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Qualitative and quantitative risk assessment of hazardous substances in the workplace

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Qualitative and quantitative risk assessment of hazardous substances in the workplace

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Editorial: Qualitative and quantitative risk assessment of hazardous substances in the workplace

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Editorial on the Research Topic
Qualitative and quantitative risk assessment of hazardous substances in the workplace

Risk refers to the possibility that an event will result in a specific outcome (an unfortunate event or adverse outcome). The definition of risk includes two meanings: the uncertainty of risk and the severity of consequences or the loss caused by events, which can be measured by relevant metrics of possibility and outcome of damage, respectively. The "occupational health risk" can be defined as the possibility of work-related diseases or occupational diseases caused by exposure to occupational hazard factors during occupational activities.

Risk assessment is divided into four classic stages: hazard identification, dose-response relationship assessment, exposure assessment, and risk characterization (1). Occupational health risk assessment (OHRA) is to comprehensively and systematically identify and analyze occupational hazards in the workplace, apply specific risk assessment methods, assess the possibility of work-related diseases or occupational diseases caused by exposure to occupational hazards during occupational activities, predict the level of occupational health risks, and provide a basis for taking appropriate risk control measures (2). Therefore, OHRA is an effective method to control occupational hazardous substances in occupational health protection and is an important content in the occupational health field (3). Many countries have developed their own OHRA criteria or guidelines; however, there is still a distance in establishing an optimal OHRA system. Each risk assessment model has advantages and limitations due to its different technical principles (4). There are many studies on methodologies and practical applications of risk assessment for harmful substances. Several studies have been conducted to examine the strengths and weaknesses of different models and assisted in their further refinement and utility (5).

This Research Topic, "*Qualitative and quantitative risk assessment of hazardous substances in the workplace*" in the "Occupational Health and Safety" section of Frontiers journal, aims to bring together the latest quality articles from researchers working in the field of Occupational Health and Safety and focuses on but not limited to (a) Research advance and policy-making on occupational health risk assessment in the workplace; (b) Development of new risk assessment methods or models for harmful substances; (c) Application of multiple qualitative and quantitative risk assessment methods in critical industries; (d) Comparative studies between different qualitative and quantitative risk assessment methods; (e) Preventive measures and occupational risk management based on risk assessment results.

Under this topic, 13 articles have been successfully published with relevant findings contributing to theoretical research and practice in OHRA. The occupational exposure limit (OEL) is often used as a judgment value for over-risk in the risk assessment. As early as the late 19th century, the concept of OEL was first established in Germany. However, due to the small number of harmful substances with OELs and the need for professional technical institutions to provide occupational health services (e.g., sampling, testing, and evaluation) for enterprises, the technology and cost are high, which cannot meet the management requirements of many small and medium-sized enterprises (SMEs) and evaluation criteria of rapidly increasing chemicals. Therefore, some occupational health risk assessment methods (mainly qualitative) have been developed to predict the risks of chemicals for which there are no OELs. These methods can be practical tools for SMEs to manage their occupational health risks.

In this Research Topic, considering the OEL plays an essential role in the exposure assessment of the risk assessment procedure, Maurer et al. developed an interdisciplinary framework for deriving the OEL based on risk assessment frameworks, including problem formulation, literature review, the weight of evidence considerations, point of departure selection/derivation, application of assessment factors, and derivation of the OEL. Xu et al. developed a strategy for comparing different OHRA methods in the workplace, considering that different risk levels would be obtained for the same hazardous factor when using different OHRA methods. The evaluation strategy included using the risk ratio (RR) to compare risk levels among six OHRA methods [e.g., the Environmental Protection Agency (EPA), Australian, Romanian, Singaporean, International Council on Mining and Metals (ICMM), and the Control of Substances Hazardous to Health models (COSHH)], analyzing correlations of the RRs of the six OHRA methods, verifying the accuracy of each OHRA method using the inherent risk (IR) of the industry. Huang et al. reported a comprehensive risk assessment model (a grading model) could effectively reflect the total risk level of critical hazards in the electronics industry. They concluded that the grading model has strong practicability. Zhou L. et al. introduced the OHRA methods developed in China using the scoping review. A wide range of OHRA methods was developed in China, including applied, comparative, and optimization studies, and each OHRA method had its strengths and limitations. Their applicability needs to be further tested through more applications in different industries, and comparative studies, optimization studies, and modeling studies are also required.

Moreover, more authors focused on assessing the risk levels of occupational hazards in critical industries or workplaces. Zhu et al. investigated the occupational health risks of n-hexane in electronics industries using multiple OHRA models. They found two semi-quantitative OHRA models developed in China might have stronger practicability for the electronics industry, and they recommended specific control measures for reducing the high health risk of workers (especially for cleaning workers). Shi et al. explored the health risk of benzene-exposed workers in the printing industry applying multiple OHRA methods. They found that the printing and pasting workers suffered a higher risk of benzene exposure and provided preventative measures for controlling the risk. Duan et al. reported the severe hazard risk of silica-dust and industrial noise in the ferrous metal foundry using a risk assessment model developed by the ICMM. In addition, some authors focused on the importance of exposure assessment in risk assessment. Wang et al. reported 31.9% of the individual noise levels exceeded 85 dB(A) of noise OEL, and 53.7% of non-coal mining enterprises were not equipped with HPD for workers, especially in small and micro enterprises, and concluded that noise exposure data was crucial for developing more feasible noise controls. Acramel et al. reported that reporting environmental contamination results to healthcare workers could play an essential role in reducing the occupational exposure to antineoplastic drugs in hospitals. Zhou Z. et al. reported that exposure characteristics of kitchen ultrafine particles were related to kitchen operations and recommended relevant protective measures since the kitchen particles were of high exposure and risk levels. Lari et al. established an exposure assessment procedure for assessing dermal exposure to pesticides among farmers using a dosimeter and hand washing methods and highlighted the importance of protective measures.

Moreover, the other two authors focused on the effectiveness of control measures based on the OHRA result. Wu et al. reported that an engineering renovation could significantly reduce the risk level of Hg in the thermometer industry. Dong et al. reported that improving protective measures in factories with acetylene hydrochlorination and ethylene oxychlorination techniques could significantly reduce risk levels and improve workers' liver health.

Progress of OHRA has been achieved. Future research in OHRA should include: (a) Speed up the formulation of OHRA guidelines. The established system needs to clarify the connotation and extension of OHRA since many occupational health practices (e.g., occupational health technique service for enterprises, physical examination for workers, occupational disease surveillance, and workplace hazardous monitoring programs) may be associated with OHRA. (b) Highlight the OHRA methodology study in the applicability of key industries, comparisons between OHRA methods, and methodology optimization since each method has strengths and weaknesses. A national-level of OHRA database in various industries is needed. Theoretical frameworks for comparative studies between different OHRA models must be improved for analyzing the accuracy, parallel, and correlation among different methods. (c) Strengthen the OHRA popularization and application. The concept and developed risk assessment methodology must be applied to occupational health practices, supervision, and law enforcement based on a new exploration of classification and hierarchical management for enterprises.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Assessment of dermal exposure to pesticides among farmers using dosimeter and hand washing methods

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Inappropriate use of pesticides followed by unsafe handling practices to control the insect infestation among the farming groups in developing countries has resulted in a high exposure risk. The use of personal protective equipment is also negligible among Indian farmers due to their affordability to access the same. Very little research has been conducted to establish an exposure assessment procedure through dermal penetration of pesticide residues. Therefore, to quantify the contamination of pesticide residues through dermal exposure along with detailed field observations and pesticide management practices, a field study was conducted in Rangareddy district, Telangana, Southern India, to assess the dermal exposure based on dosimeter and hand washing methods. The analytical method was modified and validated in-house for performance parameters such as limit of detection, quantification, linear range, recovery, and precision. The potential dermal exposure values ranged from 0.15 to 13.45 µg, while a reduction was found in exposure levels as actual dermal exposure values ranged from 0 to 0.629 µg. Contamination through hand washing was the major contributor to overall dermal exposure. Statistical analysis revealed a significant difference in the exposed dermal regions of the leg and torso after the use of PPE. Penetration factor for each anatomical region and risk evaluation in terms of the Margin of Safety implies unsafe handling of pesticides. The findings of the present study confirm the increased exposure to organophosphate pesticides among operators and highlight the importance of the use of protective measures, especially among those that focus on dermal exposure mitigation.

KEYWORDS
pesticides, personal protective equipment, risk assessment, potential dermal exposure, patch dosimeter, skin wiping, occupational exposure

Introduction

Decades ago, agrochemicals were introduced aiming at enhancing crop yields by protecting crops from pests. Due to adaptation and resistance developed by pests to chemicals and secondary pest outbreaks, every year higher amounts and new chemical compounds are used to protect crops, which not only raise the costs of food production but are also causing undesired side effects (1). This kind of non-judicious practices and unsafe use of pesticides has caused numerous problems stemming from their use through their release into the environment, while causing potential adverse effects and undesired side effects on human health (2–4). Furthermore, occupational, accidental, or intentional exposure to pesticides sometimes also resulted in hospitalization and deaths (5). Therefore, the role of exposure and the resulting risk assessment has become extremely significant, particularly for occupationally exposed groups.

Exposure to pesticides among farmers during their various preparation steps in the field applications may occur in several ways such as ingestion, inhalation, ocular, or skin contact. It is well-established that out of different routes of exposure, skin absorption is the major and relevant route of pesticide entry into the human body (6, 7). Further, as claimed by many studies, dermal exposure seemed to comprise the bulk of cumulative exposure; consequently, the protection afforded by garments or personal protective clothing must be considered essential for minimizing dermal exposure among pesticide handlers (8). However, the pesticide handlers in tropical countries including India do not usually use PPE, mainly due to their inaccessibility and discomfort associated with its use under hot and humid climatic conditions (9, 10). This in turn leads them to be more vulnerable to dermal exposure than their counterparts in temperate countries.

The developed countries, such as the European Union and North American countries, have established exposure data requirements, and do not allow a pesticide to be authorized for its use unless there is a specific data or adequate model prediction to show that, in normal use, the operator exposure levels would be below the acceptable exposure levels (11). On the contrary, in India, no such data are available, as very little research has been performed to establish exposure assessment among Indian farming groups. Moreover, most pesticide poisonings occur in developing countries because of unsafe pesticide handling practices such as poor knowledge of Good Agricultural Practices, improper training, inadequate application techniques, lack of awareness of toxicity, and negligible use of PPE (12–14).

Therefore, the importance of assessing human exposure to pesticide risk reliably has been growing. Several methods to quantify dermal exposure are available; however, they depend upon the availability of trained personnel, appropriate sophisticated equipment, elaborate chemical analyses, the inherent toxicity of pesticides, repeated exposure intensity, duration, and frequency to understand the mass of substance likely to be absorbed (15). Over the last decades, dermal exposure assessment has been the focus of research and regulations, which has resulted in the development of various methods and models addressing dermal absorption and ill health effects (16–18). However, the development of proper dermal exposure models is scarce due to different methods used to generate sound data (16).

The objectives of the present study were to evaluate the magnitude, patterns, and determinants of dermal exposure to pesticides among farmers of Rangareddy district, Telangana state, India, where the use of PPE is relatively limited and to assess the impact of the use of PPE on the minimization of exposure to pesticides. The current pesticide exposure situation in the study area selected is only representative of a large agricultural region and may generally reflect the situation in India. In the present study, field trials were conducted among six local farmers who are pesticide operators using organophosphate insecticides (OP) for the control of a variety of insect pests on different crops. An established analytical method was used for the determination of OP pesticides, and the performance parameters checked were fully validated to evaluate the dermal exposure by analyzing contamination through hand washings and the dosimeter method for patch and wipe washings. Primary objectives of the study were to identify the parameters which are likely to affect the intensity of exposure by in-field evaluation of operational modalities of the operators engaged in different farming activities through field observation and pesticide management as well as to quantify the potential dermal exposure (PDE) and actual dermal exposure (ADE) during pesticide treatment in an actual field scenario. We also aimed to evaluate the protection against pesticides by measuring skin loading rate and penetration factor (PF) and a risk indicator in terms of margin of safety (MOS).

Materials and methods

Study area and subjects

The study was conducted in an identified village in the Rangareddy district of Telangana state in Southern India. The annual normal rainfall of the district is 781.0 mm and the major crops grown include cotton, maize, red-gram, rice, jowar (*Sorghum*), green-gram, black-gram, castor, and other commonly grown vegetables (19). Continuous pest infestation in the region due to consecutive cultivation has led to repeated use of pesticides. From out of the larger study conducted among 217 farmers/farm workers, three subjects each of vegetables (okra, eggplant, tomato) and commercial crop (cotton) cultivators who are engaged in different farming activities were randomly selected as study operators, who also previously took part in the pesticide use survey conducted in the study area who had expressed their interest to participate.

Ethical clearance and consent

The operators (farmers/farm workers) were made clear that the study was only in the interest of the authors' academic research to avoid any potential bias. Written consent was taken and they were also explained that they are free to decline their participation at any given point of time without any fine or penalty. The names of the participants were replaced with specific codes to use in data analyses and to ensure confidentiality. The study protocol was reviewed and approved by the ethical committee of the Indian Council of Medical Research - National Institute of Nutrition, Hyderabad, India (REF NIN Protocol number 11/I/2016).

Field observations and pesticide management

The following information from each operator on each separate occasion was recorded using standardized field data sheets: (1) types and quantity of active ingredients handled during the day; (2) number and total duration of different phases (methods of mixing of pesticides formulation, spraying, cleaning); (3) types of work clothing (shirt/T-shirt, cotton cloth fabric, length of sleeves, trousers, shoe, scarf, if any) used; (4) use of any PPE and if not, reasons for not using; (5) crop height and farm size; (6) incidences of spills and leakages; (7) data recorded on meteorological parameters of maximum and minimum temperature (°C), relative humidity (%), wind velocity (km/h), and direction using Digital Anemometer (LM 8010, Lutron Electronic, Taiwan) two times in an hour and at every place of treatment each time on the day of samples collection; and (8) details of precautions if any followed by the operators while handling pesticides. Observations such as their re-entry into the treated fields, walking direction during spraying, incidental contaminations, and events such as breaks for equipment repairs, talking, smoking, or eating/drinking during handling of pesticides were also noted.

In the second phase of the study, the same operators were provided with a fresh set of PPE as per European Food Safety Authority guidelines and the Pesticide Handler Exposure Database (8, 20) free of cost which includes a Tychem "C" category III cover-all (DuPont™); a safety splash goggle; a cup type respirator; a pair of nitrile gloves and a pair of PVC gumboot, all procured from Usha Fire, Hyderabad (DuPont supplier, India). The operators were advised to wear the PPE provided for a period of 90 days over their regular farm clothes before handling the pesticides. The purpose of this sampling procedure is to ensure the capture of the pesticide residues that might have/not penetrated operators' clothing during farming activities and their potential absorption through their skin, followed by the adherence of residues onto their body regions which are normally not covered by their regular farm clothing.

Monitoring of dermal exposure

A certified reference material of the pesticide—acephate, chlorpyrifos, monocrotophos, profenofos, and quinalphos and internal standard—triphenyl phosphate (TPP), were purchased from Sigma-Aldrich Chem. Pvt. Ltd., India with a certified purity of ≥97%. Pestanal grade organic solvents of acetonitrile and methanol (LC-MS grade) were purchased from Sigma-Aldrich, Merck KGaA Darmstadt, Germany with 99% purity, while formic acid (analytical grade) was purchased from Fluka Pvt. Ltd., Mumbai, India. The analytical grade reagent ethanol and anhydrous sodium chloride and sodium sulfate were purchased from Merck, Mumbai, India. The HPLC column was purchased from Agilent Technologies Pvt. Ltd., India.

The patch dosimeter, surface wipe, and hand washing methods were adopted to measure the external dermal exposure to pesticide residues among the operators (21). Trained staff has collected the samples of exposed dermal regions from the operators following the SOPs under the field conditions.

Operators were instructed to wash their hands with water before their work shift to rule out any background contamination if present. Further, the hand washing samples were collected at the end of the shift after handling the pesticides. Each operator was instructed to rinse one hand at a time approximately for at least 30 s in a Ziploc™ bag made of poly-ethylene material (thickness 0.025 mm and 17.8 cm wide) containing 200 mL of ethanol (70% v/v) (22). Further, they were also provided with hypo-allergenic soap to wash their hands and water for moisturizing purposes after rinsing their hands.

Dermal exposure of other exposed body parts was also accessed by placing the patch samplers using the dosimeter method. The patch sampler was made of a surgical cotton gauze pad of approximately 1 mm thickness and 100 cm^2 surface area, backed with an impermeable material (aluminum foil) to prevent seepage of collected residues through the patch to the skin and/or clothing. Ten of such patch samplers were attached using surgical tapes over the clothing worn by each operator (external patch) and were placed on the inner clothing under the PPE (internal patch) at different places of the exposed dermal regions. Patch samplers from corresponding exposed dermal regions were pooled and analyzed as one sample, which resulted in three patch samples per measurement (on back between shoulder blades and over the sternum [pooled as torso patch], the upper surface of right/left forearm, midway between elbow and wrist forearm [pooled as arm patch], front of right/left leg, mid-thigh and at front of right/left leg, above the ankle-below knee [pooled as leg patch]) and the same was removed

TABLE 1 Key information about the pesticides used by operators.

Operator	Trade name of pesticides	Amount of pesticides used (mg)	Active ingredient (%)	Chemical group	WHO classification*	AOEL[a] or NOAEL[b] (mg/kg bw/ day)[#]
1V	Acemain/Acestar	250	Acephate (75% SP)	Organophosphate (OP)	II	0.0008[a]
2V	Orax	210	Profenofos (50% EC)	OP	II	1.0 [b]
3V	Dhanulux	480	Quinalphos (25% EC)	Organothiophosphate	II	0.05[b]
1C	Hilban	220	Chlorpyrifos (20 % EC)	OP	II	0.001[a]
2C	Orax	300	Profenofos (50% EC)	OP	II	1.0[b]
3C	Monocil	180	Monocrotophos (36% SL)	OP	Ib	0.005 [b]

*World Health Organization - classification of acute toxicity (2004): Ib-highly hazardous; II-moderately hazardous.
[#]Source: EU Database, 2012.

using tweezers (triple-rinsed with ethanol) before changing their work clothes and after spraying tasks. This method aims to estimate the amount of a particular substance deposited on clothing/skin/penetrating through outer clothing layers.

Skin wiping technique, using surgical cotton gauze pad wetted with 2 mL of 70% ethanol as it is soluble for most compounds and causes less irritation to the skin, was employed as wipe sampler to assess the dermal penetration of pesticide residues on exposed dermal regions of face/forehead and neck at the end of work shift (21). Exposed forehead, face, and neck regions were wiped five times by repeatedly folding and turning wipe samplers by the trained personnel using surgical gloves on.

At the end of the sampling event, the samples of the patch, wipe, and hand washing were collected in the Ziploc bags closed by twisting the upper part of the bag to make an air-tight seal, labeled appropriately for each operator, and transported in chilled condition using ice-packs from the field to laboratory and stored at −20°C (deep-freezer HF 500 CHP; Carrier, USA) until extracted. All the extractions were completed not later than 7 days after the collection of samples.

Assessment of dermal exposure

In the present study, measurements of dermal exposure were used to quantify the potential and actual dermal exposure of operators on each work shift. The potential dermal exposure (PDE) is defined as the total amount of pesticide in contact with the body surface of farmers, namely, protective clothing, work clothing, and uncovered skin; actual dermal exposure (ADE), in contrast, is the amount of pesticide in contact with the uncovered skin, and therefore, the fraction passed through protective and work clothing and that poses a risk of being percutaneous absorption (8, 21). All external and internal patches were used to estimate PDE and ADE, respectively, for the exposed body regions. The PDE and ADE were calculated using Equations (1) and (2), respectively. Further, to check the PDE calculations for the face and neck region, the skin wipes of the exposed region of the face and neck of the operator without using the face mask/PPE were considered, while for ADE calculations also the same procedure was followed, but after the use of face mask/PPE.

$$\text{PDE} = \text{Measured conc. (ng/cm}^2\text{) on sampler attached over work clothes} \times \text{Exposed anatomical area (cm}^2\text{)} \quad (1)$$

$$\text{ADE} = \text{Measured conc. (ng/cm}^2\text{) on samplerattached over skin inside work clothes and PPE x Exposed anatomical area (cm}^2\text{)} \quad (2)$$

where measured ng/cm^2 is the total value given for deposition and exposed dermal region for the patch or wipe sampler which makes the summation of surface area torso (7,100) [back (3,550) + chest (3,550)], arms (4,120) [upper arms (2910) + forearms (1,210)], legs (6,200) [upper legs (3,820) and lower legs (2,380)] and wipe (760) [face and forehead (650) and neck (110)], whereas the surface areas used include both right and left arms and legs of the adult body (80th percentile man) (8).

Further, the measured PDE was transformed to percentual PDE (%PDE) by normalizing the PDE value with the total amount of the active ingredient used, and expressed as a percentage, to allow comparisons between different trials, where different active ingredients and consequently dissimilar pesticide amounts were used (23). The %PDE was calculated using Equation (3):

$$\%\text{PDE} = [\text{PDE / amount of active ingredient (mg)}] \text{ x } 100 \quad (3)$$

The concentration of pesticide in each extract combined with the duration of each experience gives a time-rate value for the dermal exposure. The skin loading rate (μg h^{-1}) was calculated from the operators' estimated number of hours of applications per day (24). From the questionnaire survey data, the estimated duration of the number of hours spent was also obtained.

For each operator, the percentage coverall penetration was calculated in terms of penetration factor (PF), which can be defined as the fraction of pesticides that cross the clothing barrier and is available for contact with the skin (25). Further, the resulting data of both PDE and ADE were used to calculate the percentage of PF using Equation (4):

$$\text{PF anatomical region (\%)} = [\text{ADE} / (\text{ADE} + \text{PDE})] \text{ x } 100 \quad (4)$$

The margin of safety (MOS), a risk indicator, was measured as previously reported (26–28) for each tested pesticide residue using Equation (5):

$$\text{MOS} = [\text{AOEL} \times \text{average body weight} / (\text{DE x AF})] \quad (5)$$

where DE is the total dermal exposure and AF is the absorption factor.

A value of MOS ≥1 would indicate safe working conditions, while the MOS <1, the unsafe conditions. If acceptable operator exposure level (AOEL) is not available, then no observed adverse effect level (NOAEL) was used based on the average body weight of 60 kg adult (Table 1). The AF value was taken as 0.11, which indicates the dermal absorption of 10%, with an addition of 1% extra to consider the inhaled fraction also, whereas DE is equal to the summation of PDE obtained from patch and wipe (μg) and final residues (μg) from washings of hands. Further, for MOS calculation, a "worst case scenario" was assumed by taking into account the practice of not using appropriate gloves and hence, any additional coefficient was not added to consider the use of protective measures (23). Therefore, the MOS was calculated using Equation (6).

$$\text{MOS} = [\text{AOEL x } 60 / (\text{DE x } 0.11)] \quad (6)$$

Extraction procedure and instrumental analysis

The hand washing samples collected were filtered using Whatman filter paper (29) and then passed three times through anhydrous sodium sulfate. The filtrate was then completely evaporated to dryness using a rotary evaporator (AD 2C, Aditya Scientific, India) at 30°C and 80 rpm. The residues were reconstituted using 1 mL of acetonitrile. While the wipe and patch samples were also subjected to ultra-sonication (Ultrasonic Cleaner, Equitron, India) for 15 min using 20 mL of methanol. The methanol extract was transferred to a glass test tube and dried under a gentle stream of nitrogen using Turbo-Vap (LV concentrator, Caliper Life Sciences, India) at 30°C and 15 psi. Re-constitution was done using 1 mL of methanol. Both the extracts were then filtered into an auto-sampler vial using a 0.22 μm PTFE cellulose syringe filter (Nupore Filtration Systems, India), and stored at −80°C (ultra-low temperature freezer, Haier, China) until analyzed.

A liquid chromatography system (Shimadzu LC 20AD) equipped with a mass spectrometer (Applied Biosystems MDS Sciex 4000-Q TRAP triple quadruple) and auto-sampler (SIL-HTC model) controlled using Analyst Software (version 4.1.2) was used for the quantitative analyses and qualitative confirmation. The chromatographic separation was carried out on the Zorbax SB-C18 HPLC column (internal diameter of 4.6, 250 mm length, and 5 μm particle size), maintaining a minimum of 25°C and maximum of 85°C oven temperature. The analysis was done in the multiple reaction monitoring (MRM) positive turbo ion spray (ESI) mode with high resolution. Two mobile phases (mobile phase A – Milli-Q water containing 0.1% formic acid and mobile phase B - methanol with 0.1% formic acid) were used in gradient mode. Initially, Pump B was maintained at 10% for 0.01 min subsequently for 20 min, changed to 98% at 25 min, and again to 10% at 32 min giving a total run time of 32 min. A constant flow rate of 800 μL min^{-1} was maintained with an injection volume of 35 μL. The ion spray voltage (IS) of 5,500 eV was used and the interface heater was held at a temperature of 500°C.

Quality control

The standardized method used for the quantitative and qualitative determination of OP in hand washings and patch/wipe samples was modified and the same was validated in-house prior to commencing the sample analyses (30); ICH

TABLE 2 Optimized MS/MS parameters for organophosphorus compounds in multiple reaction monitoring (MRM) mode using different energy profiles.

Analyte	MRM transition (parent/quantifier)	DP	EP	CE	CXP	R_T (min)
Acephate	184/143	46	10	11	12	8.0
Monocrotophos	224.1/127.1	46	6	21	12	11.9
Quinalphos	299.1/147	60	5	30	7	13.2
Profenofos	375/305	61	10	27	26	14.6
Chlorpyriphos	350/198	56	10	19	8	19.0
TPP (IS)	327.1/77.1	96	8	63	4	22.1

DP, De-clustering potential; EP, entrance potential; CE, collision energy; CXP, collision cell exit potential; R_T, retention time.

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TABLE 3 Performance parameters of the LC-MS/MS method for the determination of pesticide residues in hand washings.

Analyte	LOD (ng mL^{-1})	LOQ (ng mL^{-1})	Precision at different concentration levels (%RSD)						% Recovery ± SD ($n = 6$)	
			Intra-day Rp			Inter-day Rc				
			1 ng mL^{-1}	50 ng mL^{-1}	500 ng mL^{-1}	1 ng mL^{-1}	50 ng mL^{-1}	500 ng mL^{-1}	50 ng mL^{-1}	500 ng mL^{-1}
Acephate	0.5	5	2.1	3.8	3.2	4.3	10.7	3.8	96 ± 1	100 ± 2
Monocrotophos	1	2	3.3	3.5	5	14.7	6	2	94 ± 2	99 ± 3
Quinalphos	0.5	1	6.1	2.7	4.3	11.7	8.5	8.4	96 ± 1	97 ± 2
Profenofos	0.5	1	7.3	6.7	2.8	8.4	3.7	6.2	96 ± 3	98 ± 1
Chlorpyriphos	1	2	4.6	3.7	7.4	10.2	7.2	6.8	95 ± 3	79 ± 4

Rp, repeatability (n = 6); Rc, reproducibility (n = 6); SD, standard deviation; RSD, relative standard deviation.

TABLE 4 Performance parameters of the LC-MS/MS method for the determination of pesticide residues in wipe/patch.

Analyte	LOD (ng mL^{-1})	LOQ (ng mL^{-1})	Precision at different concentration levels (%RSD)						% Recovery ± SD ($n = 6$)	
			Intra-day Rp			Inter-day Rc				
			1 ng mL^{-1}	50 ng mL^{-1}	500 ng mL^{-1}	1 ng mL^{-1}	50 ng mL^{-1}	500 ng mL^{-1}	50 ng mL^{-1}	500 ng mL^{-1}
Acephate	0.2	0.5	2.7	3.0	1.8	13.3	3.9	4.7	104 ± 3	104 ± 2
Monocrotophos	0.5	5	7.6	3.3	2.9	7.2	12.6	10.9	104 ± 2	100 ± 3
Quinalphos	0.2	0.5	1.6	3.9	4.3	5.6	11.1	9.9	100 ± 3	101 ± 3
Profenofos	0.5	5	4.6	2.3	3.3	10.2	11.5	9.8	102 ± 2	100 ± 2
Chlorpyriphos	0.5	1	1.6	3.6	1.3	7.7	10.9	14.0	99 ± 3	98 ± 3

Rp, repeatability (n = 6); Rc, reproducibility (n = 6); SD, standard deviation; RSD, relative standard deviation.

TABLE 5 Details of operational modalities for each pesticide treatment at the field level.

Operator	Active ingredient	Crop under cultivation	Work period (min)	T (°C)[a]	RH (%)[a]	Wind speed (km/h)[a]	Garments	Potential regions of body that can get exposed
1V	Acephate	Tomato	20	32.3	51.4	7.4	Long trousers, long sleeved cotton shirt, rubber shoe	Head, face, neck, hands
2V	Profenophos	Eggplant	25	34.3	50.8	9.4	Short trousers, long sleeved cotton shirt	Head, face, neck, hands, feet
3V	Quinalphos	Okra	80	35.6	46.4	8.7	Long trousers, long sleeved cotton shirt	Head, face, neck, hands, feet
1C	Chlorpyrifos	Cotton	30	33.4	42.2	6.6	Long trousers, short sleeved T-shirt, casual shoe	Head, face, neck, hands, forearms
2C	Profenophos	Cotton	20	30.9	47.6	9.3	Long trousers, short sleeved shirt	Head, face, neck, hands, forearms, feet
3C	Monocrotophos	Cotton	37	36.4	52.5	7.9	Short sleeved shirt, sarong	Head, face, neck, hands, forearms, lower legs, feet

[a]Mean of work period.

Q2 (R1) guidelines (1995). Individual analyte standard was prepared by dissolving 1 mg of neat standard in 1 mL of acetonitrile:distilled water in a 1:1 ratio (1,000 mg L^{-1}) and a working standard mixture of 20 mg L^{-1} was prepared from the stock solutions. Primary and secondary working solutions were prepared and TPP was used as the internal standard at 200 ng mL^{-1} concentration. All the standard solutions were sealed and stored at −80°C for future analyses. Mass parameters for OPs were optimized in multiple reaction monitoring (MRM) mode (Table 2). The absence of an analyte peak in the blank run indicates the selectivity of the method. The analytes showed consistent retention over 10 runs with a retention time variation of ±0.2 min and the RSD of the obtained peak areas over the 10 runs was observed to be <3%. The calibration plots obtained by plotting the peak area vs. analyte concentration for all the pesticides showed good linearity with correlation coefficients (r) ranging from 0.9986 to 0.9999. Performance parameters of the LC-MS/MS method for the determination of pesticide residues in hand washings (Table 3) and wipe/patch were determined (Table 4). Briefly, the concentration range used for hand washing varied from 0.5 to 1,000 ng mL^{-1}, while that for wipe/patch was in the range from 0.2 to 1000 ng mL^{-1}. The sensitivity of the method was evaluated by determining the experimental limit of detection (LOD) and the limit of quantitation (LOQ) for each analyte at a signal-to-noise ratio (S/N) of 3:1 and 10:1, respectively. It was found that the LOD ranges from 0.5 to 1 ng mL^{-1} in hand washing and 0.2 to 0.5 ng mL^{-1} in wipe/patch. The LOQ in hand washing and wipe/patch ranges from 1 to 5 ng mL^{-1} and 0.5 to 5 ng mL^{-1}, respectively. The recoveries determined at two different concentrations were in the range from 75 to 102% for hand washing and from 95 to 107% for wipe/patch, which proves the accuracy of the method. The precision was determined as relative standard deviation (RSD) in terms of repeatability (intra-day) and reproducibility (inter-day) at three fortification levels (1, 50, and 500 ng mL^{-1}) for hand washing and wipe/patch were ≤15%.

Statistical analysis

The raw data collected using the questionnaires and LC-MS/MS were coded, entered into specially designed databases (Microsoft Access), and transferred to appropriate spreadsheets (Microsoft Excel) for statistical analysis using the SPSS software (version 23). The descriptive variables were represented as mean (standard deviation), frequency, and percentages. A statistical correlation was determined among different exposed dermal regions of the operators, before and after the use of PPE. Therefore, the t-test was carried out to assess the association between exposure levels among the operators before and after the use of PPE for different exposed dermal regions, and the associations were studied with a 95% confidence interval (CI) and, statistical significance was considered at $p < 0.05$.

Results

Field observations

All the operators were men and mean age was 35.2 years with an average farming experience of 16.2 years. Further, they were marginal farmers with a land holding of 2.66 acres.

The field observations and pesticide management data collected for the present study involved a single event of pesticide treatment for each operator on each separate occasion. The operators were asked to carry out the pesticide spraying operations as how they practiced and as always. It was observed that the five OPs were the most commonly applied insecticides which were registered under the Insecticides Act for use in the country (31), using hand-pressurized knapsack spraying devices (backpack pump with hand or motorized spray) which were carried on their back. It was found that the sprayings were done with the lance positioned in front of the operators, while they walk forward in different directions in the treated field areas. Further, the spraying activities were found to have been done in the morning time between 7 and 10 a.m., when the temperature was relatively cool. It was found that the number of pesticides sprayed was not done as per the Good Agricultural Practices (GAPs) and also varied as per the crop cultivated, the intensity of the pest infestation and the area to be treated. Also, none of the six operators used any PPE of their own while handling the pesticides, except one who was found to have covered his head/mouth using a handkerchief. The discomfort in using the PPE coupled with un-affordability and inaccessibility was found to be some of the self-reported major reasons for not using the PPE. Further, no one was found to have taken training from authorized agricultural officials. Also, all the operators stored pesticides at farms in a separate shed. Further, they were also disposing of empty containers after their use without even rinsing the same in the agricultural fields in which they were performing the agricultural activities. Details of meteorological conditions were recorded indicating high temperature and low humidity throughout the duration of the operators' work in the field (Table 5). It was also observed that they sprayed pesticides against the wind direction.

Pesticide management

The pesticide management practices were undertaken in three phases: the preparation of the pesticide followed by the application, and the cleaning of the spraying equipment (Table 1). The operator took about 15 to 60 min for completing the farming tasks of mixing, loading, spraying, cleaning the sprayer, removing work garments, etc. However, it depends on the area of the field and the quantity of pesticides to be applied.

The preparation involves mixing up the pesticide formulation with water, followed by loading it into the tank of the knapsack sprayer. While in the case of solid formulation, they were mixed with their bare hands in approximately 10 to 15 L of water in a tank of 20 to 50 L capacity without following any GAPs. Of the six operators chosen for the study, only one was found to have mixed the solution with the aid of a wooden stick, while the rest mixed with bare hands. The mean concentration of the active ingredient in the liquid mixture was found to be 21.87 mg/L. It was observed that there were some technical errors during the preparation of the pesticide formulation such as spillages, overflow of tanks with excessive foaming, blockage of pipes, etc. due to which the formulations were found to be directly coming in contact with the operator's body such as hands, arms, chest, and legs.

The pesticide application starts with the knapsack sprayer being mounted on the back of the operator to initiate the spraying in the field. During this process, it was found that the operators' body was exposed to the droplets emitted by the nozzles of the knapsack sprayer if the operator was using a defective sprayer. The hand pressure sprayer used for spraying was found to be 10 years old and was hardly rectified for its leakages. Operators were found to be spraying with the lance approximately 30 cm above the top of the crop in front of them by swinging it from side to side, which will, in turn, form the spray aerosol in front of him into which he walks forward. The spray tank usually has a high-discharge nozzle that discharges pesticide formulation at a pressure of 0.90 ± 0.18 L min^{-1}. It was further found that the pesticides applied to the crop ranged from 180 to 480 mg $acre^{-1}$. It was further observed that most of the operators (67%), before initiating the spraying task/entering the agricultural field, were checking the speed of the spray nozzle to close proximity and keeping the spray machine in "on mode" resulting in the splashes of pesticide solutions falling onto their body parts like chest, face, hands, and eyes. Further, to clear blockages of the nozzle if any, they were found to be blowing the air through their mouths which will have a direct impact on the operator's health due to unsafe handling practices/GAPs (Figure 2).

Cleaning was done by pouring the clean water from the nearby water tank/tap to ensure that all the accessories of the tank were washed thoroughly and it was repeated at least two times. During this process, it was observed that the spillage from the washings of the equipment fell on the operator's body, as they do not wear any protective gear.

Further, most of the operators were found to have re-entered the treated/sprayed fields within 2 days of application without following any proper protection. Apart from working on their own land, the operators were found to have been engaged in the farming activities such as spraying, planting, pruning, weeding, threshing, cutting, picking, and harvesting on other farms also. They were also found to be using the same clothes used during spraying till the next spray without washing them and this may result in possible substantial exposure to the pesticides. On the whole, it was noted that on average, the operator was spending 6.2 hours per day on farming activities.

TABLE 6 Pesticide residues levels in hand washings (μg) among operators before and after use of PPE.

Operator	Before use of PPE	After use of PPE
1V	1.65	0.952
2V	44.8	0.1064
3V	53.2	0.264
1C	0.206	0
2C	0.07	0
3C	2.16	1.122

Pesticide residues concentration in hand washing

The hand washings evaluated for each operator were found to be the major contributors compared to the overall dermal exposure. From the results, it could be revealed that the residue levels ranged from 0.07μg (operator 2C) to 53.2μg (operator 2 V) among those who worked without using gloves, while, a reduction in the residues was found among those who used gloves (0 to 1.12μg) (Table 6).

Assessment of dermal exposure

Potential and actual dermal exposure

The data on dermal exposure, representing the results of PDE, ADE, percentual dermal exposure, and loading rates are summarized (Table 7). Of the different exposed dermal parts of the body, the PDE and %PDE levels were found to be more in the torso parts of the operator followed by arm, face, and neck regions. Overall, the PDE values ranged from 0.15 to 13.45 μg, while in contrast a reduction was found in exposure levels in ADE as compared to PDE (0 to 0.629 μg). The zero value here suggests the partial protection provided by the PPE against pesticide exposure. After considering the duration of exposure to be 6.2 h per day, the skin loading rates, PDEh and ADEh, ranged from 0.024 to 2.17 μg/h and 0 to 0.026 μg/h respectively. It was further found that the dermal exposure values were also influenced by the type of the crop that was cultivated, as the mean (SD) values were found to be 4.19 (0.19) among the vegetable cultivators, while it was 1.12 (0.4) among the cotton cultivators.

PF values of operators who worked with a complete set of PPE (Tyvek coverall, full face mask, boots, and gloves) ranged from 0.0 to 25.1%. Negligible values of PF of arm, leg, and trunk for the operators 2V and 3V and for face and neck for the operators 1C, 2C, and 3C indicate complete body protection from dermal exposure to pesticides; in these cases, PPE functioned as a complete barrier to the penetration of pesticides and provides absolute protection. For other operators,

TABLE 7 Potential and actual dermal exposure (PDE and ADE, expressed in μg), %PDE, %ADE and skin loading rates for all operators.

Operator	Exposed dermal regions	PDE (μg)	%PDE	PDEh (μg/h)	ADE (μg)	%ADE	ADEh (μg/h)
1V	Arm	5.614	2.25	0.905	0.629	0.25	0.102
	Leg	0.265	0.11	0.043	0.022	0.01	0.003
	Torso	2.9	1.16	0.468	0.16	0.06	0.026
	Face + neck	13.452	5.38	2.17	0.138	0.06	0.022
2V	Arm	3.368	1.6	0.543	0	0	0
	Leg	0.837	0.4	0.135	0	0	0
	Torso	9.124	4.34	1.472	0	0	0
	Face + neck	0.337	0.16	0.054	0.056	0.03	0.009
3V	Arm	6.716	1.4	1.083	0	0	0
	Leg	0.901	0.19	0.145	0	0	0
	Torso	6.284	1.31	1.013	0	0	0
	Face + neck	0.477	0.1	0.077	0.16	0.03	0.026
1C	Arm	0.49	0.22	0.079	0.002	0	0
	Leg	0.149	0.07	0.024	0.007	0	0.001
	Torso	1.111	0.51	0.179	0.005	0	0.001
	Face + neck	0.92	0.42	0.147	0	0	0
2C	Arm	0.561	0.19	0.091	0.006	0	0.001
	Leg	0.147	0.05	0.024	0.023	0.01	0.004
	Torso	0.536	0.18	0.086	0.035	0.01	0.006
	Face + neck	4.051	1.35	0.653	0	0	0
3C	Arm	0.558	0.31	0.09	0.026	0.01	0.004
	Leg	0.815	0.45	0.132	0.047	0.03	0.008
	Torso	2.574	1.43	0.415	0.123	0.07	0.02
	Face + neck	1.581	0.88	0.255	0	0	0

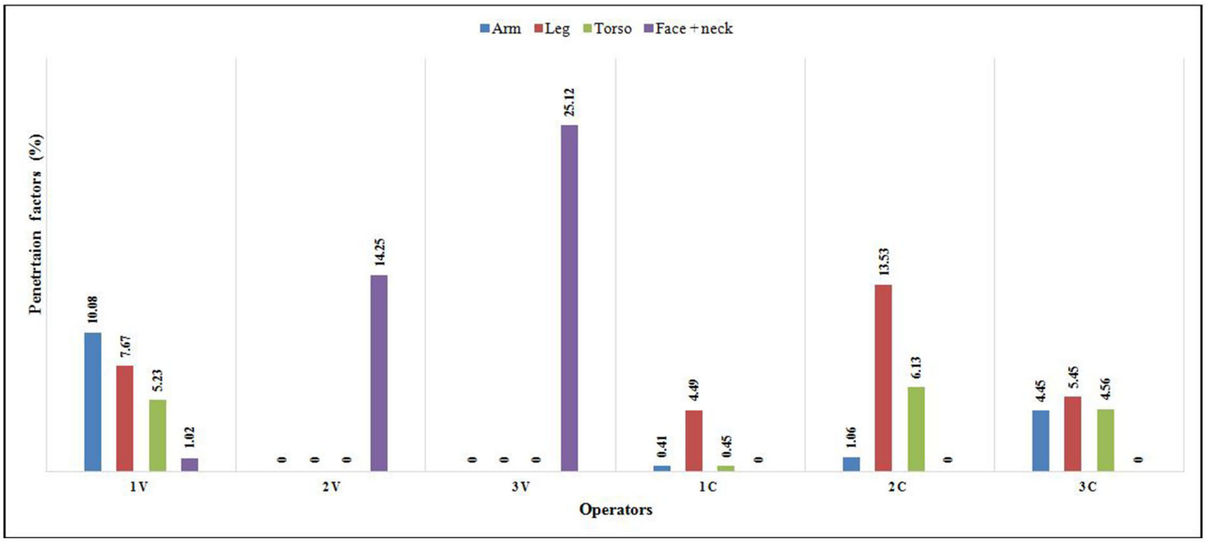

FIGURE 1
Penetration factor for each anatomical region.

the protection was not complete as the mean values of PF ranged from 2.67% for arm to 6.73% for the face and neck region (Figure 1).

MOS was calculated for each case to determine if the spraying operation was done by following safe handling practices or not. It was observed that out of the six operators studied, four had not adopted safe handling practices (Table 8).

Results revealed a significant difference ($p < 0.05$) concerning exposure levels in leg and torso regions among operators who have used PPE (Table 9 and Figure 3).

Discussion

In the present study, the dermal exposure was accessed among the vegetable and cotton crop cultivators using and not using PPE while engaged in farming activities in Rangareddy district, Telangana, Southern India. From this study, it was evident that the dermal contamination was found to be relatively less among those who have used PPE. For the last six decades, researchers have stressed that the adoption of GAPs and the use of PPE are the ideal methods to minimize the risk of exposure (32, 33).

Assessment of an operator's dermal exposure to pesticide is a very critical task as it depends on multiple factors such as type of equipment used, type and quantity of pesticide formulation used, their application rate, duration of application, climatic conditions prevailing at the time of application, use of PPE, their attitude in following safety measures, and any training undertaken as per the GAPs (33). In the present study, self-reported information gathered on the operational modalities of pesticide handling both in terms of field observations and the pesticide management practices adopted by the operators provided possible evidence of likely substantial exposures at all phases of pesticide handling during spraying and other agricultural activities. In the Indian agro-economy, the majority (85%) are small and marginal farmers, who have no access and cannot afford to use the automated spraying equipment is lacking as part of GAPs and is being observed in the present study also (34).

Further, the operators were also observed to undertake spraying activities with bare bodies sometimes to avoid the heat in the prevailing tropical climatic conditions, which would have increased the rate of dermal penetration. In the present investigation, the unsafe agricultural practices such as blowing the nozzle of the knapsack sprayer with the mouth, re-entry into the treated fields/crops at short intervals, and consuming the food/drinking water near the sprayed field areas followed by the lack of PPE use by the operator might aid in exacerbating the exposure resulting in the elevated PDE values. This may be attributed to poor training and handling practices, technical knowledge on the safe use of pesticides, lack of awareness of the hygienic practices, and inadequate knowledge on the adoption of protective measures during spraying coupled with low education levels. Similar observations were reported by earlier researchers among the pesticide handlers (35). Further, it was also observed from the present investigations that the operators were not considering the meteorological parameters such as the direction of the wind, humidity, temperature, etc., recorded on the day of spraying, which also would influence the drifting of the pesticide residual droplets followed by volatility which will not only affect the environment but also the perspiration rate of the operators (7).

Widespread use of the dosimeter and hand washing methods can be observed in earlier studies for assessing dermal exposure, since these methods have the clear advantage of low capital costs and ease of use (35–37). From the present study findings, it was observed that contamination through hands was found

TABLE 8 MOS for different pesticides.

Operator	Crop	Pesticide used	MOS
1V	Tomato	Acephate	0.02
2V	Eggplant	Profenophos	9.33
3V	Okra	Quinalphos	0.40
1C	Cotton	Chlorpyrifos	0.19
2C	Cotton	Profenophos	101.67
3C	Cotton	Monocrotophos	0.35

TABLE 9 Association among different exposed dermal regions of the operators.

Exposed dermal regions	Before use of PPE		After use of PPE		*t*-value	*p*-value
	Mean (μg)	SD	Mean (μg)	SD		
Face + neck	3.470	5.076	0.059	0.073	1.646	0.161
Arm	2.885	2.790	0.111	0.254	2.426	0.059
Hand washing	17.014	24.931	0.407	0.500	1.631	0.164
Leg	0.519	0.367	0.017	0.018	3.347	0.020*
Torso	3.755	3.308	0.054	0.070	2.740	0.041*

*Statistical significance at $p < 0.05$ and CI at 95%.

FIGURE 2
Operators mixing and spraying pesticides without following any safety protocol.

FIGURE 3
Operator involved in spraying activity after wearing provided PPE.

to have been the major contributor to all the dermal exposure parameters that were analyzed among the operators, who have not followed any GAPs. Further, in the present study, it was observed that all the operators have used liquid formulations of pesticides for spraying purposes. It was further found that exposure through hands accounted for >62% of the total dermal exposure, which would have been due to the operators mixing/loading with bare hands when using a liquid formulation of pesticides for spraying purposes, touching the spraying equipment frequently, and/or most of the times due to the deposition of droplets on hands from spray clouds/drifts. Studies conducted earlier reported that the exposure via hands often accounted for a significant portion of total dermal exposure (35, 38). A study reported that the exposure through hands was found to be 22–62 times greater than that of the solid formulation of pesticides when mixed and loaded with the liquid formulation of pesticides (23). From the current study, it was found that hand contamination was the highest contributor among the operators who have not used gloves and found to be in line with the previous findings reported among those who have not used PPE, there was found only slight contamination through hands among those operators who have used gloves (26).

In the present investigation, the PDE levels evaluated in the patch and wipe methods revealed that the torso region (14%) followed by the arm and the face/neck regions (13%) were the major contributors to dermal exposure among most of the operators. A significant reduction of the pesticide residual concentration was found in leg and torso regions among the operators who have used the PPE for 90 days. It was further found that facial exposure was another important dermal region for exposure among most of the operators as they were found to be frequently wiping their sweat on their faces with their contaminated bare hands. Of the different kinds of exposure, the exposure of the head and face was found to have been rarely reported as an important component of pesticide exposure, although this route was identified as one of the major contributors to dermal exposure among the hand-held applicators (39). Further, higher levels of percentual dermal exposure (% PDE) were found among the operators, while showing a reduction in the same after using the PPE (%ADE). Further, it is noteworthy that the lower values of ADE, %ADE, and ADEh indicate the importance of using PPE, which has also been reported by earlier researchers (40, 41).

Further, it was also found from the present study that the PDE values were higher among the vegetable cultivators as compared to the cotton cultivators as different crop heights and densities can explain the differences in the mean PDE values for different crop cultivators. Though the influence of different crops on the exposure amount and distribution pattern has been previously investigated elsewhere, the crop-wise distribution of PDE values reported among the Indian farmers is meager (42, 43). In the present investigation, the PF values vary among the operators, probably due to differences in pesticide handling methods and the types of different classes/groups of the pesticides used, and the type of work clothing that was used which might have determined the penetration and thereby having an impact on the exposure (25, 44). Further, in the present study, the higher PF values for the face, neck, and lower parts of the body (upper and lower legs) were found to have agreed with the earlier finding (36). This indicates that the PF depends not only on the actual use of the PPE but also on the proper use of PPE as the penetration of the pesticide residues among the operators in the present study has been observed to be more, if the closure of the coverall is incomplete or wearing cloth with sleeves rolled-on while during spraying and/or frequent opening/closing of the masks in between during the spraying operations and thereby paving the way for the penetration of pesticide residues through seams and zips (45).

Of the various indicators that were used to assess the dermal exposure among the operators in the present study, the MOS was found to be a better indicator than the PDE, as the risk estimation is strongly affected by the toxicological properties such as AOEL/NOAEL for each active ingredient, as the exposure levels cannot be considered as safe or unsafe based on the PDE values. Further, the MOS establishes a comparative frame under different field situations such as the types of different pesticides used/concentrations applied/application techniques adopted, etc. (43). Results from the present study revealed that 67% of the operators were found to have adopted unsafe practices, emphasizing the associated risk. The limitation of the study is that it has been done using a smaller sample size; however, a large prospective study is warranted to validate the findings of the present field trial with a larger sample size and also to assess the exposure impact on gender. Additionally, the persistence of the pesticide residues in the body fluids among the exposed is also needed to be undertaken in order to assess the adverse health effects.

Conclusion

With the use of the patch dosimetry, hand washing, and wipe technique, the present field trial study highlights the dermal exposure to pesticides among Indian farmers in a real-time field scenario. The data on field observation and pesticide management indicate the variability in operative modalities among the operators and majority of them demonstrated an insufficient level of risk perception. Study results revealed higher PDE, %PDE, and PDEh levels and unsafe working conditions, as reflected by the low MOS risk evaluation which demonstrates that it is reasonable to expect possible health effects for farmers engaged in farming activities regularly without wearing PPE and by not adopting any specified GAPs. Further, the evaluation of dermal exposure after the use of supplied PPE by the operators in the trials indicated lower ADE, %ADE, and ADEh levels, highlighting the use of adequate PPE as a major important parameter for the operators' safety. To the best of our knowledge, so far the assessment of dermal exposure among Indian farmers using dosimeter and hand washing methods was not studied as part of the dermal exposure assessment. The exposure dataset from the present study could be used as a surrogate for the estimation of the operator's dermal pesticide exposure under similar pesticide use scenarios. This might also help in developing databases for risk assessment through dermal penetration/absorption and emphasizing the need for thorough training and comprehensive understanding of the safe handling practices to protect them from exposure.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethical Committee of the Indian Council of Medical Research - National Institute of Nutrition, Hyderabad, India (REF NIN Protocol number 11/I/2016). The participants/farmers/operators provided their written informed consent to participate in this study.

Author contributions

SL participated in the analysis of the data and interpretation of the results and wrote the first draft of the manuscript. PJ contributed to the conception and design of the study. PJ, SM, and BJ wrote sections of the manuscript. JV, PY, AP, and MN were involved in the fieldwork, sample collection, and processing. All authors contributed to manuscript revision, read, and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Reporting environmental contamination results to healthcare workers could play a crucial role in decreasing the risk of occupational exposure to antineoplastic drugs

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Introduction

Antineoplastic drugs (ADs) are still the standard treatment of cancer by acting on dividing cells to inhibit the uncontrolled reproduction of cancer cells but also on healthy cells by a non-targeted action. As a consequence, the majority of those medications are regarded as being hazardous to reproduction, carcinogenic, or mutagenic (CMR). In the past, nurses would prepare anticancer medications on the bench top without taking any special safety measures, which had negative effects on the workers who were exposed. There have been reported incidents of rashes, allergies, infertility, miscarriage, birth abnormalities, leukemia, and other malignancies (1). These hazardous drugs are also referenced in the monographs of the International Agency for Research on Cancer (IARC) according to a classification considering the risk of carcinogenicity for humans (2). Several methods have been used to assess occupational exposure directly in biological fluids or indirectly by searching for traces of ADs in the environment.

The implications of long-term exposure to ADs residues in hospitals are still unknown, despite the fact that this risk is now well-documented. The exposure is primarily caused by skin contact with contaminated surfaces. Subsequent biological (3) and toxicological (4) research also confirm that healthcare practitioners continue to be exposed to residual levels of contaminants. Hence, it's critical to manage and reduce the risk of exposure for healthcare professionals.

The European Union emphasized the significance of protecting workers who are exposed to carcinogens or mutagens as a result of the preparation, management, or disposal of hazardous drugs and all work involving exposure to carcinogens or mutagens in light of the fact that 1,5 million healthcare workers in Europe are exposed to ADs [DIRECTIVE (EU) 2019/130].

In western countries, injectable chemotherapy preparations are mainly centralized in hospital pharmacies. It has led to the implementation of additional protective measures throughout the chemotherapy process and setting of environmental monitoring (5) or healthcare workers biological fluids monitoring (3). Nevertheless, a lack of adherence to safety protecting measures and cleaning procedures (6–9), and poor knowledge of contamination risk (10–12) still described in healthcare population.

As we are convinced that the lack of communication conducts to a slackening of daily basis vigilance, we are focusing here on establishing proper feedback and discussions with healthcare workers regarding environmental monitoring campaigns.

State of art

Environmental monitoring: A useful tool since the 90's

Analysis of biological fluids are more informative about the contamination of healthcare workers than environmental monitoring but much more complex to conduct. Environmental monitoring by surface wipe sampling is the most commonly used method to evaluate the contamination throughout the chemotherapy process. It's therefore based on the choice of drugs tracers and the development of an exact, precise and as sensitive as possible analytical method (13).

Manual handling or automatic manufacturing of preparations, infusion of treatment, patients care waste management, and cleaning procedures are all steps during which the risk of contamination is present. Healthcare workers might be exposed when aerosols, leaking or spillage are generated, or when they come in contact with contaminated surfaces during the manufacturing of the preparations, infusion procedure disposal of waste, or cleaning (armchair, toilets, floor or bedding) (14–22).

Regular monitoring of environmental contamination has been carried out for several years in German (23), Italian (24), Czechoslovakian (19), Canadian (20) or American hospitals (21). These monitoring have shown that the risk of healthcare exposure is not systematically related to the level of environmental contamination or to the activity of the chemotherapy process but more to the practices and awareness of healthcare workers. However, these monitoring are useful to evaluate the efficacy of protective equipment, cleaning procedures (25–27), medical devices used for preparation or infusion [for example, Closed System Drug-Transfer Device (CSTDs) (28)], etc.

In some countries environmental monitoring are mandatory and some threshold values have been proposed to graduate the level of contamination and particularly for cyclophosphamide (23, 29–31). Considering the diversity of Ads used throughout the same facility, a multi-component analyzes is advisable. Analytical method must be representative of the activity and take into account the physio-chemical properties of the different ADs used. Several but reasonable number of tracers (5–10 tracers) should be considered but trying to analyze all the ADs of the chemotherapy process could complicate the interpretation. Liquid chromatography in tandem with mass spectrometry is an adequate method for environmental monitoring (13).

Risk of occupational exposure: healthcare worker's view

Fazel et al. described in a recent paper the "barriers and facilitators for the safe handling" of ADs (10). Although there are recommendations on safe-handling of ADs, evidence suggests that compliance is usually very low. The most common barriers and facilitators identified in this review are, respectively, "poor training" and "adequate safety training." These authors also emphasize the importance of "creating work environments where safety is a priority for the safe handling" of ADs.

In another paper, Boiano et al. described examples of activities which increase exposure risk reported by workers: "failure to wear appropriate nonabsorbent gown"; "intravenous tubing primed with antineoplastic drug"; "contaminated clothing taken home"; "spill or leak of antineoplastic drug during administration"; "failure to wear chemotherapy gloves"; and "lack of hazard awareness training" (8). In this study, respondents believed that dermal exposure to ADs was minimal and therefore did not wear the required PPE during administration. However, it has been demonstrated that skin contact during handling and administration is possible without precautionary work practices and use of personal protective equipment (PPE). Nowadays, dermal exposure resulting from skin contact with contaminated environmental surface is the main source of contamination. Similarly, despite the fact that safe handling recommendations have long been available, respondents did not always adhere to the advised procedures, highlighting the significance of training and education for both employers and employees. Curiously, the majority of respondents stated that they had received instruction on how to handle antineoplastic medications safely. The risk of exposure perceived by the workers is therefore an important factor in adherence to these safe handling recommendations. Thus, the authors suggest that "employers may be unaware of the adverse health risks," but also that "better communication is needed to ensure that employers and workers are fully aware of the hazards and precautionary measures" to decrease exposures to ADs.

Experience at Institut Curie: The CurieCONTA project

Annual environmental monitoring

We described in a recent paper a comparative study of environmental contamination by cyclophosphamide on the two hospital sites of Institut Curie (22). Not surprisingly, this work has shown that our preparation and administration areas are contaminated in very specific locations with cyclophosphamide and we know that other toxic drugs could be detected. The observations conducted in this study, allowed us to assess procedure compliance and identify potential determinants of environmental contamination.

Recently, the French Agency for Food, Environmental and Occupational Health & Safety (Anses) published a report classifying work involving exposure to cytotoxic substances as carcinogenic processes. There is no obligation to make periodic environmental monitoring in France. However, identifying a few representative points of contamination and follow their evolution over times is a pertinent approach of quality improvement and risk management. It seemed essential to us to set up an environmental monitoring procedure in order to periodically check the state of contamination, to assess preventive measures, process changes or decontamination procedures. This also helps educational purposes, specifically to re-sensitize the healthcare workers who trivialize this risk as part of their daily practice. Considering the data available, an annual surface wipe sampling procedure was validated to assess the impact of the corrective measures. This annual surface wipe sampling procedure also include an assessment of professional practices and experience feedback related to contamination. This project, named "Curie CONTA," is coordinated by a multidisciplinary working group (i.e., the Curie CONTA Committee) composed by pharmacists, pharmacologists, Occupational physicians, Health managers and a Hygiene Health Environment manager. The general procedure of this environmental monitoring is described in Figure 1.

Communication strategy

To our knowledge, the communication of results to healthcare workers is poorly detailed in the literature. That is why we proposed an example of annual communication strategy usually carried out in our hospital since 2018 (Figure 1). In the first place, the Curie CONTA Committee meets to discuss about the evolution of practices and feedback on contamination incidents, to define the mapping of the samples and the corrective measures to be evaluated during the environmental monitoring campaign. The collection of samples is planned with enough time to implement the corrective measures. After the analysis of the surface wipe samples, the results are discussed by the Curie CONTA Committee and if needed, immediate actions are validated. Then the results are presented to the management of the hospital, to the Occupational physician and to the Health, Safety and Working Conditions Committee. Finally, the results are presented to the healthcare workers including cleaning staff. These presentations are adapted for the different audience and validated by the Curie CONTA Committee This communication not only presents the evolution of the environmental contamination but also provides recommendations for controlling this risk of occupational exposure (i.e., long term action measures). Details of this annual environmental monitoring procedure and communication strategy is described in Figure 1.

We are convinced that this descending/ascending communication to healthcare workers is essential. It need to include every worker in order to answer questions, sensitize them to the risk of exposure, and encourage them to follow the defined recommendations. The feedback from the healthcare workers during these presentations are very positive. However, we should assess our approach, for example by using a questionnaire. In our experience, reporting these results of surface contamination measurements is an essential educational tool that raises awareness and helps healthcare professionals to decrease the risk of occupational exposure.

Discussion

Even if ADs are defined as hazardous drugs, they are still extensively used in hospitals because of the continuous increasing number of cancers. Despite established guidelines, studies indicate poor compliance with current best practices, placing healthcare workers and their family at risk of exposure. The misuse of protective gloves and gowns suggest that there is a perception that exposures are inconsequential or so rare that they do not justify their use (8). The exposures observed through urine (32) or blood samples (33, 34) clearly reflect this lack of effectiveness or compliance with the preventive measures put in place.

Surface wipe sampling is now currently used as a standard method to determine workplace contamination in many countries. It is well-established that success of preventive and corrective measures occurred when surface contamination data are obtained but also properly communicated. The restitution of the results is therefore an important step for an awareness of the risk of exposure and a reminder of good practices. Improvements in prevention actions are therefore necessary and they must relate both to the information and training of workers and to the provision of suitable PPE and organizational measures allowing the control of contamination. An assessment of the impact and effectiveness of these preventive measures must therefore be carried out regularly. In the near future, we are waiting for a European harmonized definition of

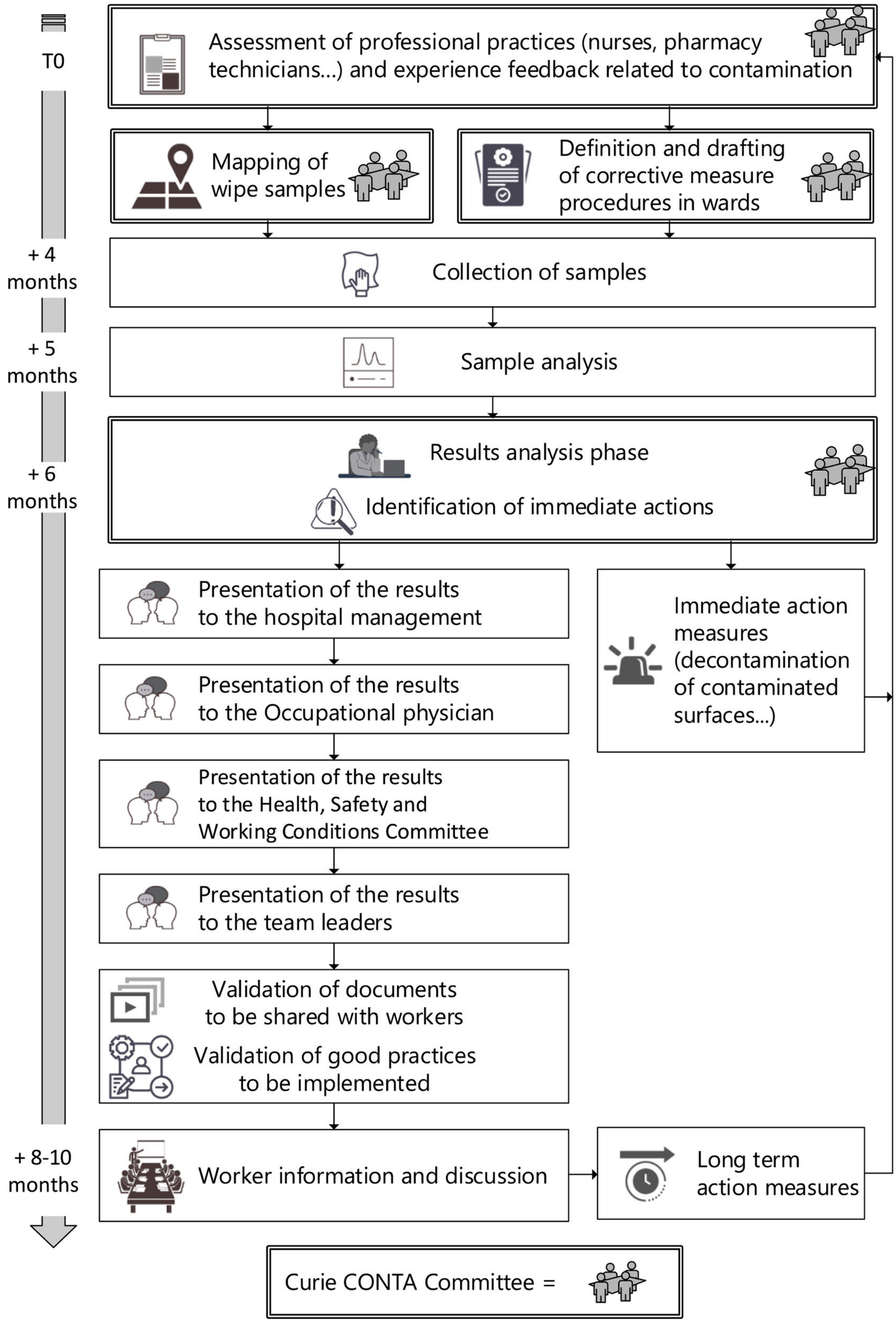

FIGURE 1
Annual environmental monitoring procedure and communication strategy at Institut Curie.

hazardous drugs. We are also waiting for new independent but comparable environmental monitoring studies from more and more hospitals. To help with this, those monitoring could be centralized by certified laboratories that have the expertise and the means to perform these analyses. Creating a European or International database and defining reference levels for hazardous drugs, specifically ADs would be an ambitious perspective but essential to meet the expectations of this issue. At last, we are also waiting for more ongoing training and education on this issue.

Finally, exposure monitoring and his management are essential. Our opinion is that reporting environmental contamination results to healthcare workers could play a crucial role in decreasing the risk of occupational exposure to hazardous drugs.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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Conflict of interest

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Exposure characteristics and risk assessment of air particles in a Chinese hotel kitchen

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Background: The hazards of kitchen particles have attracted social attention, but their distribution characteristics and risk assessment are rarely reported.

Objective: To explore the temporal and spatial distribution characteristics of kitchen particles, analyze the variations in characteristics of number concentration (NC), mass concentration (MC), surface area concentration (SAC), and particle size distribution, provide reference indexes for evaluating worker exposure, evaluate the risk of kitchen particles, as well as suggest improvements and control measures.

Patients and methods: Different cooking posts in a Chinese hotel kitchen were selected to monitor exposure to particles, explore the temporal and spatial distribution characteristics of NC, MC, and SAC of particles in the cooking post, analyze changes in the particle size, compare the individual exposure of particles between the cooking and steaming posts, and analyze the correlation between NC, MC, and SAC. Risk assessment of kitchen ultrafine particles was performed using a Nanotool.

Results: The sizes and fluctuation ranges of $NC_{10-500nm}$ at cooking posts during lunch preparation and at peak periods were significantly higher than those at the end of the lunch period. The mean values of $MC_{10-500nm}$ during the lunch preparation peak and ending periods were 0.149, 0.229, and 0.151 mg m^{-3}, respectively. The mean values of $SAC_{10-500nm}$ were 225, 961, and 466 $\mu m^2 \cdot cm^{-3}$, respectively. The mode diameter of exposed particles at the cooking post [(34.98 ± 2.33) nm] was higher than that at the steaming post [(30.11 ± 2.17) nm] ($P < 0.01$). The correlation between $SAC_{10-500nm}$ and $NC_{10-500nm}$ ($r = 0.703$) was the strongest. Nanotool gave a hazard rating ratio, exposure rating ratio, and risk ratio of 0.75.

Conclusion: The sizes of the NC, MC, and SAC of the particles at the cooking post were related to the kitchen operations. Since kitchen particles are of high exposure and risk levels, protective measures should be formulated and implemented to deal with them safely.

KEYWORDS

particles, quantity concentration, mass concentration, surface area concentration, risk assessment

Introduction

Catering-related kitchen fume pollution is increasing in severity. It is now one of the main air pollutants in indoor living environments. Kitchen oil fumes are aerosols composed of gas, solids, and liquids (1), which can float in the air for a long time, and contain many ultrafine particles smaller than 0.1 μm. Ultrafine particles are generally defined as aerodynamic, geometric, or having migration diameters <100 nm, and are marked by particularity, diversity, and potential harm (2). The new physical and chemical characteristics of ultrafine particles lead to complex exposure characteristics and different biological effects (3). Results from *in vitro* and animal experiments have shown that ultrafine particles have greater toxicological effects than large particles of parent materials (4). The health risks caused by the characteristics and widespread existence of ultrafine particles have attracted extensive attention, but there is a lack of population exposure data. The direct reason is that there is no perfect method for the exposure assessment of ultrafine particles in China or elsewhere. One reason for the lack of exposure assessment methods is that people do not know much about the exposure characteristics of ultrafine particles in the workplace. This paper mainly studied the distribution characteristics of particulate matter in Chinese kitchens, the relationship between Sac, Mc and Nc, and risk assessment methods, focusing on the relationship between SAC, MC and NC, which is the difference between related studies (5).

Currently, there is not much literature in China and worldwide on the harm of kitchen oil fume particles to the human body and how to control the amount of oil fume particles (6, 7). Studies have shown that kitchen oil fume particles can cause cardiovascular and cerebrovascular diseases, cancer, skin damage, respiratory diseases and so on (8). Researchers have reported the induced damage of kitchen oil fume particles to DNA (9), the source of indoor ultrafine particles (10), the differences in the number of particles produced by different cooking methods (11), the impact of different energy heating methods on particles in the kitchen (12), and differences in the number of particles produced by variations in oil heating. Few studies have examined the distribution and exposure characteristics of oil fume particles and assessed the risks of kitchen particles. However, assessment methods and improvements that should be made and adopted still need to be discussed. Similarly, due to their unique nature and specific size, these particles may cause different health hazards than other dust materials. Therefore, the method for evaluating their exposure concentrations and risk should be different from that for other dust material counterparts. The toxicity of ultrafine particles may be due to their small size, high surface activity, charge, and dissolution rate. Kitchen particles have high surface activity, which can promote the ability of nanoparticles to enter cells, resulting in damage to the cells, proteins, and genes in the lungs, as well as the cardiovascular and nervous systems (13). Kitchen oil fumes contain a large number of free radicals with large molecular weight and high stability, which can generate reactive oxygen free radicals and lipid peroxides when entering the body, an important cause of lung cancer, tracheitis, pneumonia, and emphysema (14).

Thus far, the existing studies cannot clarify their damage to the body. Moreover, the international standard of exposure limit has not yet been determined. Due to the potential toxic effect of kitchen particles on human health, it is very important to conduct a risk assessment of these particles. The impact of kitchen particles on human health is a research field worthy of discussion. Thus, we used existing data to evaluate the risk of occupational exposure to kitchen particles, as well as to establish a comprehensive and systematic kitchen particles database. This study examined the number concentration (NC), mass concentration (MC), surface area concentration (SAC), and size distribution of particles in a Chinese kitchen. It also explored the temporal and spatial distribution characteristics of each index and focusing on the correlations between MC, NC, and SAC, which is the difference between related studies (5). This study is expected to preliminarily clarify the exposure characteristics of particles in kitchen fumes, suggest better indicators for the exposure assessment of kitchen workers, provide a basis for the health risk management of exposed people, and lay an experimental foundation for future studies on the health effects of kitchen fumes.

Abbreviations: Abbreviations: NC, number concentration; MC, mass concentration; SAC, surface area concentration; NIOSH, National Institute for Occupational Safety and Health; PPE, personal protective equipment; LEV, local exhaust ventilation; LSD, least-significant difference.

Materials and methods

Kitchen selection

A Chinese hotel kitchen was selected as the survey site. The kitchen is set on the second floor of the north side of the hotel, which connects to the outside world only by the smoke exhaust duct. The kitchen has an area of 5 m × 16 m, and is divided into a storage room, preparation area, and cooking area. There were vegetables, frozen food, and other food materials in the storage room, from which they were taken out by the food preparation personnel in that order during preparation. The preparation area was the operation area for cold dish preparation, cleaning, and chopping food materials. The cooking area was an operation area for cooking food materials. The hood ventilation facilities were set above the front of the five cooking stoves in the operation area, but there was only one hood ventilation system in this kitchen. During operation, the air velocity at the capture

TABLE 1 The main instruments and parameters.

Exposure metrics	Instruments	Particle sizes (nm)	Measuring range	Sampling rate (L·min^{-1})	Log interval (min)
Total NC	3007 (TSI, USA)	10–1,000	0–100,000 particles·cm^{-3} (pt·cm^{-3})	0.1	1
Personal NC	DiSCmini (TESTO, Germany)	<700	0–5,000,000 pt·cm^{-3}	1.0	1
Total respirable MC	Dust Trak 8533 (TSI, USA)	100–1,000	0.01–150 mg·m^{-3}	3	1
SAC	Aero TrakTM 9000 (TSI, USA)	10–1,000	1–10,000 μm^2·cm^{-3}	2.5	1
Size distribution by number	SMPS 3034 (TSI, USA)	10–487	1–2.4 × 10^6 pt·cm^{-3}	1.0	3
	OPS 3330 (TSI, USA)	300–10,000	0–3,000 pt·cm^{-3}	1.0	1

point was about 0.8 m · s^{-1}. The chef did not wear protective masks or noise-proof earplugs, and lunchtime was mainly from 10 a.m. to 2 p.m. The preparation area was adjacent to the cooking area. Therefore, both work areas were exposed to the oil fumes generated during cooking.

Measurement indicators and instruments

The measurement indices were divided into exposure concentration and particle size distribution. The exposure concentration indices were MC, NC, and SAC (referring to the sum of all particle surface areas in unit volume), and the particle size distribution index was the particle size distribution of NC. In addition, the auxiliary measurement indicators include air temperature, air pressure and wind speed in meteorological conditions. Table 1 shows the main instruments and parameters. The instruments used included the aerosol monitor Dusttrak 8533, the ultrafine particle counter 3007, the nanoparticle aerosol monitor Aero Trak 9000, the scanning electromigration particle size meter SMPS 3034, the optical particle sizer OPS 3330, the meteorological condition meter 9565 (TSI, USA), and the nanoparticle analyzer Discmini (Testo, range 10–700 nm, Germany). All instruments are returned annually to the original factory for calibration.

Sampling scheme

Firstly, through on-site investigation and pre-detection of the workplace with 3007, the emission source of particles at the detection posts was determined, as well as the sampling time. The specific detection scheme was as follows: (15) ① Background concentration measurement: the concentration of particles in the air in the kitchen between 9 and 9:59 am before cooking on the same day was selected as the background concentration. When detecting the background concentration, there were no workers or other particle release sources. ② Particle detection based on operation activities: the detection location was based on the early field investigation data and pre-detection, and the influences of the chef's operation mode, instruments, and equipment on the chef's operation were considered. The main cooking methods included stir-frying, pan-frying, and deep-frying, which were generally operate under rapid high-heat conditions. There were also steaming posts, which were usually operated under continuous heating. The combination of fixed-point sampling and individual sampling was adopted within the same day at different times, and individual samples were collected for different indicators. The temporal and spatial distributions of particles in cooking posts were analyzed by fixed-point sampling (180 groups of data were collected throughout the preparation, peak, and ending periods). An individual sampling method was used to analyze the particle exposure characteristics of different posts (133 groups of data were collected during the preparation and peak periods). For individual sampling, the instrument was hung on the chef, and the sampling air inlet was clamped at the breathing belt position on the chef's collar. During fixed-point sampling, the sampling and testing instrument was placed at the downwind side of the testing post. The instrument and equipment were as close to the chef as possible without affecting his operation. The point distribution position is shown in Figure 1. The detection height was the worker's respiratory belt level. The detection time was from the beginning of preparation to the end of operation activities. The detection period was 10:45–13:44. Simultaneously, the background value in the kitchen during non-working hours before lunch was detected, and the detection period was 9:00–9:59. Table 2 illustrates the detailed events of each stage.

Risk assessment method

According to previous studies (16), the Nanotool (http://www.controlbanding.net/) is suitable for nanoparticles and has comprehensive advantages in risk assessment; thus, it was selected for use in this study. It was developed by Paik and Zalk at Lawrence Livermore National Laboratory in the United States. The Nanotool uses a scoring system to allocate risk and exposure levels, as well as combines

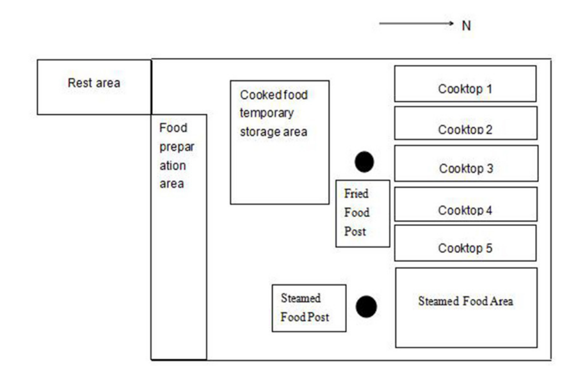

FIGURE 1
Locations of monitoring sites. •: Detection point.

TABLE 2 Record of activities in each lunch period.

Activity period	Time	Activity
Before lunch	9:00-—9:59	No operation
Lunch preparation	10:45-—11:44	Opening and closing of furnaces 1 and 2; 3 times each
Lunch peak	11:45-—12:44	Furnace 1 was opened and closed 5 times, furnace 2 was opened and closed 3 times, furnace 3 was opened and closed 3 times, furnace 4 was opened and closed 5 times, and furnace 5 was opened and closed 3 times
Lunch closing	12:45-—13:44	No operation

the risk and exposure levels to obtain the risk level in the two-dimensional decision matrix, followed by dividing them into four levels on average. Table 3 shows the hazard and exposure input parameters. Hazards were determined based on particle shape, concentration, surface activity, and toxicity (including carcinogenicity, mutagenicity, and reproductive toxicity). Exposure levels were determined by substance emission potential, activity emission potential, and exposure control.

Statistical analysis

The comparison of NC and the background concentration of particles exposed to different cooking posts and the comparison of the SAC of particles under different modes were analyzed using one-way ANOVAs. The pairwise comparison was performed using the Least-SignificantDifference (LSD)method when the variances were homogeneous. The pattern diameter of particles, or the particle diameter corresponding to the maximum NC of the particles at lunch peak, exposed to different cooking posts was analyzed using a one-way ANOVA with repeated data. The Pearson correlation method was used to analyze the correlations between NC, MC, and SAC. The significance level was set at $\alpha = 0.05$.

TABLE 3 Hazard parameters and exposure scenario parameters of oil fume.

Input information	Required information	Oil fume
Nanotool base metal hazard classification input parameters	Carcinogen	Yes
	Reproductive harm	No
	Mutagen	Yes
	Skin hazards	No
	Sensitization	No
Nanotool - nanomaterial hazard classification input parameters	Surface reactivity	Unknown
	Particle shape	Anisotropy
	Particle size	11–40 nm
	Solubility	Insoluble
	Carcinogen	Yes
	Reproductive harm	Yes
	Mutagen	Yes
	Skin hazards	No
	Sensitization	No
Exposure classification input parameters	Aerosol concentration	11–100 mg
	Current engineering control	Local exhaust ventilation
	Number of employees with similar exposures	8
	Operating frequency (year)	Everyday
	Operating time	>4 h

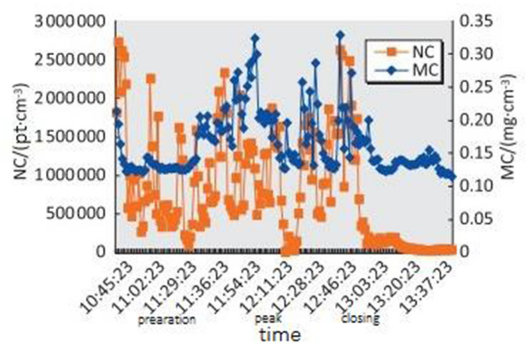

FIGURE 2
Distribution of $NC_{10-500nm}$ and $MC_{10-500nm}$ of fried food posts in the Chinese kitchen in different time periods.

Results

Time-concentration particle changes at the fried food post

As shown in Figures 2, 4, the sizes and fluctuation ranges of $NC_{10-500nm}$ during the lunch preparation and peak periods were significantly higher than those during the lunch ending period. These were related to operational activities. The lunch preparation period was 10:45–11:44, which mainly focused on vegetable preparation, as well as cooking and heating preparation, with no cooking activities. The average $NC_{10-500nm}$ particle value was $\sim 10^6 \cdot pt \cdot cm^{-3}$. The lunch peak period was 11:45–12:44. Cooking activities were frequent during this stage, and the average $NC_{10-500nm}$ value was about $9.8 \times 10^5 \cdot pt \cdot cm^{-3}$. There was no significant difference between lunch preparation and lunch peak $NC_{10-500nm}$. Lunch ended at 12:45–13:44. There were a few cooking activities from 12:45 to 13:00, after which there were none. The average value of $NC_{10-500nm}$ was $4.2 \times 10^5 \cdot pt \cdot cm^{-3}$, which was lower than that during the preparation and peak period ($P < 0.01$), but higher than the background value (about $0.4 \times 10^5 \cdot pt \cdot cm^{-3}$; $P < 0.01$).

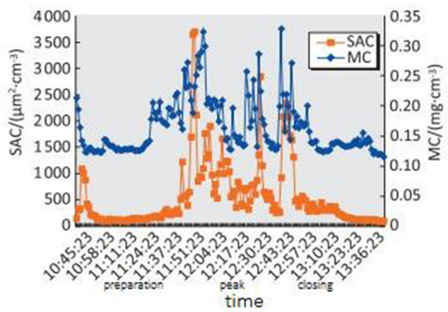

FIGURE 3
Distribution of $SAC_{10\sim500nm}$ and $MC_{10\sim500nm}$ of particles at fried food posts in the Chinese kitchen in different time periods.

$MC_{10-500nm}$ fluctuated less than $NC_{10-500nm}$ throughout the whole process. The mean values of $MC_{10-500nm}$ during the lunch preparation, peak, and closing periods were 0.149, 0.229, and $0.151 mg \cdot m^{-3}$, respectively. $MC_{10-500nm}$ in the peak period was higher than that in the preparation and closing periods ($P < 0.05$); however, there was no difference in $MC_{10-500nm}$ between the lunch preparation and closing periods ($P > 0.05$).

As shown in Figures 3, 4, the mean values of $SAC_{10-500nm}$ during the lunch preparation, peak, and closing periods were 225, 961, and 466 $\mu m^2 \cdot cm^{-3}$, respectively. The $SAC_{10-500nm}$ value was higher during the peak period than during the preparation and ending periods and was higher during the ending period than during the preparation period ($P < 0.05$).

Particle size characteristics for the fried food posts

During the lunch peak, the number of particles was distributed from large to small, as shown in Figure 5: within 100nm, > 100–200nm, > 200–300nm, > 300–400nm, and > 400–500nm. The proportion of particles with a

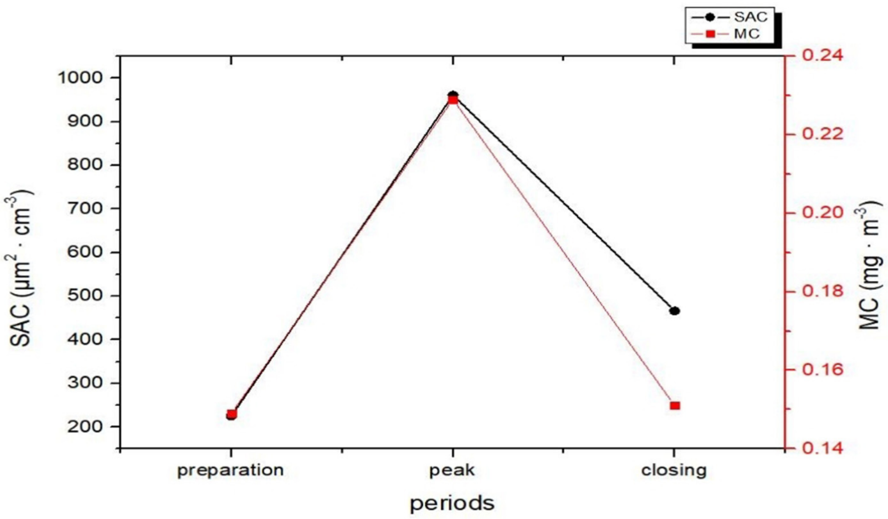

FIGURE 4
Mean values of $SAC_{10\sim500nm}$ and $MC_{10\sim500nm}$ of particles at fried food posts in the Chinese kitchen in different periods.

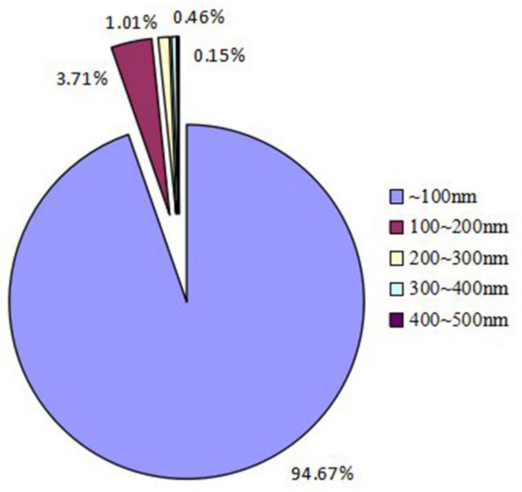

FIGURE 5
Percentages of particle number distribution with different particle size at lunch peak.

TABLE 4 Analysis of variance of $NC_{20-700nm}$ and mode diameter of particles in different posts ($n = 133$).

Post	$NC_{20-700\ nm}$ size (nm)	Mode
Fried food post ($n = 133$)	1,032,352 ± 158,231[1,2]	34.98 ± 2.33[3]
Steamed food post ($n = 133$)	668,771 ± 23,623[2]	30.11 ± 2.17
Background values	42,485	

[1]P < 0.01, compared with steaming posts.
[2]P < 0.01, compared with the background values.
[3]P < 0.01, compared with steaming posts.

particle size less than 100nm and less than 200nm was 94.67% and 98.38%, respectively. When the particle size was less than 200 nm, the NC of the particles of 19nm was the largest, so the mode diameter at the lunch peak was 19nm.

Individual particle exposure levels at different cooking posts

The $NC_{10-700nm}$ [(1,032,352 ± 158,231), (668,771 ± 23,623) pt·cm^{-3}] of the particles exposed to the cooking and steaming posts was higher than the background value (42,485 pt·cm^{-3}) ($P < 0.01$). The $NC_{10-700nm}$ of the cooking posts was higher than that of the steaming posts ($P < 0.01$), and the mode diameter of the particles exposed to the cooking posts [(34.98 ± 2.33) nm] was higher than that of the steaming posts [(30.11 ± 2.17) nm] ($P < 0.01$), as shown in Table 4.

TABLE 5 Correlation Analysis between $MC_{10-500nm}$, $NC_{10-500nm}$ and $SAC_{10-500nm}$ ($n = 180$).

Index	$SAC_{10-500\ nm}$	$NC_{10-500\ nm}$	$MC_{10-500\ nm}$
$SAC_{10-500nm}$ (μm^2/cm^3)	1.00	0.703[1]	0.351[2]
$NC_{10-500nm}$ (×10^{4}p/cm^3)	–	1.00	0.412[a]
$MC_{10-500nm}$ (mg/m^3)	–	–	1.00

[1]P < 0.01.
[2]P < 0.05.

Correlations between MC, NC, and SAC

The correlation between $NC_{10-500nm}$ and $SAC_{10-500nm}$ was the strongest, with a correlation coefficient of 0.703 ($P < 0.01$). The correlation coefficients of $NC_{10-500nm}$ and $MC_{10-500nm}$, as well as $SAC_{10-500nm}$ and $MC_{10-500nm}$ were 0.412 and 0.351, respectively ($P < 0.05$), as shown in Table 5.

Risk assessment of kitchen particles and control measures to be improved

Table 6 shows the risk assessment results of the control classification tool and the preventive measures recommended by the National Institute for Occupational Safety and Health (NIOSH) regulations. Nanotool's hazard and exposure level ratios were 0.75, and the risk ratio was 0.75, suggesting high exposure and risk levels and indicating that protective measures should be formulated and implemented for kitchen oil fumes. According to NIOSH regulations, the prevention and control of ultrafine particles include five elimination steps: replacement, engineering control, administrative control, and personal protective equipment (PPE). Since it is impossible to eliminate and substitute ultrafine particles during cooking, the following control levels should be adopted: engineering control, administrative control, and PPE. Table 5 lists the current control measures and other control measures that need improvement.

Discussion

The $NC_{10-500nm}$ values and particle fluctuations during the lunch preparation and peak periods were greater than those of the background value. However, there was no difference between the preparation and the peak periods. The kitchen operation during preparation is mainly the pretreatment of some dishes, and a small amount of cooking operation will also produce soot particles. The above factors will increase the exposure of $NC_{10-500nm}$ during lunch preparation (17).

TABLE 6 Risk assessment and control measures.

Tool	Hazard level ratio	Exposure grade ratio	RR	Existing control measures	Other control measures to be improved
Nanotool	0.75	0.75	0.75	(1) Engineering control: the gas stove is equipped with LEV (2) Occupational health management system: regular occupational health training, reduce exposure time and conduct occupational health examination for workers. The preventive maintenance plan for ultrafine particles is missing	(1) Engineering control: reasonably arrange the position of air supply and exhaust outlets, distribute air volume, and select the form of air outlet. It is necessary to increase the exhaust speed of LEV (2) Occupational health management system: LEV regular maintenance and inspection plan shall be formulated to ensure the effectiveness of engineering control measures (3) PPE: NIOSH certified N95 or P100 filter mask respirator shall be used, and regular inspection shall be conducted to ensure that workers wear PPE correctly

$SAC_{10-500nm}$ was different in the three lunch periods, with peak period > ending period > preparation (P < 0.05). The particle $SAC_{10-500nm}$ in the peak period of operation was higher than that of the preparation and ending periods, which was related to the particle $NC_{10-500nm}$ in the peak period. Thus, the value in the ending period was higher than that in the preparation period, which may be related to the presence of many particles floating in the air during the ending period (18). This study also found a correlation between $SAC_{10-500nm}$ and $MC_{10-500nm}$, consistent with the results from a study by Zou et al. (19).

The focus of this study was mainly ultrafine particles within the 100 nm limit. When analyzing the composition of particles according to size, we also analyzed particles with other sizes. Particles above 500 nm have a short residence time in the air and low concentration, which is difficult for the sampling instrument to capture. Regarding composition, the number of particles <100 nm accounted for over 94%, occupying an absolute advantage, which may be related to the agglomeration effect of ultrafine particles (20).

When studying the $NC_{10-700nm}$ exposure characteristics of individual particles at the cooking and steaming posts, we found that the $NC_{10-700nm}$ exposure values of the two posts were both statistically significant according to a one-way ANOVA (P < 0.01). Considering that the components of particles in contact with the cooking and steaming posts were not the same, it can be inferred that the cooking post was mainly exposed to a large amount of grease. In contrast, the steaming post was exposed to a large amount of steam. Therefore, the harm of particle exposure at the cooking post may be much greater than that at the steaming post.

Correlation analysis showed that the correlation between $SAC_{10-500nm}$ and $NC_{10-500nm}$ was higher than that between $SAC_{10-500nm}$ and $MC_{10-500nm}$, which is consistent with the results of a study by Heitbrink et al. (21). Toxicological studies have also shown a strong dose-response relationship between the surface area dose of very low solubility fine particles and ultrafine particles and inflammatory lung response (22). Moreover, epidemiological studies have shown a correlation between SAC and population health risk (23). Further, there was no linear correlation between the measurement results of daily air pollution with MC as the index and death (24). However, by applying the same detection index and converting MC data into SAC analysis, we found a linear correlation between the SAC of particles in the ambient air and death data, indicating that SAC may be more suitable as an air exposure index (25). These studies suggest that MC alone cannot replace NC or SAC indicators.

Although we had selected the most common Chinese hotel kitchen in this study, it is still a case report. The sampling results of ultrafine particles were closely related to sampling location, distance, wind direction, air inlet direction, operation conditions, and protective measures (26, 27). The wind speed in the kitchen environment was relatively stable. Still, the movement of operators as well as equipment interfered with the wind speed and direction, leading to changes in the distribution of ultrafine particles. Therefore, this study recorded the activity events and meteorological conditions of the sampling process in detail. According to the characteristics of kitchen operation posts, the components of kitchen oil fumes (28) are complex, mainly including over 200 kinds of aldehydes, ketones, hydrocarbons, fatty acids, alcohols, aromatic compounds, esters, lactones, and heterocyclic compounds, most of which are toxic or even strong carcinogens (such as benzopyrene, and heterocyclic amines). The workers were tracked and sampled during a complete lunch cycle. The results showed that a slight change in the surrounding environment had different effects on different detection instruments, however, specific reasons need to be further discussed. Since the physical and chemical characteristics of ultrafine particles are different from those of general particles (29), eliminating the influence of background mixing and external interference in the workplace environment on the results is a problem that needs to be addressed in future research.

The exposure, hazard level, and risk ratios for this scenario given by the Nanotool model were all 0.75, which is high. The revealed high proportion of carcinogens in cooking smoke supports the results of high-risk levels obtained from control banding tools, and the results of NC, MC, SAC, and individual NC confirm the high exposure risk.

Epidemiological studies reported that cooking fumes contain many carcinogens and exposure to them increases cancer risk, which provides evidence for the high-risk nature of such air pollution. Controlling occupational hazard exposure is the primary method for protecting workers with high-risk exposure. According to NIOSH regulations, a series of controls, including elimination, substitution, engineering, administrative, and PPE, have been used to implement feasible and effective controls. For the restaurant investigated in this study, elimination, and substitution were not feasible, and instead, the best way to control kitchen fumes was to use engineering control. Results of the risk assessment showed that prevention and control measures should include local exhaust ventilation (LEV), indicating that the effectiveness of the existing LEV of the restaurant was insufficient, the air velocity at the capture point should be at least $1.2\,\mathrm{m} \cdot \mathrm{s}^{-1}$ (30). The reasons for this may include insufficient wind speed, the unreasonable position of the exhaust hood, and rising airflow in response to high temperatures. The following prevention and control measures should be added to the existing measures to protect workers in similar restaurants: (1) The capture efficiency of LEV needs to be improved. (2) A preventive maintenance plan should be formulated to ensure the effectiveness of engineering control measures. (3) NIOSH certified N95 or P100 filter mask respirators should be used, and regular inspection should be conducted to ensure that workers wear PPE correctly.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

ZZ contributed to the conceptualization, data curation, investigation, funding acquisition, supervision, and writing of the original draft. XG contributed to the investigation, data curation, methodology, funding acquisition, and formal analysis. YC contributed to the investigation and funding acquisition. HZ and YJ contributed to the conceptualization, funding acquisition, review, and editing of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Impact of engineering renovation on dynamic health risk assessment of mercury in a thermometer enterprise

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The occupational health risk assessments (OHRA) of inorganic mercury (Hg) are rarely reported. We conducted an internal and external exposure monitoring of employees in a thermometer enterprise which experienced the renovation of occupational health engineering, followed by an evaluation on the health risks of Hg exposure with four OHRA methods in order to find out a most suitable model. The results showed that the concentrations of airborne and urinary Hg in all testing positions and subjects obviously decreased after the engineering renovation, meeting the occupational exposure limits (OELs) of China. Subsequently, four OHRA models, namely the models from US Environmental Protection Agency (EPA), Ministry of Manpower (MOM), International Council on Mining and Metals (ICMM), and Classification of occupational hazards at workplaces Part 2: Occupational exposure to chemicals (GBZ/T 229.2-2010) were applied in the qualitative risk assessment. And the evaluation results of different methods were standardized by risk ratio (*RR*), which indicated MOM, ICMM risk rating, and GBZ/T 229.2 models were consistent with the order of inherent risk levels in those working processes. The order of *RR* between four models was: $RR_{EPA} > RR_{ICMM} > RR_{MOM} > RR_{GBZ/T229.2}$ ($P < 0.05$). Based on the strict limits of Hg, GBZ/T 229.2, and MOM methods may have more potentials in practical application. Though the working environment has been significantly improved via engineering renovation, it is strongly suggested that the thermometer company conduct more effective risk management covering all production processes to minimize Hg exposure levels and health risk ratings.

KEYWORDS

mercury, thermometer, occupational health risk assessment, renovation, risk ratio, concentration, occupational exposure

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Introduction

Mercury-containing thermometers are widely used in medical institutions because of their stable performance, convenient operation, and low price (1). Mercury, as the only liquid metal element on the earth (2), is recognized by the World Health Organization (WHO) as one of the top 10 chemicals or groups of chemicals of major public health concern (3), which is the most common chemical hazardous agent for thermometer manufacturing enterprises. It often invades the human body in the form of vapor during production activities, and long-term exposure can cause occupational mercury poisoning, affecting the nervous system, the digestive system, and the immune system, and damaging human health. In recent years, domestic and foreign scholars have identified and analyzed workplace hazards through occupational health risk assessments (OHRA) (4–8), and many researchers have conducted corresponding studies on the occupational hazard risks of mercury (9, 10). Zhu et al. (11) studied the characteristics of mercury pollution at the site of a thermometer manufacturer and conducted the health risk assessment. Han et al. (12) used the Environmental Protection Agency (EPA) model to assess the non-carcinogenic risk of mercury in fluorescent lamp manufacturing enterprises, and found that the mercury concentration in the exhaust mercury-injecting post exceeded the standard, which was high risk. Ruan et al. (13) used the Ministry of Manpower (MOM) model to assess occupational hazards in energy-saving lamp production enterprises, and found this model can objectively reflect the actual risk level of the workplace. In this paper, EPA, MOM, International Council on Mining and Metals (ICMM), and GBZ/T 229.2 (14) were used to carry out OHRA of mercury in a thermometer enterprise, comparing the risk differences before and after the renovation of occupational disease protection facilities longitudinally, and focusing on the correlation between risk levels and occupational exposure under different methods transversely, to obtain suitable methods for dynamic occupational risk assessment of mercury.

Object and methods

Object

A thermometer manufacturing enterprise in Jiangsu was selected to conduct on-site testing and analysis in December 2019 and September 2020. The products of the enterprise conclude trigonal thermometers and internal scaling thermometers. The technological process can be seen in Figure 1. According to the early survey, the main occupational health hazard is mercury. The posts where workers could be exposed to mercury were all taken into considerations.

Methods

Five OHRA models were used to classify the risk of occupational diseases for employees, including EPA, MOM, ICMM, and GBZ/T 229.2. Several representative posts were chosen to carry out short time sampling in accordance with GBZ/T 159-2004: Sampling Practices for Monitoring Harmful Substances in workplace Air (15). The detection factor was tested according to GBZ/T 300.18-2017: determination of toxic substances in workplace air-Part 18: Mercury and its compound (16). The occupational exposure limits (OELs) in China stipulate that the 8-h time-weighted average allowable concentration of mercury is 0.02 mg/m^3. The judgment of whether the concentration of mercury in the workplace exceeds the standard is made according to the OELs.

EPA

In this model, the method can be divided into cancer risk assessment and non-carcinogenic risk assessment, having two steps in the process of OHRA: exposure concentration (*EC*) estimation and health risk assessment (17–19). *EC* is determined by *CA*, *ET*, *EF*, *ED*, and *AT*, as calculated by Equation (1):

$$EC = (CA * ET * EF * ED)/AT \tag{1}$$

where *CA* is the concentration of the toxic and hazardous chemicals in the air of the workplace (g/m^3). *ET* is the exposure time of employees in the workplace (h/day). *EF* is the exposure frequency of employees in the workplace (day/year). *ED* is the duration of exposure during the exposure period (y). *AT* is the average exposure time (h), the value of which is $ED*24*365$. The non-carcinogenic risk, hazard quotient (*HQ*) of mercury is calculated by Equation (2):

$$HQ = EC/RfC \tag{2}$$

where *RfC* is the inhalation toxicity reference value of the toxicant to be evaluated, also known as the reference concentration (mg/m^3). The *RfC* of mercury is 0.3 $\mu g/m^3$ according to the IRIS database.

MOM

In the MOM semiquantitative risk assessment model (20, 21), the risk is determined by hazard level (*HR*) and exposure level (*ER*). The hazard classification of chemicals is divided by toxicity of the chemicals with five levels: no risk (grade 1); low risk (grade 2); moderate risk (grade 3); high risk (grade 4); extreme risk (grade 5), and that of mercury is 5 (13, 22). *ER* is determined by comparing the weekly time-weighted average exposure level (*E*) with the long-term OEL. *E* is calculated by Equation (3) (23):

$$E = (F * D * M)/W \tag{3}$$

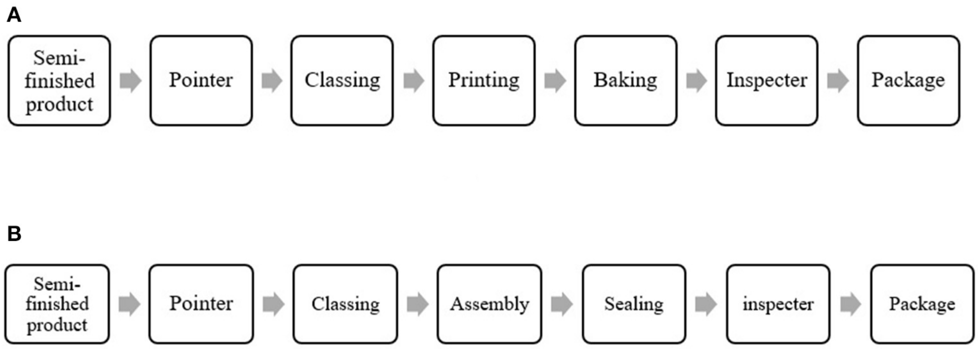

FIGURE 1
Main technological process of the thermometer manufacturing enterprise: **(A)** Trigonal thermometer, **(B)** Internal scaling thermometer.

where F is the weekly exposure frequency; D is the average exposure time (h); M is the air detecting concentration (PPM or mg/m^3); W is the average working time per week (40 h). The risk is calculated by Equation (4):

$$R = \sqrt{HR * ER} \quad (4)$$

ICMM

The ICMM model involves two methods (24, 25), one is ICMM risk rating method, and the other is ICMM quantitative method of assignment. The former determines the risk level based on the level of occupational exposure, the effectiveness of protection, and the likelihood of occupational exposure, depending on subjective judgment to a great extent. When using ICMM quantitative method of assignment, the occupational risk is calculated by Equation (5):

$$rr = C * PrE * PeE * U \quad (5)$$

When rr is risk rank, C is the occupational health consequences, according to the degree of harm, the value of mercury in this study is 100. PrE is exposure probability, which is assigned according to the result of onsite testing: <50% OEL is assignment 3; 50–100% OEL is assignment 6; ≥100% OEL is assignment 10. PeE is exposure time. Supplemental Table 1 presents the assignment. U is the uncertainty parameter: certainty is assignment 1; uncertain is assignment 2; very uncertain is assignment 3. Risk grades are determined by rr, as shown in Supplemental Table 2.

GBZ/T 229.2

GBZ/T 229.2 considers the hazard of chemicals, occupational exposure ratio, and physical workload of workers. The weights of the three factors correspond to W_D, W_B, and W_L, respectively, and the values are shown in Supplemental Tables 3–5. W_B is determined by B, which is the ratio of occupational exposure level to OELs in particular.

The grading index of occupational hazards is defined as G, calculated by Equation (6), corresponding to four types of operations, as illustrated in Supplemental Table 6.

$$G = W_D * W_B * W_L \quad (6)$$

Standardization of assessment results

To better compare the assessment results of different models, the risk ratio (RR) was put forward to standardize the occupational risk, which was calculated by Equation (7),

$$RR = \frac{Risk\ Grade}{Total\ Grade} \quad (7)$$

In the method of EPA, MOM, and ICMM quantitative method of assignment, there are five risk levels corresponding to the risk grades 1–5, and the larger the value, the higher the risk level. While in the method of ICMM risk rating and GBZ/T 229.2, the total grade is 4.

Statistics

SPSS 27.0 software was used for statistical analysis. RR between the 2 years were tested by a non-parametric test. $P < 0.05$ was considered statistically significant. Kendall's W-test was executed to assess agreement among the RRs obtained from different OHRA models, which was a non-parametric statistic. Kendall's coefficient of concordance W ranges from 0 (no agreement) to 1 (complete agreement) (26, 27). Spearman correlation analysis was used to analyze the correlation between RRs and occupational exposure, and $P <$ 0.05 was considered significant.

TABLE 1 Results of mercury concentration tests in 2019 (mg/m^3).

Production process	Post	Duration of exposure	Median (Range)	TWA	STEL	Judgment
Trigonal thermometer	Pointer	10	0.073 (0.071–0.074)	0.091	0.074	Unqualified
	Classing	10	0.061 (0.025–0.074)	0.066	0.074	Unqualified
	Printing	10	0.053 (0.035–0.063)	0.063	0.063	Unqualified
	Baking	10	0.039 (0.037–0.040)	0.039	0.040	Unqualified
	Package	10	0.050 (0.023–0.070)	0.060	0.070	Unqualified
Internal scaling thermometer	Pointer	10	0.018 (0.013–0.028)	0.024	0.028	Unqualified
	Classing	10	0.013 (0.011–0.020)	0.019	0.020	Qualified
	Assembly	8	0.018 (0.011–0.019)	0.016	0.019	Qualified
	Sealing	8	0.024 (0.013–0.024)	0.020	0.024	Qualified
	Package	10	0.023 (0.017–0.028)	0.029	0.028	Unqualified
Inspection area	Inspecter	10	0.023 (0.014–0.029)	0.028	0.029	Unqualified
Solid waste treatment	Crushing	0.8	0.115 (0.105–0.254)	0.016	0.254	Unqualified

TABLE 2 Results of mercury concentration tests in 2020 (mg/m^3).

Production process	Post	Duration of exposure	Median (Range)	TWA	STEL	Judgment
Trigonal thermometer	Classing	8	0.009 (0.003–0.018)	0.016	0.018	Qualified
	Printing	8	0.010 (0.006–0.019)	0.015	0.019	Qualified
	Baking	8	0.011 (0.003–0.015)	0.013	0.015	Qualified
Internal scaling thermometer	Classing	8	0.004 (0.002–0.008)	0.006	0.008	Qualified
	Assembly	8	0.005 (0.002–0.011)	0.007	0.011	Qualified
	Sealing	8	0.008 (0.005–0.017)	0.012	0.017	Qualified
	Pointer	8	0.010 (0.005–0.018)	0.011	0.018	Qualified
	Package	8	0.003 (0.002–0.006)	0.004	0.006	Qualified
Inspection area	Inspecter	8	0.010 (0.004–0.017)	0.013	0.017	Qualified
Solid waste treatment	Crushing	4	0.010 (0.004–0.015)	0.007	0.015	Qualified

Results

Results of on-site survey and mercury concentration tests

As illustrated in Table 1, the concentrations of mercury in 75% of the posts were beyond the OEL in 2019. In terms of the on-site survey, the main control measures applied throughout the factory include isolating equipment, submerging broken thermometers in trays of water, and conducting a continuous clean-up program. Actually, the size of the isolation cabinet did not fit well with the degassing machine, leaving doors not fully closed. The floor of the rooms was laid by terrazzo, and the surface of the walls was uneven. The height of the side wall exhaust fans was set too high. There was no exhaust hood installing at the mouth of the crusher. The exhaust gas treatment device was set on the top of the workshops, greatly affecting the efficiency of ventilation and detoxification. What's more, the number of tail gas treating units was small. In a word, the lack of rationality in the setting of protective measures for occupational diseases was the main reason for the excessive mercury concentration.

In 2020, the enterprise experienced the renovation of occupational health engineering, and the main measures were as followed, laying smooth pads on the workbench, setting up a local exhaust hood at the workstation, changing the location of the exhaust gas treatment device from the high position to the low position, etc. These measures greatly promoted the emissions of inorganic mercury vapor. All the operations involving mercury were performed over impermeable surfaces without crevices, which helped to reduce the mercury exposure of workers. In a word, the engineering facilities appeared to run in good condition compared to that in 2019. In terms of process transformation, the fixed point and packaging process of the two thermometers were merged. The test results shown in Table 2 indicated that the mercury concentration of each post after the transformation was qualified. And the mean level of TWA in 2020 decreased significantly ($P = 0.002$) in comparison with that of 2019, indicating that engineering renovation greatly reduced the mercury concentration in the air of workplaces.

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Furthermore, the internal exposures of the subjects were analyzed. The urinary Hg values declined obviously among 51 frontline workers after engineering renovation (median levels: 132.1 µg/g Cr before the renovation and 54.9 µg/g Cr after the renovation, $P < 0.001$).

Results of OHRA

The risk assessment results of each model were shown in Tables 3, 4. Table 5 illustrated the percentage of posts with different risk. In 2019, the assessment results of EPA model and ICMM quantitative method of assignment were consistent. Over 90% of the posts were unacceptable risks, corresponding to the risk rating scaling of 5. As a result of MOM, 33% of the posts were extremely high risk, mainly distributed in the triangular thermometer production area. The risk of the other posts was high. In all, the general risk level of MOM model is lower than that of EPA model and ICMM quantitative method of assignment. When using ICMM risk rating method, 75% of the posts were extremely high risk. The results of GBZ/T 229.2 showed that 42% of the posts were severe hazard operations, and 33% of the posts were moderate hazard operations.

In 2020, the results of MOM and ICMM quantitative method of assignment remained unchanged, maintaining the level of extremely high risk. In MOM and ICMM risk rating methods, the risk level of major posts declined significantly, and the number of high-risk posts decreased. The posts of pointer, classing, printing, and package in the triangular thermometer production area changed from extremely high risk to high risk. In the method of GBZ/T 229.2, there was no post with severe hazard operation in 2020. All the posts were relatively harmless operations.

Tables 6, 7 show *RRs* of different models. The order of *RRs* between four models was: $RR_{\text{EPA}} > RR_{\text{ICMM}} > RR_{\text{MOM}} > RR_{\text{GBZ/T229.2}}$ ($P < 0.05$) on the whole. There was no significant difference in the risk level before and after the transformation using EPA and ICMM assignment quantitative methods. Among the three assessment methods of MOM, ICMM risk rating method, and GBZ/T 229.2, *RRs* in 2020 were significantly reduced compared with 2019. Non-parametric tests were used to analyze the differences of *RRs* for each assessment model in 2019 and 2020. The results showed that the risk level of each post changed significantly after the transformation of occupational disease protection facilities in 2020 (MOM model, $P = 0.006$; ICMM risk rating method, $P = 0.002$; GBZ/T 229.2, $P = 0.002$).

The results of Kendall's coefficient of concordance W-test illustrated that the *RRs* obtained from the model of MOM, ICMM risk rating method, and GBZ/T 229.2 were comparable (2019, $W = 0.51$, $P < 0.05$; 2020, $W = 0.8$, $P < 0.05$). To further compare the applicability of MOM, ICMM risk rating method, and GBZ/T 229.2, the correlation analysis between *RR* and TWA

TABLE 3 Results of the health risk assessment of mercury exposure at each position in 2019.

Post	EPA			MOM			ICMM risk rating method				ICMM quantitative method of assignment					GBZ/T 229.2				
	EC (µg/m³)	*HQ*	Risk level	E/PEL	*ER*	Risk level	Exposure level	Effectiveness of protective facilities	Likelihood of exposure occurring	Risk level	*PrE*	*PeE*	*U*	Risk value	Risk level	W_D	W_B	W_L	*G*	Classification
Pointer-T	27.01	90.03	5	4.55	5	5	High	Poor	Medium	4	6	10	1	6,000	5	8	4.55	1.5	55	III
Classing-T	19.59	65.30	5	3.30	5	5	High	Poor	Medium	4	6	10	1	6,000	5	8	3.3	1.5	40	III
Printing-T	18.70	62.33	5	3.15	5	5	High	Poor	Medium	4	6	10	1	6,000	5	8	3.15	1.5	38	III
Baking-T	11.58	38.58	5	1.95	4	4	High	Poor	Medium	4	6	10	1	6,000	5	8	1.95	1.5	23	II
Package-T	17.81	59.36	5	3.00	5	5	High	Poor	Medium	4	6	10	1	6,000	5	8	3	1.5	36	III
Pointer-I	7.12	23.74	5	1.20	4	4	High	Poor	Medium	4	6	10	1	6,000	5	8	1.2	1.5	14	II
classing-I	5.64	18.80	5	0.95	3	4	Medium	Poor	Medium	3	6	10	1	6,000	5	8	0	1.5	0	0
Assembly-I	3.80	12.66	5	0.80	3	4	Medium	Poor	Medium	3	6	10	1	6,000	5	8	0	1.5	0	0
Sealing-I	4.75	15.83	5	1.00	4	4	High	Poor	High	4	6	10	1	6,000	5	8	1	1.5	12	II
Package-I	8.61	28.69	5	1.45	4	4	High	Poor	Medium	4	6	10	1	6,000	5	8	1.45	1.5	17	II
Inspecter	8.31	27.70	5	1.40	4	4	High	Poor	High	4	6	10	1	6,000	5	8	1.4	2	17	II
Crushing	0.38	1.27	4	0.80	3	4	Medium	Poor	High	3	6	2	1	1,200	5	8	0	2	0	0

TABLE 4 Results of the health risk assessment of mercury exposure at each position in 2020.

Post	EPA			MOM			ICMM risk rating method				ICMM quantitative method of assignment					GBZ/T 229.2				
	EC ($\mu g/m^3$)	HQ	Risk Level	E/PEL	ER	Risk Level	Exposure level	Effectiveness of protective facilities	Likelihood of exposure occurring	Risk level	PrE	PeE	U	Risk value	Risk level	W_D	W_B	W_L	G	Classification
Classing-T	3.80	12.66	5	0.80	3	4	Medium	Good	Medium	3	6	10	1	6,000	5	8	0	1.5	0	0
Printing-T	3.56	11.87	5	0.75	3	4	Medium	Good	Medium	3	6	10	1	6,000	5	8	0	1.5	0	0
Baking-T	3.09	10.29	5	0.65	3	4	Medium	Good	Medium	3	6	10	1	6,000	5	8	0	1.5	0	0
Classing-I	1.42	4.75	5	0.30	2	3	Rare	Good	Medium	2	6	10	1	6,000	5	8	0	1.5	0	0
Assembly-I	1.66	5.54	5	0.35	2	3	Rare	Good	Medium	2	6	10	1	6,000	5	8	0	1.5	0	0
Sealing-I	2.85	9.50	5	0.60	3	4	Medium	Good	High	3	6	10	1	6,000	5	8	0	1.5	0	0
Pointer	2.61	8.71	5	0.55	3	4	Medium	Good	Medium	3	6	10	1	6,000	5	8	0	1.5	0	0
Package	0.95	3.17	5	0.20	2	3	Rare	Good	Medium	2	6	10	1	6,000	5	8	0	1.5	0	0
Inspecter	3.09	10.29	5	0.65	3	4	Medium	Good	High	4	6	10	1	6,000	5	8	0	1.5	0	0
Crushing	0.83	2.77	5	0.35	2	3	Rare	Good	High	3	6	6	1	3,600	5	8	0	1.5	0	0

was carried out, as shown in Table 8. Significant correlation was found in this study, indicating that the three models apply to the OHRA of mercury, among which the applicability of GBZ/T 229.2 is the best, followed by the MOM model, and finally ICMM risk rating method.

Discussion

In the comparison of results of on-site surveys in 2019 and 2020, the main changes happened in the renovation of protective facilities, which directly affects the concentration of mercury in the air of workplaces. There were few changes in the use of personal protective equipment and the occupational health management over the 2 years. The analysis was carried out from two dimensions.

From the vertical perspective, the most intuitive change in this dynamic assessment was a significant reduction in on-site mercury concentration. However, from the assessment results of EPA model and ICMM quantitative method of assignment, there was no statistically significant difference in the *RRs* over the 2 years. Environmental Protection Agency model is a comprehensive and quantitative method, and there are several factors involved in the OHRA of mercury, including the concentrations, exposure time, exposure frequency, and working ages, which is suitable for assessing the long-term chronic effects of substances. On one hand, in the comparison of assessment factors of the 2 years, factors except the concentrations remained unchanged, and the concentration had weak influence on the assessment results. On the other hand, The *RfC* used in EPA model is 0.3 $\mu g/m^3$, having a smaller order of magnitude compared to exposure concentration. Under the premise that the mercury concentration decreased significantly, the calculated *HQ* was still large, so the risk level did not change significantly, which reflected the limitations of the model in dynamic assessment during a short period of time with changes in the mercury concentration in the workplaces. What's more, the calculation of the model is based on the IUR and *RfC* of chemicals in the IRIS database in the United States, which cannot be used to assess the occupational health risk of chemicals that are not included in the database.

In the model of ICMM quantitative method of assignment, which was refined based on the ICCM risk rating method, the factor of exposure time was taken into consideration. Similar to the EPA model, the change of the single factor of concentration in a short period of time did not have significant impacts on the evaluation results. What's more, the assignment range of the four parameters varies greatly, which can easily amplify the risk level and reflect the high requirements of occupational health protections in the mining industry. When the assignment of material consequences is large, the risk value can easily exceed the threshold, and the overall assessment result is high. It is recommended to

TABLE 5 Post risk distribution in 2019 and 2020.

Method	Percentage of posts with extremely high risk in 2019	Percentage of posts with high risk in 2019	Percentage of posts with extremely high risk in 2020	Percentage of posts with high risk in 2020
EPA	92%	8%	100%	0
MOM	33%	67%	0	60%
ICMM risk rating method	75%	25%	10%	60%
ICMM quantitative method of assignment	100%	0	100%	0
GBZ/T 229.2	42%	33%	0	0

TABLE 6 *RRs* of exposure to mercury at each position in 2019.

Post	EPA	MOM	ICMM		GBZ/T 229.2
			Risk rating method	Quantitative method of assignment	
Pointer-T	1	1	1	1	1
Classing-T	1	1	1	1	1
Printing-T	1	1	1	1	1
Baking-T	1	0.8	1	1	0.75
Package-T	1	1	1	1	1
Pointer-I	1	0.8	1	1	0.75
classing-I	1	0.8	0.75	1	0.25
Assembly-I	1	0.8	0.75	1	0.25
Sealing-I	1	0.8	1	1	0.75
Package-I	1	0.8	1	1	0.75
Inspecter	1	0.8	1	1	0.75
Crushing	0.8	0.8	0.75	1	0.25

TABLE 7 *RRs* of exposure to mercury at each position in 2020.

Post	EPA	MOM	ICMM		GBZ/T 229.2
			Risk rating method	Quantitative method of assignment	
Classing-T	1	0.8	0.75	1	0.25
Printing-T	1	0.8	0.75	1	0.25
0.75 ng-T	1	0.8	0.75	1	0.25
Classing-I	1	0.6	0.5	1	0.25
Assembly-I	1	0.6	0.5	1	0.25
Sealing-I	1	0.8	0.75	1	0.25
Pointer	1	0.8	0.75	1	0.25
Package	1	0.6	0.5	1	0.25
Inspecter	1	0.8	1	1	0.25
Crushing	1	0.6	0.75	1	0.25

TABLE 8 Results of Spearman correlation analysis.

Method	r_s	*P*
MOM	0.821	0.001
ICMM risk rating method	0.754	0.005
GBZ/T 229.2	0.94	<0.001

adjust the assignment range of the four parameters to refine the division of risk levels when the method was used in other industries. Although the risk level was judged by the specific values, the model was still considered as a qualitative assessment method. At the same time, there is a need for evaluators to extensively review and discuss data to reduce subjective bias.

From the horizontal perspective, *RRs* derived from the three methods applicable to dynamic risk assessment of mercury also differed in their association with occupational exposure. International Council on Mining and Metals risk rating method is based on the actual exposure concentration of the substance, but the effectiveness of the protective facilities and the possibility of exposure depend on subjective judgment. The evaluation parameters are few and the operability is strong, but the stability of the evaluation results needs to be strengthened. The semi-quantitative characteristics of the MOM model can objectively reflect the risk level of the evaluation system. In the calculation process, the exposure level is assigned according to the exposure concentration, which has been widely used in the OHRA of chemical substances. However, it cannot be used for risk assessment of physical occupational hazards such as high temperature and noise. The method of GBZ 229.2 was the most practical in this study, in which the assessment process considered the degree of harm of chemical substances, occupational exposure, and the intensity of manual labor of workers. It was also improved since the *RRs* were obtained after standardizing the grading results regarding foreign methods. Compared with MOM's assignment of exposure level, this method directly used the on-site detection concentration to calculate the classification index, so the *RRs* and occupational exposure correlation in GBZ/T 229.2 are the most significant.

Conclusions

Mercury is an ancient and traditional poison. However, there are still few studies on OHRA of mercury in thermometer manufacturers. In this study, multiple methods were used to carry out the OHRA of mercury. The results showed that the mercury exposure was significantly improved after the renovation of occupational protection facilities, while the EPA and ICMM quantitative method of assignment failed to reflect this change and may not be suitable for the dynamic assessment of occupational health risks of mercury. The model of MOM, ICMM risk rating method, and GBZ/T 229.2 have good applicability in this study, the applicability of GBZ/T 229.2 is the best, followed by MOM, and finally the ICMM risk rating method. What's more, though the working environment has been significantly improved via engineering renovation, it is strongly suggested that the thermometer enterprise conduct more effective risk management covering all production processes to minimize Hg exposure levels and health risk ratings.

This study focused on the occupational health risks of mercury in different years. Sustained attention can be paid to the concentration of mercury exposure in major positions to obtain more data, which can be used to monitor job risk and optimize the existing risk assessment model.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethical Committee of Jiangsu Provincial Center for Disease Control and Prevention (REF JSJK2022-B002-01). The participants provided their written informed consent to participate in this study.

Author contributions

PW and JD participated in the analysis of the data and interpretation of the results and wrote the first draft of the manuscript. XL, HZ, and BZ contributed to the conception and design of the study. YX, LH, ZY, and HZ were involved in the fieldwork, sample collection, and processing. All authors contributed to manuscript revision, read, and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1037915/full#supplementary-material

SUPPLEMENTAL TABLES 1–6
Illustrated the values of the main indexes used in the several OHRA models.

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Evaluation of strategies for the occupational health risk assessment of chemical toxicants in the workplace based on a quantitative analysis model

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Objectives: The commonly used methods for the occupational health risk assessment (OHRA) of chemical toxicants cannot fully meet the needs of practical work. This study evaluated OHRA strategies for chemical toxicants in the workplace by establishing a quantitative analysis model.

Methods: Five typical industries in China that implement OHRA using the six common models (the Environmental Protection Agency, Australian, Romanian, Singaporean, International Council on Mining and Metals, and the Control of Substances Hazardous to Health models) were selected as the research objects. We established a quantitative analysis model to compare the six models and applied it to compare the results obtained using each model and preliminarily analyze the advantages, limitations, and application scope of each method.

Results: The risk ratio (RR) values of the six methods decreased in the following order: $RR_{EPA} > RR_{COSHH} > RR_{ICMM} > RR_{Australia} > RR_{Singaporean} > RR_{Romanian}$ ($P < 0.05$). Among the six models, the Singaporean model had the strongest RR correlation with the other models ($P < 0.01$). The sequence of RRs obtained from the Singaporean, ICMM, Australian, and Romanian models in the five industries was consistent with the sequence of the three inherent risk levels in those industries. Only the Romanian model could distinguish between the RRs of all five industries. The EPA and Singaporean models could effectively distinguish the differences in inherent risk for four hazard factors (manganese and inorganic compounds, benzene, xylene, and ethyl acetate), with the assessment accuracy being relatively higher for the EPA model.

Conclusions: Among the six models, the EPA model had the relatively highest accuracy in assessing chemical toxicants, followed by the Singaporean model. The EPA and Romanian models were strongest in differentiating the differences in toxicity risk. More studies on OHRA methodology are needed.

KEYWORDS

methodology, occupational health, risk assessment, workplace, chemical toxicants

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Introduction

Occupational injuries caused by exposure to chemical toxicants are serious problems worldwide. Globally, air pollution-related diseases kill approximately seven million people each year (1). Over 140 million chemicals are registered in the International Chemical Abstracts Society, and ∼10,000 new chemicals are registered each year (2), making chemical-related occupational injuries complicated. Occupational chemical poisoning has a high fatality rate and can easily result in a public health emergency (3).

At present, the common methods for assessing chemical hazards in the workplace are based on occupational exposure limits (OELs) and threshold limit values (TLVs) from the American conference of governmental industrial hygienists (ACGIH). However, the ACGIH values include only a few hundred chemicals, and values are not available for most chemical toxicants. These methods also depend on the concentration of chemical toxicants in the workplace, which creates problems in cases where the on-site concentrations of chemical toxicants cannot be obtained. Moreover, new chemicals are introduced in industry and commerce much faster than new occupational exposure limits can be established. Due to these technical limitations, assessment methods based on OELs and TLVs are unable to meet the actual work requirements.

Occupational health risk assessment (OHRA) is a comprehensive and systematic identification and analysis of workplace hazards based on the identification and analysis of hazard factors and protective measures in the workplace. OHRA provides a quantitative assessment of the level of occupational health risk that can inform corresponding control measures to supplement existing prevention and control strategies for occupational diseases. In 1983, the National Research Council of the United States first proposed the theory of risk assessment, which divided OHRA into four stages: hazard identification, dose-response relationship assessment, exposure assessment, and risk characterization (4). Since then, various OHRA methods have been promulgated by European and American agencies and international organizations. At present, over 10 OHRA methods are employed worldwide, including qualitative, quantitative, and semi-quantitative methods; among them, the following six are the most common: the United States Environmental Protection Agency (EPA) model (5), the United Kingdom's Control of Substances Hazardous to Health Essentials (COSHH) model (6), the Singaporean model (7), the International Council on Mining and Metals (ICMM) model (8), the Australian model (9), and the Romanian model (10). Based on the EPA, Singaporean, and COSHH models, China launched technical guidelines for the OHRA of chemicals in the workplace (GBZ/T 298-2017).

The OHRA methods have different principles and methodological characteristics due to their different backgrounds, national conditions, and initial fields of application, resulting in model-specific advantages and limitations (11, 12). Little research has been conducted to understand the differences among methods and develop guidance on the appropriate assessment methods for specific poisons or sites. This is because we do not fully understand the theoretical underpinnings, scope of applicability, and classification parameters of the degree of hazard for each method.

To identify a suitable OHRA strategy for chemical toxicants in the workplace, we have studied OHRA methods for nearly 10 years. Through a literature review, we qualitatively compared six commonly used OHRA methods (EPA, COSHH, Singaporean, ICMM, Australian, and Romanian), revealing the strengths and limitations of each method (13), which provide some guidance for our practical work, but they are still not precise enough. In order to evaluate the applicability of each method in practice guidance work, we applied six methods for risk assessment in typical industries in China. We found that using different methods to assess the same hazard often produces inconsistent results (14–19). In order to understand which method is relatively more reliable in assessing the risk of chemical toxicants, we introduced the concept of risk ratio (RR) to compare the assessment results of each method, and used various methods to verify the comparison results. We applied the methodology to over 70 enterprises in seven typical industries (e.g., wood furniture manufacturing, electroplating, crane manufacturing, printing and dyeing, printing, leather products manufacturing and mining) and found that the EPA and Singaporean models exhibited good reliability since they could distinguish the inherent risk of the industry or risk factor and tended to get higher risk levels (20–23). Through the above research, it can be seen that the quantitative comparison framework introduced by RR can be used as a method to evaluate the relative reliability of each method. And the framework that we've created is open, we can develop more reliable validation models and apply them in more and more extensive hazard sites to understand more differences among the models based on solve practical problems.

Chemical toxicants seriously endanger human health. OHRA is an effective way to control the occupational health risk of harmful toxicants in the case of inadequate standards and regulations. Understanding the differences between methods and the scope of application of each method is of great significance for guiding practical work. On the basis of previous research, we selected five typical industries in China (soil sand mining, ferrous metal casting, ship repair, equipment repair, and gasoline station) as the research objects and performed OHRA for exposure to chemical hazards using six OHRA methods (EPA, COSHH, Singaporean, ICMM, Australian, and Romanian). Using the established quantitative analysis model that improved on early-stage qualitative and quantitative analysis model, we discussed the correlation and accuracy of the evaluation results for each method along with the differences among methods. We also preliminarily analyzed the advantages, limitations, and application scope of each method. The results provide a scientific basis OHRA-based occupational health management in countries facing occupational hazards. The findings also provide valuable information for further application and methodological research on OHRA.

Materials and methods

Description of typical industries

Soil sand mining, ferrous metal casting, ship repair, equipment repair, and gasoline station were selected as typical industries for the following reasons. According to the "Management catalog of occupational hazard risk classification of construction projects" issued by the State Administration of Work Safety of China (2012 edition) (24), the inherent risk (IR) for occupational hazards in the soil sand mining and ferrous metal casting industries was classified as "severe." The IR for the ship repair and equipment repair industries was classified as "medium," while that for the gasoline station industry was classified as "low." Thus, these five industries represent a range of IR levels in China (severe, medium, and low IR). Among the five industries, IR for occupational hazards decreases in the following order: IR_{mining} and $IR_{ferrous} > IR_{ship}$, and $IR_{equipment} > IR_{gasoline}$.

A total of 151 enterprises in Zhejiang Province in eastern China were selected as typical enterprises. These included three large enterprises, eight medium-sized enterprises, 29 small enterprises and 111 micro-enterprises (25). A total of ~16,000 workers exposed to hazard factors were involved. Basic information is shown in Table 1.

Identification and detection of hazard factors

The hazard factors and levels of exposure were identified through occupational health field investigations, air sampling, and laboratory testing. Air sampling and laboratory testing were carried out in accordance with the Chinese standard "Specifications of air sampling for hazardous substances monitoring in the workplace (GBZ 159)" and "Determination of toxic substances in workplace air (GBZ/T160 and 300)." Table 1 shows the basic information and levels of exposure to hazard factors (e.g., silicon dust, welding dust, manganese and inorganic compounds, grinding wheel dust, xylene, and iron ore powder) in each industry. The exposure levels of hazard factors at some locations in the soil sand mining, ferrous metal casting, and ship repair industries exceeded the permissible concentration-time weighted average (PC-TWA) permitted by China or the threshold limit values-time weighted average (TLV-TWA) permitted by ACGIH. This was not the case for the equipment repair and gasoline station industries.

Introduction to the six commonly used OHRA methods

The six common OHRA methods (EPA, COSHH, Singaporean, ICMM, Australian, and Romanian) have similar assessment frameworks (22). The main assessment framework is based on the degree of hazard, exposure level, and probability of occurrence and includes hazard identification, hazard characteristic assessment, exposure assessment, and risk description. The detailed principles of the six methods have been reported previously (5–10) and are briefly described below.

(1) EPA method (quantitative evaluation). The EPA inhalation risk assessment consists of two parts: carcinogenic and non-carcinogenic risk assessments. The non-carcinogenic risk assessment was mainly applied in this study and involves two primary steps:

A) Estimating exposure concentration (EC, in $\mu g/m^3$):

$$EC = (CA \times ET \times EF \times ED)/AT \quad (1)$$

where CA ($\mu g/m^3$) is the concentration of hazard factor in the air; ET (h/d) is the exposure time; EF (days/year) is the exposure frequency; ED (years) is the exposure duration; AT [ED (years) × 365 days/year × 24 h/day] is the average exposure time.

B) Non-carcinogenic risk assessment:

The hazard quotient (HQ), which indicates the risk level, is defined as

$$HQ = EC/RfC \times 1,000\ (\mu g/mg) \quad (2)$$

where RfC (mg/m^3) is the reference concentration of inhalation toxicity.

The EPA model can calculate the occupational health risk level of chemical toxicants with relative accuracy, but can only assess the health risk caused by inhalation route, and is limited to chemical toxicants with reference concentration (RfC) and inhalation unit risk (IUR), which can only be retrieved from the EPA website poison database.

(2) COSHH model for qualitative evaluation. In this method, the health hazard levels and exposure levels of chemical substances (solid or liquid) are considered comprehensively, and the control level is provided by a matrix method. The health hazard level of a chemical is determined according to a hazard band using risk phrases or OELs. The exposure level is determined according to the dustiness of a solid or the volatility of a liquid and the scale

TABLE 1 General information and exposure levels of hazard factors in five typical industries.

Industry (*n*)	Location	No. of locations	Hazard factor	Exposure levels by ratio (mean, range) (mg/m^3)	Evaluation by China PC-TWA	Evaluation by ACGIH TLV-TWA
Mining of soil and sand (12)	Rig operator	19	Silicious dust	2.275 (0.186–21.6)	Disqualified	Disqualified
	Excavator driver	26	Silicious dust	0.892 (0.143–2.986)	Disqualified	Disqualified
	Transport driver	25	Silicious dust	1.107 (0.200–3.429)	Disqualified	Disqualified
	Stope inspector	11	Silicious dust	0.989 (0.333–2.186)	Disqualified	Disqualified
	Discharge	15	Silicious dust	2.216 (0.357–10.729)	Disqualified	Disqualified
	Crushing inspector	26	Silicious dust	1.218 (0.186–4.714)	Disqualified	Disqualified
	Forklift driver	15	Silicious dust	0.901 (0.171–4.233)	Disqualified	Disqualified
	Sprinkler driver	11	Silicious dust	0.617 (0.143–0.943)	Qualified	Disqualified
Ferrous casting (17)	Molding	43	Silicious dust	1.372 (0.200–7.200)	Disqualified	Disqualified
	Smelting	6	Other dust	0.158 (0.050–0.363)	Qualified	/
	Casting	20	Silicious dust	0.761 (0.020–1.660)	Disqualified	Disqualified
			Other dust (iron)	0.136 (0.030–0.363)	Qualified	/
	Sand stripping	23	Silicious dust	1.237 (0.150–7.500)	Disqualified	Disqualified
	Shot blasting	5	Silicious dust	5.900 (0.500–13.60)	Disqualified	Disqualified
Ship repairs (11)	Electrowelding	208	Welding fume	1.355 (0.050–7.575)	Disqualified	/
			Manganese and inorganic compounds	0.956 (0.003–28.98)	Disqualified	Disqualified
			Nitrogen oxides	0.013 (0.002–0.038)	Qualified	Qualified
	Polishing	176	Grinding wheel dust	0.618 (0.025–5.378)	Disqualified	/
	Spraying	44	Benzene	0.037 (0.008–0.200)	Qualified	Qualified
			Xylene	1.149 (0.001–12.89)	Disqualified	Disqualified
			Ethyl acetate	0.002 (0.0003–0.031)	Qualified	Qualified
	Sanding	55	Iron-ore dust	1.549 (0.060–5.483)	Disqualified	Qualified
Equipment repair (11)	Electrowelding	12	Welding fume	0.071 (0.025–0.225)	Qualified	/
			Manganese and inorganic compounds	0.027 (0.007–0.073)	Qualified	Qualified
	Polishing	11	Grinding wheel dust	0.032 (0.014–0.074)	Qualified	/
	Paint mixing	3	Benzene	0.05	Qualified	Qualified
			Xylene	0.023 (0.010–0.030)	Qualified	Qualified
			Ethyl acetate	0.0007	Qualified	Qualified
	Spraying	9	Benzene	0.068 (0.008–0.1)	Qualified	Qualified
			Xylene	0.0468 (0.001–0.16)	Qualified	Qualified
			Ethyl acetate	0.001 (0.0004–0.005)	Qualified	Qualified
	Polishing	15	Talc dust	0.127 (0.025–0.525)	Qualified	Qualified
Petrol station (100)	Oiling	100	Ggasoline	0.044 (0.0003–0.491)	Qualified	Qualified
	Oil discharge	100	Gasoline	0.006 (0.0003–0.096)	Qualified	Qualified

ACGIH TLV-TWA, threshold limit values-time weighted average permitted by the American Conference of Governmental Industrial Hygienists; PC-TWA, permissible concentration-time weighted average.

of use. While this method is simple and feasible, it may not always be accurate because it does not consider protection measures or on-site toxicant concentrations.

(3) Singaporean method (semi-quantitative evaluation). The risk level is calculated according to the hazard ratings (HR) and exposure ratings (ER), and the formula is as follows:

$$\text{Risk} = (\text{HR} \times \text{ER})^{1/2} \quad (3)$$

The HR is determined based on carcinogenicity classifications from the ACGIH and the International Agency for Research on Cancer, or on the acute toxicity data of chemicals (LD50 and LC50). The ER is classified according to the ratio of field exposure concentration to occupational exposure limits.

(4) ICMM method (qualitative evaluation). This method comprehensively considers the possible health hazards, probability of exposure, and exposure time. The risk level is determined using a quantitative method or matrix method.

(5) Australian method (qualitative evaluation). In this method, the risk levels are determined manually using a diagram or a calculator based on the likelihood of occurrence, frequency of exposure, and severity of consequences. This method is simple and easy to apply and is suitable for a wide range of assessments (e.g., risk assessments carried out by occupational health management personnel in small- and medium-sized enterprises (26).

(6) Romanian method (qualitative assessment). In this method, the risk level is evaluated using a matrix method based on the severity and probability of consequences resulting from hazard factors. This method can be used to calculate the overall risk level of the workplace and has obvious advantages in comprehensive risk assessment.

Quantitative analysis model

Risk ratio (RR)

The six OHRA methods produced different levels of risk (22). To compare the results of each method, the risk levels obtained using the six methods were converted into RRs for quantitative comparison.

(1) Conversion of risk level: The EPA method produces quantitative data. The output of the COSHH method is control method classification. The risk assessment results of the other four methods are classifications of risk level. Thus, to compare the assessment results among different methods, the EPA non-carcinogenic risk assessment results (HQ) were converted into risk level by referring to the classification standard of exposure concentration of the Singaporean method, which includes five levels. The results of the COSHH method were converted by referring to the risk level of the Singaporean method (Table 2).

TABLE 2 Conversion of risk assessment results for the EPA and COSHH models.

The EPA model		**The COSHH model**	
Hazard quotient (HQ)	**Risk level†**	**Control strategy**	**Risk level‡**
<0.1	1	–	–
0.1–0.5	2	CS1	2
0.5–1.0	3	CS2	3
1.0–2.0	4	CS3	4
≥2.0	5	CS4	5

†Modified based on the classification standard of exposure concentration of the Singaporean model.
‡Modified based on the risk level of the Singaporean model.

(2) RR calculation: After risk level conversion, the results for the six methods were converted to the classification of risk level. The risk assessment results of the EPA, Australian, Singaporean, and ICMM models were divided into five levels, while those of the Romanian and COSHH models were divided into seven and four levels, respectively. The concept of RR was introduced to allow comparison among the risk assessment results of different methods. RR was defined as the ratio of the risk level of an occupational hazard factor assessed by a method to the highest risk level of the model. The RR represents the relative risk level of hazard factors derived from a certain method.

Concentration ratio (CR)

To make the exposure concentration of hazard factors of different positions comparable, CR was defined as the ratio of the exposure concentration of a hazard factor to the OEL of the hazard factor (22). CR represents the relative exposure level of a certain hazard factor in a certain position; thus, CR can be used to compare the exposure levels of different hazard factors or different positions. CR $>$ 1 indicates that the exposure to a hazard factor exceeds the OEL for that factor.

Quantitative analysis

Comparison of RRs among the six OHRA methods

The statistical differences among the RRs evaluated by the six OHRA methods reflect the differences among the evaluation results of the OHRA methods for the same occupational hazard factors.

Correlations among the RRs of the six OHRA methods

The correlations among the RRs obtained by the six methods were statistically analyzed.

Verification of relative accuracy of six OHRA methods

(1) The relative accuracy of the OHRA results obtained using the six OHRA methods in different industries was verified by comparing the consistency in RR values for different industries and inherent risks (IR) levels. Refer to Section "Description of typical industries," for the classification of inherent risks in each industry.

(2) The relative accuracy of the evaluation result of each method was verified by evaluating the consistency in the RRs for different chemical toxicants and IRs. We selected four chemical toxicants (manganese and inorganic compounds, benzene, xylene, and ethyl acetate) to evaluate the accuracy of each method. The IR of a hazard factor depends on its inherent hazardous consequences and exposure probability. The IR increases as the inherent hazardous consequences become more severe and as the exposure concentration increases. In this study, the inherent hazardous consequences of a hazard factor were determined based on the RfC value of the EPA method. A larger RfC indicates less severe inherent hazard consequences. Table 3 shows the RfC values and exposure concentrations for each hazard factor. The IR values of the four hazard factors in the five industries decreases in the following order: $IR_{manganese} > IR_{benzene} \approx IR_{xylene} > IR_{ethyl\ acetate}$.

Statistical analysis

The Kruskala–Wallis H(K) method was used to analyze the RRs and CRs of multiple independent samples. The Mann–Whitney *U* method was used to compare the RR or CR between two independent samples. The correlations between RR values were analyzed by Spearman correlation analysis (abnormal distribution).

Results and discussion

Comparison of RRs among the six OHRA methods

As shown in Table 4, among the six models, the highest RR was obtained by the EPA model [1.0 (0.4–1.0)] followed by the COSHH model [0.8 (0.4–1.0)], the ICMM model [0.8 (0.4–1.0)], the Australian model [0.6 (0.4–0.6)], the Singaporean model [0.4 (0.4–0.6)], and the Romanian model [0.4 (0.3–0.4)]. Thus, the RRs of the six methods decreased in the following order: $RR_{EPA} > RR_{COSHH} > RR_{ICMM} > RR_{Australian} > RR_{Singaporean} > RR_{Romanian}$ ($P < 0.05$). This order is similar but not the same as the previously reported order: (22) $RR_{EPA} > RR_{COSHH} > RR_{Singaporean} > RR_{Australian} > RR_{ICMM}$ and $RR_{Romanian}$ ($P < 0.05$).

The above results show that using different methods to evaluate the same risk produces different risk assessments, and the EPA and COSHH models result in the highest RR values. This may be because the EPA, Singaporean, and COSHH models are relatively objective, while the Australian, ICMM, and Romanian models are more subjective because they rely on the professional knowledge and work experience of evaluators. The EPA model produces a high RR because it evaluates risk using an order of magnitude formula (HQ = EC/RfC). The COSHH model does not consider the field exposure concentration, and the exposure concentration of each hazard factor in this study was less than the standard (CR < 1), resulting in a relatively high RR for this method. The Australian, ICMM, and Romanian methods rely on the experience and subjective judgment of an evaluator along with accurate accident occurrence data. However, the Romanian model has a more detailed rating (seven levels), which may explain why its evaluation results were relatively low (Tables 3, 4).

The results show that the different OHRA methods produce different risk assessment results for the same risk. Among the six OHRA methods, the EPA model is the most sensitive and produces the highest RR values, while the Romanian model results in the lowest RR values.

Correlations among the RRs of the six OHRA methods

Table 5 shows the correlations among the RRs of the six OHRA methods. The RR of the COSHH model was not correlated with those of the ICMM and Romanian models, while correlations were found among the RRs of the other methods. Only the RR of the Singaporean model was positively correlated with those of the other five methods ($P < 0.01$), and the correlation coefficients were relatively greater and positive value. The RRs of the ICMM, Romanian, and Australian models were all positively correlated with each other. In a previous study, we found that the RR of the EPA model was not correlated with those of the COSHH, Romanian, and Australian models, while it was correlated with the RR of the ICMM model; meanwhile, the RR of the Singaporean model was positively correlated with those of the other five methods ($P < 0.01$) (22).

The RRs of the COSHH and EPA models were weakly correlated with those of the other methods, while the RR of the Singaporean model was positively correlated with those of the other five methods ($P < 0.01$). The EPA and COSHH models assess the hazard consequences of hazard factors based on their own unique parameters of hazard factors. The EPA model is based on IUR and RfC, while the COSHH model is based on risk-phrase. However, as

TABLE 3 Quantitative comparison of RRs among the six OHRA models for four hazard factors.

Hazard factors		Manganese and inorganic compounds	Benzene	Xylene	Ethyl acetate
RfC (μg/m^3)		0.05	30	100	3,500
CR [median (range)]		0.21 (0.06–0.62)[a,b,c]	0.05 (0.01–0.05)[a]	0.04 (0.019–0.66)[a]	0.000 (0.000–0.0004)
n		234	56	56	56
EPA	Risk level (range)	5	2–5	2–5	1–1.15
	RR [median (range)]	1.0 (1.0–1.0)[a,b,c]	0.4 (0.4–0.4)[a,b]	1.0 (1.0–1.0)[a]	0.2 (0.2–0.2)
COSHH	Risk level (range)	2	5	2	2
	RR [median (range)]	0.4[c]	1.0[a,b]	0.4	0.4
Singaporean	Risk level (range)	2–4	2–3	1–3	1–3
	RR [median (range)]	0.6 (0.4–0.6)[a,b,c]	0.4 (0.4–0.4)[a,b]	0.2 (0.2–0.6)[a]	0.2 (0.2–0.2)
ICMM	Risk level (range)	3–5	4–5	2–5	1–5
	RR [median (range)]	0.8 (0.6–1.0)[a,b]	0.8 (0.8–0.8)[a,b]	0.4 (0.4–0.8)[a]	0.2 (0.2–0.2)
Australian	Risk level (range)	2–3	3	1.7–2	2
	RR [median (range)]	0.6 (0.4–0.6)[a,b,c]	0.6[a,b]	0.4 (0.4–0.4)	0.4
Romanian	Risk level (range)	3–6	4–6	3–4	1
	RR [median (range)]	0.4 (0.3–0.4)[a,b,c]	0.4 (0.4–0.4)[a,b]	0.3 (0.3–0.3)[a]	0.1

RfC, reference concentration for inhalation toxicity; CR, concentration ratio; n, number of risk levels or RRs for each hazard factor; RR, risk ratio.
[a]$P < 0.05$ compared with petrol station; [b]$P < 0.05$ compared with equipment repair; [c]$P < 0.05$ compared with ship repair.

TABLE 4 Quantitative comparison of RRs among the six OHRA models in five industries.

Industry		Mining of soil and sand	Ferrous casting	Ship repair	Equipment repair	Petrol station	Sum
IR		Severe	Severe	Medium	Medium	Low	/
n		148	97	989	85	200	1,519
EPA	Risk level (range)	/	/	1–5	1–5	/	1–5
	RR [median (range)]	/	/	1.0 (0.4–1.0)[b]	1.0 (0.2–1.0)	/	1.0 (0.4–1.0)[e,f,g,h,i]
COSHH	Risk level (range)	5	2–5	2–4	2–5	5	2–5
	RR [median (range)]	1.0 (1.0–1.0)[b,c,d]	1.0 (1.0–1.0)[a,b,c]	0.4 (0.4–0.8)[a,b]	0.4 (0.4–0.8)[a]	1.0 (1.0–1.0)	0.8 (0.4–1.0)[e,f,g,h]
Singaporean	Risk level (range)	3–5	2–5	1–4	1–3	2	1–4
	RR [median (range)]	0.8 (0.8–0.8)[a,b,c]	0.8 (0.6–0.8)[a,b,c]	0.4 (0.4–0.6)[a]	0.4 (0.4–0.6)[a]	0.4 (0.4–0.4)	0.4 (0.4–0.6)[e,f,g]
ICMM	Risk level (range)	5	4–5	2–5	1–5	1–2	1–5
	RR [median (range)]	1.0 (1.0–1.0)[a,b,c,d]	1.0 (1.0–1.0)[a,b,c]	0.8 (0.6–1.0)[a]	1.0 (0.6–1.0)[a]	0.3 (0.2–0.4)	0.8 (0.4–1.0)[e,f]
Australian	Risk level (range)	3–4	2–4	2–4	2–3	2	2–4
	RR [median (range)]	0.6 (0.6–0.8)[a,b,c]	0.6 (0.6–0.6)[a,b,c]	0.6 (0.4–0.6)[a,b]	0.4 (0.4–0.6)[a]	0.4 (0.4–0.4)	0.6 (0.4–0.6)[e]
Romanian	Risk level (range)	4–6	3–6	3–6	1–6	1	1–6
	RR [median (range)]	0.4 (0.4–0.6)[a,b,c,d]	0.4 (0.4–0.4)[a,b,c]	0.4 (0.3–0.4)[a,b]	0.4 (0.3–0.4)[a]	0.1 (0.1–0.1)	0.4 (0.3–0.4)

IR, inherent risk according to the "Management catalog of occupational hazard risk classification for construction projects" issued by the State Administration of Work Safety of China (2012 edition); n, the number of risk levels or RRs for all hazard factors in each industry; RR, risk ratio.
[a]$P < 0.05$ compared with petrol station; [b]$P < 0.05$ compared with equipment repair; [c]$P < 0.05$ compared with ship repair; [d]$P < 0.05$ compared with ferrous casting; [e]$P < 0.05$ compared with the Romanian model; [f]$P < 0.05$ compared with the Australian model; [g]$P < 0.05$ compared with the ICMM model; [h]$P < 0.05$ compared with the Singaporean model, [i]$P < 0.05$ compared with the COSHH model.

a semi-quantitative method, the Singaporean model has characteristics of both quantitative and qualitative methods, resulting in good RR correlations with the other methods. The Romanian, Australian, and ICMM models are strongly influenced by the evaluator; thus, the differences among the results of these three methods could be reduced if the same evaluator applied these methods at the same time to evaluate the risk.

TABLE 5 Correlations among the RR values of the six OHRA methods.

	RR_{EPA}	RR_{COSHH}	$RR_{Singaporean}$	RR_{ICMM}	$RR_{Australian}$	$RR_{Romanian}$
RR_{EPA}	1.000	–	–	–	–	–
RR_{COSHH}	−0.355*	1.000	–	–	–	–
$RR_{Singaporean}$	0.633*	0.125*	1.000	–	–	–
RR_{ICMM}	0.442*	0.010	0.750*	1.000	–	–
$RR_{Australian}$	0.472*	−0.152*	0.719*	0.815*	1.000	–
$RR_{Romanian}$	0.252*	−0.043	0.696*	0.806*	0.935*	1.000
CR	0.174*	−0.023	0.506*	0.348*	0.443*	0.509*

*P < 0.001.

Since each OHRA method has its principle and methodology, the evaluation results of the methods are not necessarily correlated.

Verification of relative accuracy of six OHRA methods in different industries

Figure 1 and Table 4 quantitatively compare the RRs among the six OHRA methods in the five industries. The EPA model could only assess risk in the ship repairs and equipment repair industries due to the lack of RfC values in the other industries. The sequence of RRs obtained from the Singaporean, ICMM, Australian, and Romanian models in the five industries was consistent with the sequence of the three inherent risk levels in those industries ($P < 0.05$), while the sequences were not consistent for the COSHH model. Only the Romanian model could distinguish the RR values of the five industries.

Most methods could distinguish differences among the industries with different inherent risk levels. This is inconsistent with our previous report in which the sequences of RRs obtained for five industries (leather, wood furniture, printing and dying of cloth or textile, printing on paper, and garment manufacturing) were consistent with the sequence of IR only for the EPA, Singaporean, and COSHH models (22).

The exposure concentration was used to determine the occurrence probability in the EPA, Singaporean, ICMM, Australian, and Romanian models. In contrast, the amount of hazard factor (ML-L-T) was used in the COSHH model, which was more rough than other methods. Compared with previous studies (22) (5,000 employees from 10 enterprises), the results of this study were more representative due to the larger amount of data (16,000 people from 151 enterprises). According to a report on surveillance and OHRA for key occupational diseases in Zhejiang province from 2010 to 2020, among 59 manufacturing sectors, soil sand mining and ferrous metal casting ranked second and fifth in risk level, respectively, while ship repair, equipment repair, and gasoline stations ranked 12th, 38th, and 57th, respectively. This further confirms that most OHRA methods can distinguish differences among industries with different IRs; however, the ICMM, Australian, and Romanian models should be applied simultaneously by the same evaluator.

In the present study, only the Romanian model could distinguish the RRs of the five industries (Table 3). This might be because the assessment results of the Romanian model are divided into seven grades, compared with four or five grades for the other five methods. As shown in Table 3, the EPA, Singaporean, and Romanian models distinguished the RRs of the four hazard factors.

Verification of relative accuracy of the six OHRA methods for different chemical toxicants

Figure 2 and Table 3 quantitatively compares the RRs obtained using the six OHRA methods for the four hazard factors (manganese and inorganic compounds, benzene, xylene, and ethyl acetate). The IR values decreased in the following order: $IR_{manganese} > IR_{benzene} \approx IR_{xylene} > IR_{ethylacetate}$. The EPA and Singaporean models effectively distinguished the IR values among the four hazard factors (manganese and inorganic compounds, benzene, xylene, and ethyl acetate) using the RRs ($P < 0.05$). According to the EPA model, the sequence of RRs for the four hazard factors at work was $RR_{manganese} > RR_{xylene} > RR_{benzene} > RR_{ethylacetate}$ ($P < 0.05$), while that for the Singaporean model was $RR_{manganese} > RR_{benzene} > RR_{xylene} > RR_{ethylacetate}$ ($P < 0.05$). Thus, the EPA and Singaporean models were highly accurate for assessing the inherent risks of chemical toxicants, in agreement with our past findings. We previously found that only the EPA and Singaporean models can effectively distinguish the IR values of xylene and ethyl acetate from the painting process. This may be related to the poor ability of the other four qualitative methods, which do not directly consider on-site exposure concentration, to assess exposure (22).

In this study, the RR values for xylene and benzene estimated by the EPA model were opposite order to those obtained by the Singapore model. The IR values of xylene and

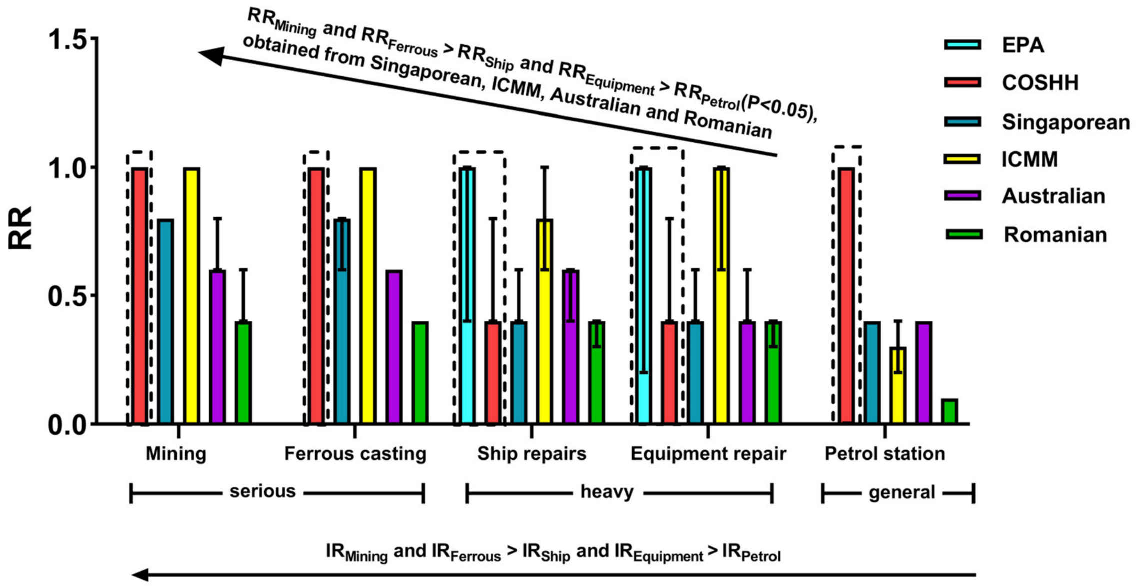

FIGURE 1
Quantitative comparison of RRs obtained for the five industries using the six models [median (interquartile spacing)]. The orders of RRs obtained using the Singaporean, ICMM, Australian, and Romanian models in the five industries were consistent with the orders of the three inherent risk levels in those industries. Only the Romanian model could distinguished the RRs of the five industries.

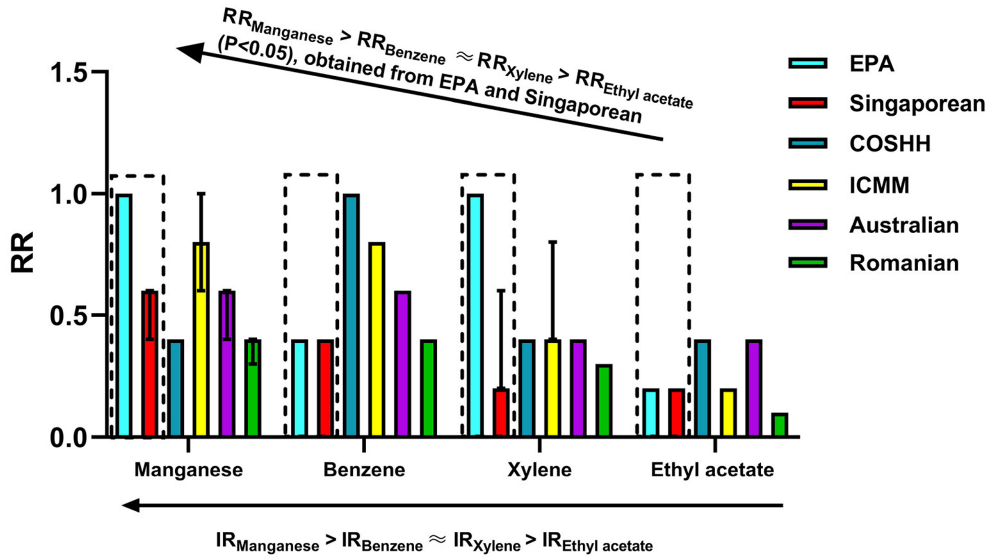

FIGURE 2
Quantitative comparison of the RRs obtained for four hazard factors (manganese and inorganic compounds, benzene, xylene, and ethyl acetate) using the six methods [median (interquartile spacing)]. The IR order of the four hazard factors in the five industries was: $IR_{manganese} > IR_{benzene} \approx IR_{xylene} > IR_{ethylacetate}$. The EPA and Singaporean models effectively distinguished the inherent risks (IRs) among the four hazard factors using the RRs ($P < 0.05$). According to the EPA method, the RRs order of the four hazard factors was: $RR_{manganese} > RR_{xylene} > RR_{benzene} > RR_{ethylacetate}$ ($P < 0.05$), while that for the Singaporean method was: $RR_{manganese} > RR_{benzene} > RR_{xylene} > RR_{ethylacetate}$ ($P < 0.05$).

benzene depend on their inherent hazard consequences and exposure concentrations. The non-carcinogenic hazard posed by benzene is more severe than that of xylene [RfC_{xylene} (100 μg/m^3) > $RfC_{benzene}$ (30 μg/m^3)], while there is no significant difference between $CR_{benzene}$ [0.05 (0.01–0.05)] and CR_{xylene} [0.04 (0.019–0.66)] ($P > 0.05$). According to the risk definition, the non-carcinogenic risk of benzene is slightly higher than that of xylene; however, based on the EPA model, the non-carcinogenic risk of xylene is greater than that of benzene. This discrepancy may be because the EPA model does not assess the health risks of chemical toxicants by simply comparing hazard consequences and exposure concentrations; rather, the EPA model uses the following quantitative assessment formula: $HQ = EC \times 1{,}000/RfC$. Although the statistical analysis [the Kruskala–Wallis H(K) method] failed to distinguish between the exposure concentrations of benzene and xylene, the EPA model could distinguish risk differences between benzene and xylene, which gave a more accurate assessment of the difference in risk, and the results of the EPA model were completely contrary to those obtained by the Singapore model.

Based on the above results, the EPA model is relatively more accurate and sensitive than the Singaporean model in assessing chemical toxicants, especially for those with carcinogenic properties. This conclusion applies only to dust-free chemical poisons and is based on the inherent risk of identifying risk factors at on-site exposure concentrations.

Conclusions

The following conclusions can be drawn based on the findings of this study.

(1) The use of different OHRA methods for the same risk produced different results. Among the six OHRA methods, the EPA model was the most sensitive and produced the highest RR values, whereas the Romanian model resulted in the lowest RR values. Thus, it is necessary to select the appropriate method based on the specific risks and working environments.
(2) Among the OHRA methods, the Singaporean model had the strongest RR correlation with the other methods ($P < 0.01$).
(3) Among the six methods, the EPA model had the relatively highest accuracy in assessing chemical toxicants, followed by the Singaporean model. This conclusion applies only to dust-free chemical poisons and is based on the inherent risk of identifying risk factors at on-site exposure concentrations.
(4) Compared to the other methods, the EPA and Romanian models better differentiated toxicity risk.

Further research is needed in this field. For example, more quantitative comparison methods are needed to explore the advantages and application fields (e.g., comparison of the risks of percutaneous absorbed substances, poisons with and without on-site concentrations, and enterprises of different sizes) of each OHRA method to provide a scientific basis for the OHRA of chemical toxicants in workplaces.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

QX studied the design, collection, analysis of data, interpretation of data, and gave final approval of the manuscript. YC, MZ, HZ, ZZ, LX, WY, HR, PW, and XS contributed to study design, collection, detection, analysis and field investigation, and manuscript writing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

Author LX was employed by Zhejiang Tianlan Environmental Protection Engineering Co., Ltd. Author XS was employed by Zhejiang Jidi Testing Technology Co., Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Occupational health risk assessment methods in China: A scoping review

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Background: Over the decades, many assessment methods have been developed around the world and used for occupational health risk assessment (OHRA). This scoping review integrated the literature on methodological studies of OHRA in China and aimed to identifies the research hot-spots and methodological research perspectives on OHRA in China.

Methods: A scoping review of literature was undertaken to explore the research progress on OHRA methods in China. Focusing on OHRA methods, the authors systematically searched Chinese and English databases and relevant guideline websites from the date of establishment to June 30, 2022. Databases included Web of Science, PubMed, Scopus, the China National Knowledge Internet, WanFang Database. Some other websites were also searched to obtain gray literature. The extracted information included the author, year, region of first author, the target industry, risk assessment model, study type, the main results and conclusions.

Results: Finally, 145 of 9,081 studies were included in this review. There were 108 applied studies, 30 comparative studies and 7 optimization studies on OHRA in China. The OHRA methods studied included: (1) qualitative methods such as Romanian model, Australian model, International Council on Mining and Metals model, and Control of Substances Hazardous to Health Essentials; (2) quantitative methods such as the U. S. Environmental Protection Agency inhalation risk assessment model, Physiologically Based Pharmacokinetic, and Monte Carlo simulation; (3) semi-quantitative methods such as Singapore model, Fuzzy mathematical risk assessment model, Likelihood Exposure Consequence method and Occupational Hazard Risk Index assessment method; (4) comprehensive method (Chinese OHRA standard GBZ/T 298-2017). Each of the OHRA methods had its own strengths and limitations. In order to improve the applicability of OHRA methods, some of them have been optimized by researchers.

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Conclusions: There is a wide range of OHRA methods studied in China, including applied, comparative, and optimization studies. Their applicability needs to be further tested through further application in different industries. Furthermore, quantitative comparative studies, optimization studies, and modeling studies are also needed.

KEYWORDS

occupational health, risk assessment, qualitative, quantitative, semi-quantitative, scoping review

Introduction

China is the most populous country in the world with a population of 1.41 billion, of which more than 783 million are workers, and more than 200 million workers are exposed to occupational hazards (1, 2). China has carried out a series of strategies and measures to reduce the health risk of occupational hazards exposure. However, occupational health in China still faces severe conditions and challenges (3). In 2021, China's National Health Commission (NHC) reported a total of 15,407 new cases of various occupational diseases nationwide (4). Occupational pneumoconiosis, noise-related hearing loss, and occupational poisoning have become the most serious occupational diseases in China (4, 5). In China, occupational diseases come from more than 30 industries, including traditional industries such as coal mining, non-ferrous metal mining, metallurgy, machinery, construction and chemical industry, and new industries such as computer and information technology, biology and medicine (3). Occupational diseases are reported in all provinces in China, but there are differences in distribution between different regions, for example, occupational tumors are predominant in Guangdong, Shandong, Liaoning, Hubei, Beijing, and Jiangsu (6), while chronic benzene poisoning is predominant in Guangdong, Jiangsu, Shandong, Beijing, Tianjin, Fujian, Zhejiang, and Sichuan (7, 8). Like many countries, China faces the important task of occupational health risk management in order to reduce the impact of occupational hazards. Occupational health risk assessment (OHRA) is an important part of occupational health management. Understanding how much exposure to a hazard poses health risks to workers is important to appropriately eliminate, control, and reduce those risks (9). The "Law on Prevention and Control of Occupational Disease," which approved by the Chinese National People's Congress Standing Committee in 2002 and recently modified in 2018, stipulates that occupational health risk assessment is one of the tasks of the health administrative department in China (10).

Risk assessment is a process that aims to identify what hazards exist in the workplace and evaluating the possibility of personal injury or harm caused by these hazards. The purpose of risk assessment is to determine and propose corresponding preventive and control measures (11). OHRA is a process of qualitatively or quantitatively evaluating occupational health risk levels by comprehensively and systematically identifying and analyzing risk factors and protective measures in the workplace, so as to take corresponding controls (12). The use of risk assessment methods to evaluate the effects of toxic chemicals had its primary origin in 1976 when the U.S. Environmental Protection Agency (EPA) (13) adopted a methodology introduced in the 1950s to conduct the evaluation of suspect carcinogens (14, 15). In 1983, the U.S. Nuclear Regulatory Commission (16) first proposed that the risk assessment process is divided into four stages: hazard identification, dose-response assessment, exposure assessment and risk characterization (16). Since then, the risk assessment techniques and methods for health risks caused by hazardous substances have been widely used. Subsequently, the U.S. EPA established a series of risk assessment guidelines, such as the supplemental inhalation risk assessment guidelines of the Human Health Risk Assessment Manual, to provided technical guidance for the risk assessment of airborne toxic chemicals in the workplace (13).

Meanwhile, some European countries, Australia, Singapore, and other countries and organizations established guidelines for OHRA and risk management in response to occupational hazards in the workplace. For example, the United Kingdom Health and Safety Executive initiated the Control of Substances Hazardous to Health (COSHH) essentials control banding strategy (17); Australia has established risk management methods in Australian Standards (AS/NZS) (18); Romania established the risk assessment method for occupational accidents and diseases with reference to European standards (EN292/1-19, EN 1050/96) in 1998 (19); Singapore established guidelines for the hazard assessment of occupational chemical exposures for hazardous chemicals (20).

China established a classification standard for hazardous operations in the 1980s and started health risk assessment research by introducing the USEPA models in the nuclear industry field (12). In the first decade of OHRA study, the health risk assessment technology in China is mainly based on the four-step process recommended by the USEPA, focusing on monitoring of exposure and epidemiological study (21). In 2007, the "Technical Guidelines for Pre-Assessment of Occupational Disease Hazards in Construction Projects" (GBZ/T196-2007) promulgated by the Chinese Ministry of Health proposed that the risk assessment methods should be applied to the assessment of occupational disease hazards in construction projects (22). In 2010, the Chinese Ministry of Health issued standards such as "Classification for Hazards of Occupational Exposure to Toxicant" (GBZ 230-2010) and "Classification of Occupational Hazards at workplaces" (GBZ/T 229-2010) to rank hazard levels from exposure to productive dust, chemical toxicants, heat and noise (23, 24). Due to the lack of OHRA method in China, the GBZ 230-2010 and GBZ/T 229-2010 were sometimes used as an alternative to occupational health risk assessment, although the results are often not accurate enough due to the low sensitivity of the method.

In recent years, Chinese government has paid more and more attention to occupational health risk assessment. Researchers in China have applied some international risk assessment methods for occupational health risk assessment in various industries (21). At the same time, some researchers improved and optimized the OHRA tools introduced from abroad, and established the first Chinese OHRA standard "Guidelines for Occupational Health Risk Assessment of Chemicals in the Workplace" (GBZ/T 298-2017) (25), which recommends a quantitative risk assessment method, a qualitative risk assessment method and three semi-quantitative risk assessment methods. As China's first OHRA guideline, researchers have carried out applied studies on it in different industries soon after it was released (26, 27). The application of OHRA methods in GBZ/T 298-2017 shows that it still needs further improvement and needs to be complemented by other risk assessment methods (28). There are numerous risk assessment methods internationally, and Chinese scholars have conducted a lot of research on various OHRA methods (12, 29, 30). Nevertheless, it is still not clear what kinds of OHRA methods are currently being applied for occupational health risk assessment studies in China, what types of methodology studies on OHRA tools are conducted by Chinese researchers, and how applicable these methods are in OHRA in the workplaces. To further understand the progress of research on OHRA methodology in China, an aggregation and generalization of these OHRA methodological studies needs to be carried out. Therefore, we conducted this scope review to summarize the methodological researches on OHRA methods in China to provide information for future research on OHRA and occupational health risk management in China.

Methods

Study design

A scoping review was conducted to explore the research progress on OHRA methodology in China. The review proceeded five stages according to a scoping review method developed by Arksey and O'Malley (31), extended by Levac et al. (32), and further modified by Westphaln et al. (33). This scoping review provides an overview of the existing evidence on studies focus on OHRA methodology in China without a formal assessment of the methodological quality. The steps of the scoping review are: (1) identifying the research question; (2) identifying relevant literature; (3) selecting studies; (4) charting the data; and (5) collating, summarizing, and reporting the results. In order to enhance the quality of this scoping review, it was conducted and reported in accordance with the checklist of Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) (34, 35).

Research questions

Specific research questions of this scoping review were:

- What kinds of OHRA methods are currently involved in OHRA methodology studies in China?
- What types of studies have been conducted on these OHRA methods by Chinese researchers?
- What are the strengths, limitations and applicability of these OHRA methods?

Search strategy

Focusing on OHRA methods, the authors systematically searched Chinese and English databases and relevant guideline websites from the date of establishment to June 30, 2022. Databases included Web of Science, PubMed, Scopus, the China National Knowledge Internet, WanFang Database. Search terms were developed based on three main concepts of "occupational health," "risk assessment," and "methods," restricted to studies conducted in China and the language of literature were in Chinese or English. We selected synonyms, Medical Subject heading (MeSH) terms, and additional keywords and altered the final search string to match the syntax requirements of each database. The detailed search strategies for the respective databases were shown in Supplementary Table 1. Retrieved articles were initially reviewed by the title and the abstract to find potentially relevant studies and exclude irrelevant ones. Reference lists of relevant articles were reviewed to identify possible additional papers. We also searched additional web-based platforms such as Google and Baidu, as well as some government websites, university homepages and other websites in June 2022 to obtain relevant gray literature.

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Inclusion and exclusion criteria

Search results were screened in a reference manager by two reviewers (LZ and PX) to reduce bias and full-text screening was conducted only by the first author. Publications unrelated to the domain of this research were removed based on a review of their titles and abstracts. Unqualified records were excluded based on the exclusion criteria. The full text of article was retrieved and reviewed for more clarity if it was not satisfactorily removed based on the information available in title and abstract. Disagreements were resolved by including the articles in an in-depth analysis and discussion involved by the third reviewer (YZ).

Inclusion criteria of the study were as follows:

- Studies conducted with the working population in China.
- Methodological studies on OHRA methods.
- Studies published in English or Chinese.
- Peer-reviewed articles, gray literature (conference proceedings, thesis, government documents, and professional publications) explaining OHRA.

Exclusion criteria of the study were as follows:

- Literature for which full text was not available, if the key information we need was not available from the abstract.
- Letters to editors, editorials, short briefs, reviews, and study protocols.
- Literature that did not describe methodological issues on OHRA such as application, comparative, optimization, or modeling.
- Although the authors of the literature were Chinese, the workplaces studied were not in China.
- The focus of the article was outside the scope of this review.

Data charting and analysis

Four researchers (FW, JZ, SW, and YH) were involved in data extraction and attended a training workshop focused on developing consistency across researchers by practicing the skills needed to reliable data extraction using a web-based form. To improve the accuracy of the literature information extracted, each researcher was randomly assigned to the same number of included publications, followed by an exchange review of the extracted information. Any disagreement was discussed and finalized by the four researchers to determine a unified opinion. A researcher (LZ) reviewed the extracted data for all the records included. The extracted information included year of publish, region of the institution of first author, type of study, OHRA tools involved, industries and types of hazardous if applicable, main results, strengths and limitations of OHRA methods, and main conclusions of the literature. A summary of the extracted data is available in Supplementary Table 2. The year of publication, the region of the researcher, the type of study, the type of hazard factors that each OHRA model can assess for the included literature were analyzed. The types of study included applied study, comparative study, and optimization study. Applied study is the practical application of occupational health risk assessment methods in one or more industries, with a description of the methodological characteristics. Comparative study focuses on the methodological principles, evaluation scope, strengths and limitations, and applicability of two or more OHRA methods to find the differences between the methods. Optimization study is conducted to optimize or improve one or more well-established OHRA methods and to compare the methodologies before and after the improvements.

Results

A total of 6,889 relevant non-duplicate records were identified from 9,081 records searched. After applying exclusion criteria, 253 articles were retrieved eligible for full-text screening, of which 145 records met inclusion criteria and were finally included for the review. The results of literature search by the two reviewers were generally consistent, except for disagreements on nine papers, which were resolved in discussion involved by the third reviewer. Figure 1 provides a summary of the PRISMA flowchart.

Characteristics of studies included in this review

Table 1 shows that this review included 145 studies focusing on OHRA methodologies in China, most of which ($n = 105$, 72.4%) were published in 2018 and later. There were 108 applied studies, 30 comparative studies and seven optimization studies. There were 12 OHRA methods included in this review, including four qualitative methods, four quantitative methods, three semi-quantitative methods, and a comprehensive method. The most covered OHRA methods were the "Good Practice Guidance on OHRA" developed by the International Council on Mining and Metals (ICMM model), GBZ/T 298-2017, the "Semi-quantitative Method to Assess Occupational Exposure to Harmful Chemicals" (Singaporean model), the "Supplementary Guidelines for Inhalation Risk Assessment in Part F of the US Environmental Protection Agency's Risk Assessment Guidelines" (USEPA model), and the "Occupational Hazard Risk Index Evaluation Method" (OHR Index model). As shown in Figure 2, among the included literature, research institutions in Guangdong ($n = 38$, 26.2%) carried out the largest number of studies on OHRA, followed by Zhejiang ($n = 25$, 17.2%) and Beijing ($n = 23$, 15.9%).

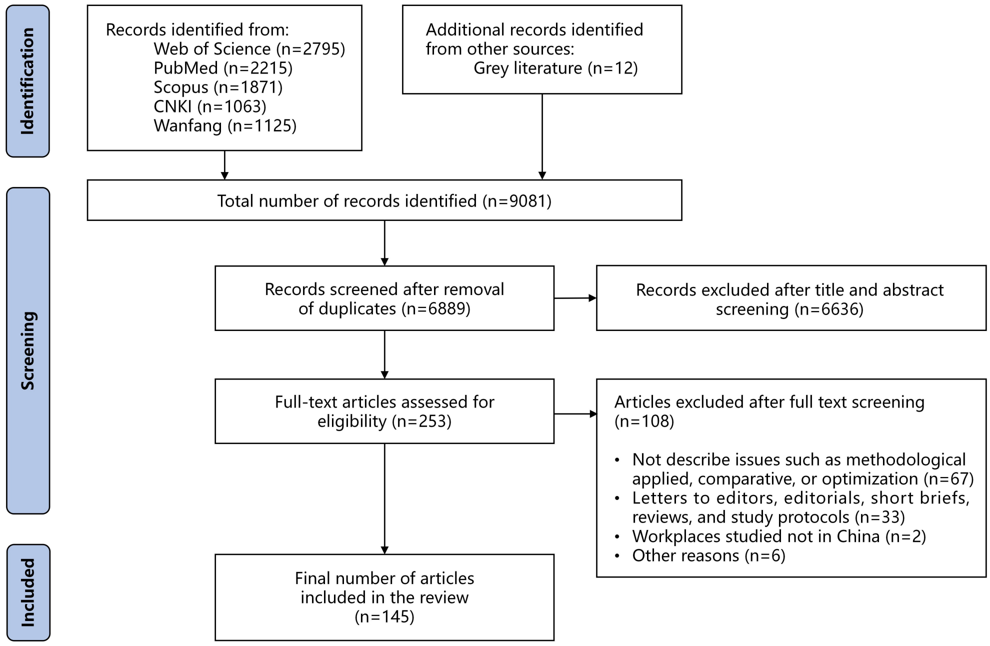

FIGURE 1
The PRISMA flowchart of this scoping review.

Classification of OHRA methods in China

Over the decades, Chinese researchers have introduced some international risk assessment guidelines, from which have been applied and technically innovated in OHRA and promoted nationwide. Similar to the core principles of internationally used risk assessment models, most of the OHRA methods in China are based on hazard level, exposure level and probability of occurrence, and can be classified as qualitative, quantitative and semi-quantitative.

Qualitative OHRA methods

Qualitative occupational health risk assessment methods studied in China were mainly: (1) the "Risk Assessment Method for Occupational Accidents and Diseases" (Romanian model) developed by the Ministry of Labor and Social Protection in Romania (19); (2) the "Occupational Health and Safety Risk Assessment and Management Guideline" (Australian model) formulated by University of Queensland in Australia (18); (3) the ICMM model (36); and, (4) the "Control of Substances Hazardous to Health Essentials" (COSHH model) formulated by the United Kingdom Health and Safety Executive (17).

The Romanian model assesses the most severe consequences on the human body and probability of occurrence of risk factors in the workplaces, and determines the risk levels based on the combination of severity-likelihood levels (19). The Australian model uses a risk assessment calculator consisting of several connecting lines to determine the risk levels based on the likelihood of an outcome, the frequency of exposure and the severity of the outcome (18). The ICMM model comprehensively considers factors such as possible health consequences, exposure probability and exposure time, and determines the risk levels by the quantitative assignment method or matrix method. The quantitative assignment method of the ICMM model is used in the situation where the monitoring results of occupational disease hazards in the workplace do not exist, and the matrix method is used in the situation where the monitoring results exist (36). The COSHH model identifies the hazard level of chemicals according to the hazard term or occupational exposure limits (OEL), determines the exposure level according to the dustiness or volatility and usage, and then reaches the risk level and corresponding control measures according to the hazard level and exposure level (17).

Quantitative OHRA methods

In China, the most widely studied quantitative occupational health risk assessment method was the USEPA model (13). This risk assessment model can evaluate both of the carcinogenic and non-carcinogenic risks of a variety of chemicals with reference concentration (RfC) and inhalation unit risk (IUR) in the U.S. EPA website. Some Chinese researchers applied Monte Carlo simulation to OHRA as a complement to the USEPA model, especially in parametric uncertainty studies (37). Monte Carlo simulation is usually used to deal with the uncertainties

TABLE 1 General characteristics of included studies.

	Number	%
Year of publication		
Before 2018	40	27.6
In or after 2018	105	72.4
Type of study		
Application study	108	74.5
Comparative study	30	20.7
Optimization study	7	4.8
Classification of OHRA methods		
Qualitative	4	33.3
Quantitative	3	25.0
Semi-quantitative	4	33.3
Comprehensive	1	8.3
OHRA methods*		
ICMM model	33	35.2
GBZ/T 298-2017	35	33.8
Singaporean model	30	31.0
USEPA model	24	22.1
OHR index model	16	15.2
Romanian model	7	11.0
Australian model	6	7.6
COSHH model	2	4.1
LEC model	4	4.1
Fuzzy model	4	3.4
Monte Carlo simulation	4	3.4
PBPK model	2	2.1

*Since a study may involve more than one OHRA method, the sum of the individual methods exceeds the total number of studies.

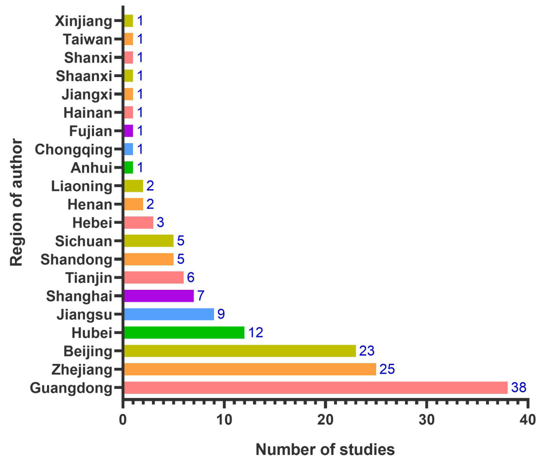

FIGURE 2
Region distribution of included studies based on the institutions of the first authors.

associated with risk-related problems (38). It extrapolates population metrics based on sampling results to provide a quantitative approach to assessing the probability distribution of health risks. The Physiologically Based Pharmacokinetics (PBPK model) was also studied in China (39). The principle of the PBPK model is to construct a differential equation of mass conservation of chemical substances in the body, which requires the collection of various physiological parameters, partition coefficients, metabolic parameters, and absorption parameters. PBPK model was mainly used in researches such as chemical safety evaluation, drug metabolism analysis and new drug research and development, and are also used in health risk assessment of carcinogens (40).

Semi-quantitative OHRA methods

The "Semi-quantitative Method to Assess Occupational Exposure to Harmful Chemicals" (Singaporean model) established by the Ministry of Manpower of Singapore was the most widely used and researched semi-quantitative OHRA method in China (20). Other semi-quantitative OHRA methods studied in China included the fuzzy mathematical model (Fuzzy model), likelihood exposure consequence (LEC) model, and the "Occupational Hazard Risk Index Evaluation Method" (OHR Index model) (28, 41).

Risk levels in Singaporean model are calculated based on hazard ratings (HR), which is assigned based on the carcinogenicity classifications established by the American Conference of Governmental Industrial Hygienists (ACGIH) and the International Agency for Research on Cancer (IARC), and exposure ratings (ER), which is based on the ratio of the exposure level and OEL (20). The fuzzy mathematical model establishes a mathematical model according to the fuzzy mathematical membership theory: $B = A \times R$. B is the total evaluation score, which is divided into excellent, good, general, poor, and very poor; A is the weight distribution set; R is a fuzzy matrix, which consists of monitoring values of occupational hazards (42). The LEC model uses the product of the index values from three factors related to occupational health to evaluate the health risk of workers (which refers to Danger, D). $D = L \times E \times C$, where D is the health risk; L is the possibility of the occurrence of the hazard; E is the frequency of the worker's exposure to the hazard; C is the possible consequence of the occurrence of the hazards (43, 44). The OHR Index model was established by Lin et al. (45) on the basis of the British occupational health and safety management system and the American occupational exposure assessment management strategy. The core principle of this method is that the risk index is the comprehensive calculation result of the health effect level, the exposure ratio and the operating condition level.

Chinese OHRA standard GBZ/T 298-2017

The GBZ/T 298-2017 is a comprehensive risk assessment guideline, including a qualitative model modified according to the COSHH model, a quantitative model modified according to the USEPA model, and semi-quantitative methods modified according to the Singapore model (25). The RfC and IUR values of some chemicals are provided in the quantitative assessment model in GBZ/T 298-2017. The semi-quantitative quantitative models in GBZ/T 298-2017 are exposure limit ratio method, exposure index method and comprehensive index method. The exposure limit ratio method and exposure index method basically follow the Singapore model. The exposure level of the comprehensive index method needs to consider the factors of chemical concentration in the air, physical and chemical properties, usage, exposure time and control measures (including engineering protection, personal protective equipment, emergency rescue measures and occupational health management) (28).

Types of OHRA methodological studies in China

Applied studies

Applied research is mainly to apply one or more OHRA models to assess occupational health risks in one or more industries to find the applicability, strengths and limitations of the applied OHRA methods in specific industries. Researchers in China have used all of the above qualitative, quantitative and semi-quantitative OHRA methods to conduct applied studies on different types of occupational hazards in various industries, so as to explore the feasibility of applying these methods to occupational health risk assessment. For example, the results of applied research of Romanian model in precious metal smelter industry (46) and fluorescent lamp manufacturing industry (47) showed that although it is subjective and the possibility of consequences is not easy to determine, it could be used for OHRA of these industries. Huang et al. (48) applied the Singaporean model to assess the occupational health risk caused by chemicals in a dyestuff factory and found that this method is applicable and effective for OHRA.

Comparative studies

A comparative study compares the results of two or more OHRA models on occupational health risks in one or more industries. By qualitatively or quantitatively comparing the evaluation results of different methods, the differences in reliability and consistency between the methods as well as the strengths and limitations of methods can be drawn, which can provide a reference for the selection of OHRA methods (49). Xu et al. (30) compared the assessment results of six common occupational health risk assessment models (i.e., ICMM model, Singaporean model, USEPA Model, Romanian model, Australian model, and COSHH model) in leather, wooden furniture manufacturing, printing and dyeing, printing, and garment manufacturing industries. The results of this comparative study implied that the order of risk ratios (RR) between the six models was: EPA > COSHH > Singaporean > Australian > Romanian and ICMM; the USEPA model and Singaporean model had higher reliability; the USEPA model was relatively independent in methodology; the Singaporean model had the strongest correlation with other models; and combination of different methodologies could be a strategy for OHRAs. Tian et al. (29) conducted a comparative study on six types of OHRA models by expert consultation, literature summarization and key informant interviews, over-grading conversion and introduction of risk ratios to compare the consistency and correlation between the methods.

Optimization studies

The aim of an optimization study is to improve or optimize the commonly used risk assessment model, and use the optimized assessment model for occupational health risk assessment, and then evaluate the optimized model. The optimization studies carried by Luan et al. (50) and Gao et al. (51) provided ideas for the formulation of the semi-quantitative method in the GBZ/T 298-2017 in China, which considered the impact of engineering protection, personal protective equipment, emergency rescue and occupational health management on health risks compared with the Singaporean model (28). Luan et al. (50) added occupational health management and engineering control measures to improve the hazard level and exposure level evaluation of the Singaporean model and then applied the optimized model to the furniture manufacturing enterprises for occupational health assessment. The improved risk assessment model not only retained the strengths of the Singapore model, but also increased the risk assessment of physical factors. Zhang et al. (52) also built a new evaluation index based on four OHRA models to evaluate the risk of the hazards between industries.

Strengths and limitations of OHRA methods

We extracted the assessment scope, strengths and limitations of all the OHRA methods included in this scoping review. The ICMM model, OHR Index model, Romanian model, Australian model, LEC model, and Fuzzy model can be applied to assess the occupational health risk caused by chemicals, physical factors, and dust. The Singaporean model, COSHH model, the GBZ/T 298-2017, Monte Carlo simulation, and PBPK model can be used to assess health risks from chemicals and dust, while USEPA Model can only assess the health risks caused by specific

TABLE 2 Qualitative comparisons between OHRA models.

Model	Classification	Scope	Strengths	Limitations
ICMM model	Qualitative	Chemicals, physical factors, and dust	1. Broad scope 2. Application to various industries	1. Rely on subjective judgment 2. Has a possibility of overestimation
GBZ/T 298-2017	Comprehensive	Chemicals and dust	1. A combination of qualitative, quantitative and semi-quantitative methods 2. Suitable for different scenarios	1. Only considering exposure through inhalation 2. Cannot evaluate risks caused by physical factors
Singaporean model	Semi-quantitative	Chemicals and dust	1. Usage of exposure index method when air monitoring data are missing 2. High consistency with other methods	1. Relatively crude classification in terms of exposure index 2. Cannot evaluate risks caused by physical factors
USEPA Model	Quantitative	Chemicals	1. Quantitative assessment for the carcinogenic and non-carcinogenic risks 2. Scientific values of RfC and IUR based on epidemiological or toxicological data	1. Limited to chemicals with IUR and RfC values 2. No consideration for personal protective equipment 3. Difficult to differentiate multiple risk level
OHR Index model	Semi-quantitative	Chemicals, physical factors, and dust	Broad scope and easy to conduct	Rely on subjective judgment to get working condition grades
Romanian model	Qualitative	Chemicals, physical factors, and dust	1. Broad scope 2. Calculation of total risk level	1. Rely on subjective judgment 2. Difficult to judge the probability of a consequence occurring
Australian model	Qualitative	Chemicals, physical factors, and dust	1. Broad scope and easy to conduct 2. Appropriate for middle- and small-sized businesses	1. Rely on subjective judgment 2. Requirement of professional knowledge
COSHH model	Qualitative	Chemicals and dust	1. Simple and easy to conduct 2. Focus on middle- and small-sized businesses 3. To provide control measures	1. Overestimation of risk levels 2. Occurrence of bias when judging liquid volatility
LEC model	Semi-quantitative	Chemicals, physical factors, and dust	Broad scope and easy to conduct	Rely on subjective judgment
Fuzzy model	Semi-quantitative	Chemicals, physical factors, and dust	1. Has a wide range of application 2. Highly consistent with the evaluation results of the Singaporean model	Need data processing, not easy to conduct
Monte Carlo simulation	Quantitative	Chemicals and dust	Quantitative calculation, relatively objective	Not easy to conduct and limited scope
PBPK model	Quantitative	Chemicals and dust	Estimate internal exposure agent, relatively objective	Not easy to conduct and limited scope

chemicals. Each method has its own strengths and limitations due to different evaluation principles, as shown in Table 2.

Discussion

Risk assessment of health risk is increasingly important to efficiently prevent and manage occupational diseases in the workplace. This scope review aimed to summarize the methodological studies on occupational health risk assessment methods in China. By searching major international and Chinese databases and relevant websites, we extracted 145 of the 9,081 searched papers that met the inclusion and exclusion criteria for this scoping review. Research on OHRA methodologies in China has increased significantly over the past 5 years, with most of the included studies published in 2018 and later. The regional distribution of first authors indicated that research institutions in Guangdong, Zhejiang and Beijing showed the highest interest in OHRA methodological research. The number of industrial enterprises and the level of economic development in these three regions are relatively developed within China (1).

The OHRA methods studied in the included literature were the ICMM model, GBZ/T 298-2017, the Singaporean model, the USEPA model, the OHR Index model, the Romanian model, the Australian model, the COSHH model, the LEC model, the Fuzzy model, the Monte Carlo simulation, and the PBPK model, ranked according to the number of studies. Researches on some of these methods has also been employed in other countries. American researchers have studied the USEPA model in the assessment of health risks of asbestos exposure and analyzed the strengths and limitations of the assess procedure (53). Golbabaei et al. (49) applied the Singaporean model to assess health risks of exposure to gases released by welding processes in natural gas transmission pipelines industry in Iran. In the U.S., Clewell et al. (54) described the process of the PBPK model development and highlighted issues related to the specification of model structure and parameters, model evaluation, and consideration of uncertainty in environmental and occupational risk assessment. Monte Carlo simulation was carried out to assess health risk of occupational exposure to heavy metals in a steel casting unit of a steelmaking plant in Iran (55).

OHRA methodological studies in China were mainly focused on applied studies, followed by comparative studies. The applied studies found that OHRA methods developed by different countries or international organizations had different principles and methodological characteristics (48, 56–63). Likewise, Mumtaz et al. (64) applied the PBPK model in some selected examples of environmental and occupational exposure assessments of chemicals and their mixtures to discuss the applicability of PBPK model in the U.S. The strengths, limitations and applicability of OHRA methods could be observed not only by carrying out applied studies, but also by conducting comparative studies (28–30, 65–67). Similar to the Chinese researchers, scholars in South Korea have also conducted a comparative study on a qualitative risk assessment method improved based on the COSHH model and a quantitative assessment improved based on USEPA model to evaluate health risks caused by 36 kinds of hazardous substances requiring management (68). In Iran, the results of a comparison study on health risk assessment on occupational exposure to styrene in a petrochemical industry using the USEPA model and the Singaporean model implied that the estimated health risk of exposure to styrene was higher in the EPA model than in the Singaporean model (69). Only a few studies included in this review were methodological optimization studies (45, 50–52, 70–72), which were conducted to improve the OHRA methods and provide insights for establishing OHRA methods suitable for the workplace in China. Optimization studies on OHRA methods have also been attempted in other countries. Ji et al. (73) in New Zealand revised the conventional risk assessment methods into a comprehensive risk assessment method with consideration of both safety accidents and chronic health issues, providing a way to include long-term health outcomes in OHRA.

The studied OHRA methods were divided into quantitative, semi-quantitative and qualitative methods, as well as a comprehensive method (i.e., the first OHRA guideline GBZ/T 298-2017 in China) that included a quantitative model, a qualitative model and three semi-quantitative models. Through this scoping review, we identified that various international and Chinese occupational health risk assessment methods have their own strengths, limitations and application scopes. The ICMM model, the OHR Index model, the Romanian model, the Australian model, the LEC model, and the Fuzzy model have the broadest range of assessments scope. These methods can be used to assess occupational health risks caused by nearly all kinds of hazards in various industries, though some of them may relatively rely on subjective judgment (42, 56, 63, 70, 74–76). Although the Singaporean model, the COSHH model, and the qualitative and semi-quantitative assessment models in GBZ/T 298-2017 cannot assess health risks caused by physical factors, they are simple and easy to operate, and are especially suitable for rapid assessment (26, 75, 77–79). The USEPA Model, the Monte Carlo simulation, and the PBPK model are objective methods, although the calculation processes are relatively complex, and the application scopes are limited (37, 39, 65, 80, 81).

Thus, there may not be a single model for a comprehensive risk assessment for all workplaces in all industries. Before applying them to OHRA in workplace, it is necessary to comprehensively consider the characteristics and evaluation principles of the methods and then choose a suitable OHRA method or combine multiple OHRA methods according to the characteristics of the workplaces (82, 83). Applicability of methodology is one of the most important issues that occupational health workers need to think deeply about. The Chinese occupational health risk evaluation standard GBZ/T 298-2017 has just been developed for 5 years and needs further improvement (27, 78, 84). Liang et al. (85) compared the results of four methods including GBZ/T 298-2017 to evaluate the risk of chemicals in the electrical appliance manufacturing industry. The result revealed that the quantitative method of GBZ/T 298-2017 may overestimate the health risk of chemicals. Tian et al. (78) carried out OHRA in battery manufacturing industries and indicated that the GBZ/T 298-2017 had several limitations, such as just considers exposure through inhalation route, cannot assess occupational health risks from physical factors, and the hazard classification of dust and chemical toxicants in semi-quantitative methods needs to be further refined. Therefore, it is necessary to strengthen the research on occupational health risk assessment methodology, and to establish and promote scientific, reasonable and operational occupational health risk assessment methods in line with China's national conditions in the future.

Using the established process outlined by Arksey and O'Malley (31) for conducting a scoping review, and reporting the results consistent with the PRISMA-ScR checklist, enhances the rigor and transparency of our review design, and trustworthiness of the results. We also anticipate that this review will provide insights for researchers focusing on OHRA methodological research. Probable limitations of this study must also be considered. Consistent with the limitations of the scope review, we did not systematically assess the methodological quality of the included studies in our review; however, this is a potential avenue for future systematic reviews and meta-analyses. Additionally, given the conceptual ambiguity regarding implementation outcome terminology (e.g., the multiple ways in which researchers define and discuss 'Applicable'), some literature that include OHRA methodological study may be excluded.

Conclusion

The results of this scoping review indicated that occupational health risk assessment methodological research in China has been very popular in recent years. The most common OHRA methodological studies in China were applied studies, with some comparative studies and limited optimization studies. There are several types of OHRA methods studied, including qualitative, quantitative and semi-quantitative methods, as well as a comprehensive guideline proposed in China. Since each method has its strengths and limitations, the application of OHRA methods in occupational health risk assessment requires comprehensive consideration. At the same time, researches on the application of OHRA methods in more industries, quantitative comparative studies, optimization studies, and modeling studies of OHRA methods are essential to explore OHRA methods more suitable for workplaces in China.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

LZ and HZ designed this scoping review, search strategy, searched databases, and conducted data analysis and interpretation. LZ, PX, and YZ conducted the article screening process. FW, JZ, SW, and YH were involved in full-text reviewing of articles during the final stage of literature screening and extract information from literature. LZ and XL drafted the manuscript. All authors reviewed and approved it, contributed to the article, and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1035996/full#supplementary-material

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Improvements in protective measures in factories with acetylene hydrochlorination and ethylene oxychlorination techniques declined risk assessment levels and affected liver health status

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Acetylene hydrochlorination and ethylene oxychlorination are the two most common methods of producing vinyl chloride monomer (VCM), which has been linked to liver impairment, hepatocellular carcinoma (HCC), and angiosarcoma of the liver (ASL) in occupational settings. However, whether and how these impairments could be effectively improved from workplace root causes has yet to be discovered. This study aimed to evaluate whether improvements in protective measures in groups Y (408 subjects) and Z (349 subjects) could have an influential impact on the alleviation of liver impairment by comparing risk assessment levels under several semi-quantitative models and results from liver ultrasound detection and liver function tests before and after the improvement. Importantly, significant differences in constituent ratio involved in parameters among age, length of employment, weekly exposure time, smoking status, alcohol consumption, and sleeping quality were found between Y and Z before improvement took place in 2020 ($P < 0.05$ or $P < 0.001$), and population distribution by gender between Y and Z was in a large homogeneity with differences in age and length of employment. C_{STE} involves ore breaking, acetylene generation, steam stripping, outward processing, and welding maintenance, was disqualified in 2020 compared to OEL, and was said to have declined to meet OEL requirements by 2021. Further, a negative correction of fresh air requirement and ventilation air changing rate with ambient concentration toward hazards in Y was stronger in 2021 than in 2020. Significant differences in risk levels in Y between 2020 and 2021 were found as ore breaking, acetylene generation, steam stripping, outward processing, VCM polymerization, welding, and repairing, decreasing to relatively lower risk levels in 2021 from the original ones in 2020 only under the semi-quantitative comprehensive index model. Abnormal rates toward other hepatic symptoms decreased in the majority of positions after the improvement, as referred to by alterations such as ALT, AST, and GGT. Overall, the effect of improvements on protective measures effectively reduced positions' risk assessment levels through ventilation enhancement and airtight strengthening, which further affected abnormal rates toward other hepatic symptoms, and alterations such as ALT, AST, and GGT were much more significant in Y than effect in Z.

KEYWORDS

acetylene hydrochlorination, ethylene oxychlorination, VCM, improvement on protective measures, occupational health risk assessment, fatty liver, other hepatic symptoms, fresh air requirement

Introduction

As an essential chemical material, vinyl chloride monomer (VCM) is used mostly in the aggregation of polyvinyl chloride (PVC), a product that is extensively used in anti-erosion pipes, construction materials, and automotive parts (1). Currently, the global market demand for PVC keeps rising, with an estimated annual production of over 30 million tons in 2021 (2). Globally, acetylene hydrochlorination and ethylene oxychlorination are presently the major procedures for synthesizing VCM and PVC. The former has taken up more than 80% of the production share and ∼40% of the capacity annually throughout the central and western regions of China due to simple crafts, low investment, and an abundance of materials in coal and calcium carbide (3). By contrast, the latter one is usually distributed in southeast coastal regions, as it requires imported ethylene, high-tech reaction equipment, and matched purification measures. As the world's largest production base for VCM and PVC, China's capacity in 2018 reached 23.53 million tons, and it is expected to reach 25.93 million tons by 2023 (4).

Given that the large-scale health conditions of workers occupationally exposed to VCM might not be so optimistic, some protective measures under recent circumstances still have room for improvement. According to the previous investigation, VCM and other identified hazards threatened workers' health status at relatively high concentrations in ambient workplaces due to volatilization from leakage of unsealed valves, open sampling ports, or noneffective ventilation, which increased accidental risks for acute poisoning and adverse effects under chronic exposure (5). In 2012, the International Agency on Cancer Research (IARC) classified VCM as a group I carcinogen based on evidence from animal and occupational epidemiological studies (6). Subsequently, sufficient evidence in humans proved that VCM caused ASL and HCC, according to the findings from two large multi-center cohort studies at PVC production plants in the USA and Europe (6, 7). In a European study, the risk of lung cancer among the 12,700 PVS workers in 19 VCM/PVC plants significantly increased with cumulative concomitant exposure to VCM (8).

Furthermore, IARC also recognized that workers who were occupationally exposed to VCM were simultaneously exposed to other hazards, indicating that more severe adverse effects might be developed through joint actions among hazards that were homogeneous in target organs, such as the liver (9). Meshakova et al. estimated that employees from several large-scale PVC production plants experienced prolonged exposure to relatively low concentrations of VCM and 1, 2-dichloroethane (1,2-DCE). Both of them predominantly affected liver enzymes, forming 2-chloroethylene oxide, monochloroacetic acid, and the conjugated metabolic product of thiodiglycolic (thiodiacetic) acid (TDAA), which tend to be mutagenic and carcinogenic (10). Particularly, workers from the VCM division were subjected to simultaneous intensive exposure to concentrations of VCM ranging from 2.0 to 14.6 $mg{\cdot}m^{-3}$ and of 1,2-DCE from 15.0 to 87.2 $mg{\cdot}m^{-3}$, while those from the PVC division were only exposed to concentrations of VCM ranging from 1.1 to 10.7 $mg{\cdot}m^{-3}$ (11). In addition to VCM, PVC was classified as a possible carcinogen (class 3) by the IARC. The inhaled PVC dust (in particular, with an aerodynamic diameter of <5 mm) may remain in the pulmonary interstitium for years, gradually releasing residual VCM, which may account for the neoplastic transformation of an epithelial cell. Due to the residual presence of VCM and other additives, the European Union's Classification, Labeling and Packaging (CLP) Regulation reports that PVC is one of the plastic polymers with the highest health hazard (hazard score of 5) (12).

In this regard, workers exposed to VCM and PVC at workplaces are facing adverse health effects. Implementing occupational risk assessment in advance would be indispensable and urgent for identifying hazard factors and promoting liver function status. Recently, the methodology toward occupational health risk assessment (OHRA) has been well-rounded for risk assessment through several available quantitative or semi-quantitative models, including the Environmental Protection

Agency's (EPA) quantitative model for carcinogens or non-carcinogens, the Singaporean semi-quantitative model, the United Kingdom's Control of Substances Hazardous to Health Essentials (COSHH Essentials), the Romania risk assessment model, and the International Council on Mining and Metal's (ICMM) quantitative model (13). Based on different models above, China formulated its own technical guideline for the occupational risk assessment model for chemicals in the workplace (GBZ/T 298-2017) from its predecessor, the Singaporean semi-quantitative model (14).

Thus, this study aimed to achieve several research purposes, including (1) systematically evaluating the effectiveness of improvements in protective measures in factories with different technological processes by comparing external concentrations among identified hazard factors before and after improvement and finding out engineering protection factors that might relate to the effectiveness if it works; (2) observing possible alterations toward risk assessment levels of VCM exposed positions affected by improvements on protective measures and comparing differences in methodology among three semi-quantitative risk assessment models; and (3) analyzing possible contributing factors that involve abnormal symptoms and morbidities on liver ultrasound detection and the liver function test. To the best of our knowledge, this could be the first study to emphasize occupational risk assessment of VCM-exposed positions in factories with techniques of acetylene hydrochlorination and ethylene oxychlorination before and after improvements on protective measures, which will pave the way for guidance implementation in occupational health surveillance and health management.

Materials and methods

Study design and subjects

A cross-sectional study of a PVC factory with the acetylene hydrochlorination technique in Tianjin City (Y) and another VCM synthesis factory with the ethylene oxychlorination technique in Guang Zhou City, Guang Dong Province (Z) was conducted in July 2020, right before their annual overhaul for repairs and maintenance (which usually takes place in November and would last for 1 or 2 months until early next year). Another retrospective investigation was carried out again in 2021 for alteration observation.

Concretely, 408 subjects from Y and 349 from Z who were occupationally exposed to VCM or others were recruited based on the following inclusion criteria: (1) employment duration longer than 1 year and longer than 3 months from current positions, (2) aged 20–55 years without gender difference, (3) work content involving operating or patrolling patterns for a certain period, (4) participants with complete questionnaire inquiries and physical examination data, and (5) workers with no medical history of allergy, asthma, allergic rhinitis, cardiovascular diseases, viral hepatitis in B and C, liver cirrhosis, or malignant liver cancer. The ethical approval of this study was approved by the Medical Ethics Committee of the National Institute of Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention, Beijing, China (NIOHP202007).

Questionnaires

All subjects who voluntarily joined this study were informed about its purposes and were requested to participate in a face-to-face questionnaire in July 2020. Precisely, parameters such as gender (men/women), age (∼35, ∼45, and ∼55 y), length of employment (∼5, ∼20, and ∼35 y), working shift system (8-h dayshift, 8-h shift, and 12-h night-shift), weekly working time (∼40 and ∼60 h), weekly exposure time (∼20 and ∼40 h), smoking status [(smokes at least one cigarette per day for 1 year or more, including those who have quit smoking in <1 year), (yes/no)], alcohol consumption [(consuming alcohol more than three times per week and more than 60 g/day each time), (yes/no)], sleeping duration (∼4, ∼6, and ∼8 h), sleeping quality (good, general, and bad), conscious ventilation effect (significant, ordinary, and negligible), individual protective masks (always wearing, sometimes if necessary, and never), and status of ventilation installment (normal operation, temporary suspension, and fully broken) were collected. All interviewers were trained in advance for objective inquiry and content integrity.

Physical examination data collection

The occupational physical examination was collected from the CDC of Binhai and Dagu New District of Tianjin City, in which the hepatic function index of alanine aminotransferase (ALT), aspartic transaminase (AST), glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), and the serum lipid parameters of total cholesterol (TC) and triglyceride (TG) were included. The results from liver ultrasound included but were not limited to fatty liver in mild, moderate, and severe grades, multiple hepatic cysts, intrahepatic calcification, thickened echo, multiple gallbladder stones, cholecystic polyps, and chronic cholecystitis. They were roughly divided into categories of normal, fatty liver (mild, moderate, and severe), and other hepatic symptoms for analysis.

Specifically, a total of 384 out of 408 workers (94.1%) from Y participated in the annual physical examination in 2021, compared to 393 in 2020 (96.3%), with a slight decrease of 2.2% in attendance rate. On the contrary, 324 out of 349 workers (92.8%) from Z joined this activity in 2021, compared to 327 in 2020 (93.7%), with a decrease of 0.9% in attendance rate. The missing participants might be due to job transfers, retirement, or rehabilitation.

Occupational on-site surveys

Identification of occupational hazards

According to an on-site survey, major occupational hazards in Y involved VCM, PVC dust, CaC_2 dust, NH_3, Cl_2, $HgCl_2$, HCl (36–38%, pH < 2), NaOH (3.5%, pH = 13.9), welding fume, O_3, manganese, and its inorganic compounds. Major hazards in Z were identified as VCM, 1, 2-DCE, Cl_2, HCl (36–38%, pH < 2), and NaOH (3.5%, pH = 13.9).

Status of protective measures before improvement

Protective measures in Y largely relied on the general ventilation effects and local dust removal, as many facilities were placed indoors, while measures in Z mainly depended on natural ventilation and airtight equipment, as most of its facilities lay outdoors. However, the effectiveness of protective measures for both of them still needed time to improve. In Y, problems such as insufficient emergency ventilation installation, malfunction on the part of ventilation equipment, irrational indoor air distribution flow, improper setting of exhaust hoods, absence of sprinkling and spraying devices, inefficient bag dust collectors, uncovered observation ports, unsealed valves or cover plates, fume cupboard malfunction, and so on were found to be potential risk factors for adverse effects. In Z, problems primarily concentrating on unsealed sampling devices, unsealed sampling ports, non-standardized settings on emergency rescue facilities, shortages of personal protective tools for certain positions, and a shortage of engineering protection measures during the loading and fueling process were potential risk factors for adverse effects.

Status of protective measures after improvement

After improvement, in Y, the raised dust of PVC and CaC_2 was suppressed mainly by the installation of anti-dust fences, bag dust collectors, and sprinkler facilities; welding fume or other hazards stemming from maintenance and repair work were effectively expelled through local exhaust fans or draft fans; and facilities such as emergency ventilation, exhaust hoods, dust collectors, and axial defective flow fans were fixed up and put to use after tests and evaluation. In Z, most pipelines, valves, observation ports, and sampling devices that originally existed at the risk of leakage had been renovated by replacing old ones with highly efficient sealing and anti-corrosion materials.

Sampling and detection

Occupational hazards were mainly categorized into two kinds: industrial dust and chemical hazards. According to Table 1, sampling and detection were conducted according to the standards of (15) GBZ 159–2004 *Sampling Practices for Monitoring Harmful Substances in Workplace Air* and (16) GBZ/T 300.1-2017 *Measurement Methods for Toxic Substances in Workplace Air, Part 1: General Principles*. In this regard, the sampling process was operated at representative sites at different time intervals and continuously sampling for three working days to ensure different individuals in identical positions were covered. Particularly, chemical hazards concentrations that related to maximum concentration (C_M) were Cl_2, O_3, HCl, NaOH, and H_2S, referred to as short-term exposure concentration (C_{STE}) were VCM, PVC dust, CaC_2 dust, NH_3, welding fume, manganese, and inorganic compounds, and 1, 2-DCE. All identified hazards were sampled using the corresponding equipment (*air sampling pump APEX-2 0.5–5.0 L·min^{-1} Casella UK; explosion-proof pump IFC-2 5.0–30 L·min^{-1}, China*). Several hazards with a simultaneous 8 h time-weighted average exposure concentration (C_{TWA}), including NH_3, VCM, welding fume, manganese, inorganic compounds, CaC_2 dust, and 1, 2-DCE, were calculated through exposure time and C_{STE} (17–26). Finally, detection results would be evaluated as qualified or disqualified in accordance with the Chinese standard of occupational exposure limits for chemical agents (27).

Detection of fresh air requirements and ventilation air changing rate

The fresh air requirements [m^3/(people·h)] and ventilation air changing rates (t/h) at plants were either detected through the electronic anemometer (ranging between 0.5 and 1 m/s and 1 and 30 m/s, China) or collected from evaluation reports, with specific detection methods lived up to the standard of (28) *GB/T 18204.1-2013 Methods of Hygienic Examination at Public Places Part 1 Physical Factors,* and corresponding Equations (1)–(3) for average wind speed, fresh air requirements, and ventilation air changing rates were displayed as follows:

$$\overline{V} = \frac{(V_1 + V_2 + ...V_n)}{n}, \quad (1)$$

where $\overline{V}$ represents the average wind speed of a certain vent (m/s), n indicates amounts of small, subdivided areas on a certain vent, and V_1 to V_n indicates the average wind speed values detected from subdivided areas in the following equation:

$$Q = \frac{\sum_{i=1}^{n} (3600 \times S \times \overline{V})}{P}, \quad (2)$$

TABLE 1 Information of identified hazards and detection standards.

Hazards	OEL mg·m^{-3}		National standards	Methods	Instruments
	MAC/PC-STEL	PC-TWA			
Ammonia (NH_3)	30	20	GBZ/T160.29-2004	Nanoreagent spectrophotometry	UNIC 2100 spectrophotometer
Chlorine (Cl_2)	1	—	GBZ/T160.37-2004	Methyl orange spectrophotometry	UNIC 2100 spectrophotometer
Ozone (O_3)	0.3	—	GBZ/T300.48-2017	Eugenol spectrophotometry	UNIC 2100 spectrophotometer
Hydrochloric acid (HCl)	7.5	—	NIOSH 7907	Volatile acids by Ion Chromatography	Hydrogen flame ionization detector
Sodium hydroxide (NaOH)	2	—	GBZ/T300.22-2017	Flame atomic absorption spectrometry	Flame atomic absorption spectrophotometer
Vinyl chloride monomer (VCM)	—	10	GBZ/T300.78-2017	Thermo desorption gas chromatography	Hydrogen flame ionization detector
Polyvinyl chloride dust (PVC dust)	—	5	GBZ/T 192.1-2007	Membrane filter sampling	Membrane weighting
Welding fume	—	4	GBZ/T 192.1-2007	Membrane filter sampling	Membrane weighting
Calcium carbide dust (CaC_2 dust)	—	8	GBZ/T 192.1-2007	Membrane filter sampling	Membrane weighting
Manganese and inorganic compounds	—	0.15	GBZ/T300.17-2017	Acid digestion Flame atomic absorption spectrometry	Acetylene-air Flame atomic absorption spectrophotometer
Sulfuretted hydrogen (H_2S)	10	—	GBZ/T160.33-2004	Silver nitrate colorimetry	Visual colorimetric determination
1, 2-dichloroethane (1, 2-DCE)	15	7	GBZ/T160.45-2007	Solvent absorption gas Chromatography	Hydrogen flame ionization detector

The OEL of calcium carbide dust had not been established in Chinese standard yet so far and it temporarily referred to the OEL of total dust category (PC-TWA = 8 mg·m^{-3}).

where Q indicates the fresh air requirements [m^3/(people·h)], n indicates the number of vents at plants, S represents the cross-sectional area at a certain vent (m^2), $\overline{V}$ represents the average wind speed of a certain vent (m/s), and P represents the actual maximum number of workers (people):

$$A = Q \times P/V \tag{3}$$

A represents ventilation rates (t/h), Q indicates the fresh air requirements [m^3/(people·h)], P represents the actual maximum amount of workers (people), and V represents the room volume (m^3).

Occupational health risk assessment models

The semi-quantitative comprehensive index model, the quantitative model of the International Council on Mining and Metals (ICMM), and the occupational hazards classification model at workplaces (dust and chemical agents) were used to evaluate risk assessment levels in Y and Z before and after improvements on protective measures.

The semi-quantitative comprehensive index model

Hazard rank (HR) and exposure rank (ER) were essential components for risk (R), as Equation (7) displayed, and it could be sequentially classified into negligible (R = 1), low (R = 2), medium (R = 3), high (R = 4), and extremely high groups (R = 5). Concretely, HR was assigned certain values with regard to toxicity classification for chemical hazards from the American Conference of Governmental Industrial Hygienists (ACGIH). ER was comprehensively evaluated through Equation (4), in which parameters from EI_1 to EI_n, respectively, symbolized vapor pressure/particle size; E/(OEL × f) includes engineering protection measures, first-aid facilities, mode of personal protective tools, emergency rescue measures, occupational health management, weekly usage amount, and

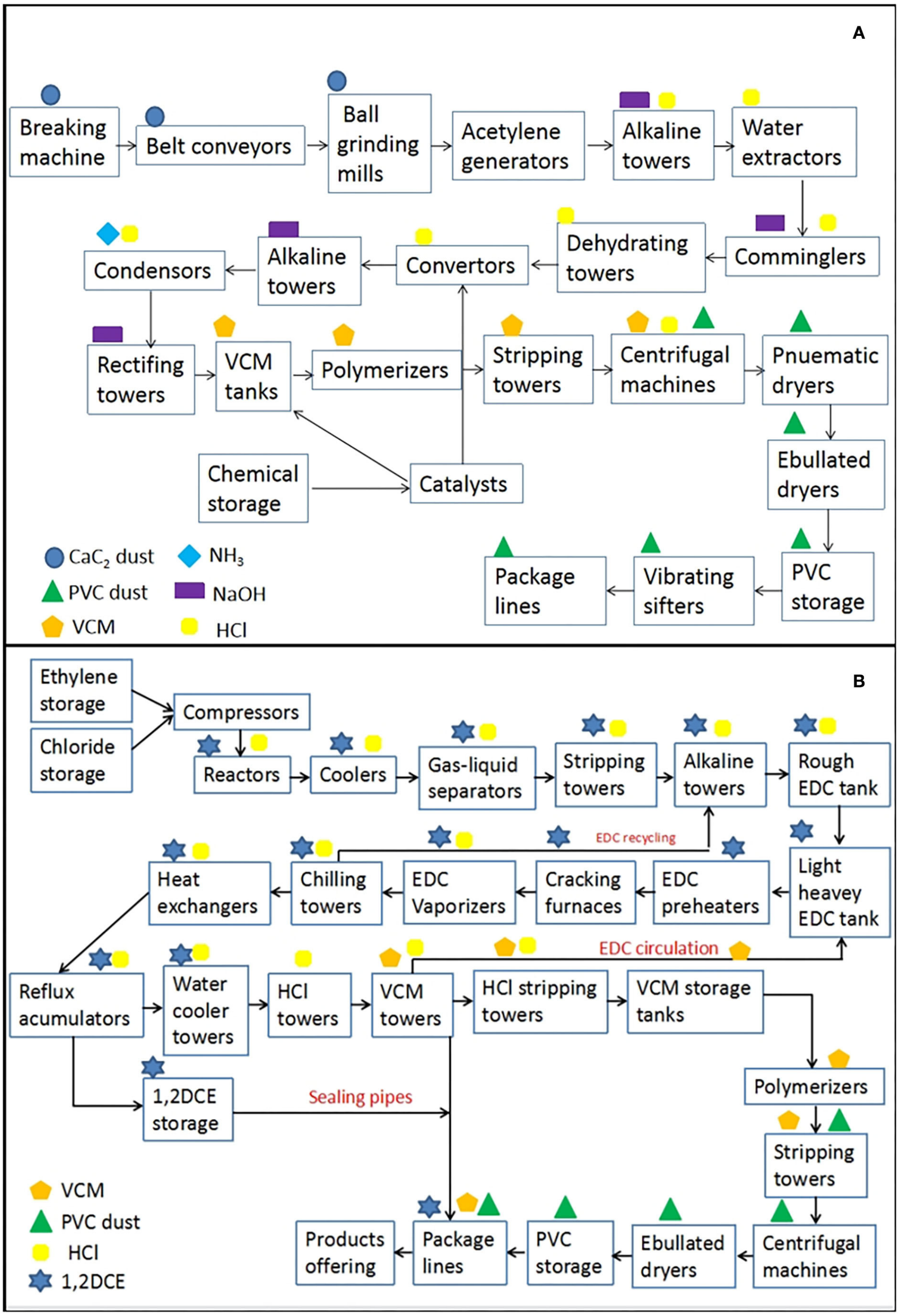

FIGURE 1
Introduction of technological processes for VCM and PVC production toward the acetylene hydrochlorination technique **(A)** and the ethylene oxychlorination technique **(B)**. In that, the technical process of **(A)** was roughly divided into sectors of ore breaking, acetylene generation,

(Continued)

FIGURE 1 (Continued)
chemical synthesis, steam stripping, outward processing, VCM polymerization, refrigeration, product packaging, and other auxiliary ones. Occupational hazards mainly contained VCM, PVC dust, CaC_2 dust, NH_3, HCl (36–38%), NaOH (3.5%), and so on. Process **(B)** were sectors of material storage, splitting decomposition, chemical reaction, oxychlorination, material recycling, field sampling, central control, maintenance, and public engineering. Occupational hazards mainly included VCM, 1, 2-DCE, HCl (36–38%), and PVC dust.

weekly contact time. Relevant equations are followed by (4), (5), (6), and (7):

$$ER = [EI_1 \times EI_2 \times EI_3 \times EI_n]^{\frac{1}{n}} \quad (4)$$

E/OEL represents the ratio between exposure concentration (E) and corresponding occupational exposure limits (OEL). E was calculated through Equation (5) when weekly working hours were mostly equal to 40 h, and the relevant OEL should multiply by a declining factor f when daily working hours (H) were longer than 8 h/day. Equations (5) and (6) are written as follows:

$$E = F \times D \times M/W, \quad (5)$$

where E represents the weekly exposure concentration (mg/m^3). F refers to the weekly exposure frequency (d/W), and D indicates the average exposure time per day (h/d), M represents the arithmetic weighted mean of exposed concentration ($mg \cdot m^{-3}$), and W means the average weekly working hours, which were limited to 40 h/w:

$$f = \frac{8}{H} \times \frac{(24 - H)}{16} \quad (6)$$

$$R = \sqrt{HR \times ER} \quad (7)$$

The ICMM quantitative model

Evaluation of the ICMM quantitative model could be calculated through Equation (8), and the risk (R) could be classified into levels of tolerable (<20), potential (20–69), high (70–199), very high (200–399) and intolerable (≥400) groups:

$$R = C \times PrE \times PeE \times U \quad (8)$$

Among these, C represents possible consequences for five grades, which are composed of minor illness (C = 1), major illness (C = 7), serious illness (C = 15), major disability (C = 50), and one or more fatalities (C = 100). PrE indicated the possibility of exceeding OEL, which could be classified as 0.5, 1, 3, 6, and 10, as it referred to the extent of the conceivable but very unlikely, only remotely possible, unusual but possible, and intermittently and continuously exceeding. Then, PeE could be classified as 0.5, 1, 2, 3, 6, and 10 according to relevant periods of exposure for rare (once per year), unusual (a few minutes per year), short periods of the month (a few minutes per month), continuous for 1 or 2 h per shift, continuous for 2 or 4 h per shift, and continuous for 8 h per shift. U represented uncertainty assignment for risk rating and exposure assessment, which was allocated to certain (U = 1), uncertain (U = 2), and even quite uncertain (U = 3) (29).

Occupational hazards classification method at workplaces

It specialized in the classification of dust and chemical agents with standards of (30) *GBZ/T 229.1-2010 classification of occupational hazards at workplaces, Part 1: occupational exposure to industrial dust,* and (31) *GBZ/T 229.2-2010 classification of occupational hazards at workplaces, Part 2: occupational exposure to chemicals*. Equations (9) and (10) for industrial dust or chemical agents are shown as follows:

$$G = W_M \times W_B \times W_L \quad (9)$$

$$G = W_D \times W_B \times W_L, \quad (10)$$

where G corresponds to the risk classification induced by dust and chemical agents, W_M indicates the weight of industrial dust, which was assigned according to the different contents (%) of free silica in the dust; $W_D$represents the weight of chemical agents, graded according to the standard of *GBZ 230–2010 "Classification for Hazards of Occupational Exposure to Toxicants"* (32), W_B represents the weight of E/OEL in chemical agents or industrial dust, and W_L was the weight of workers' physical labor intensity, estimated through the standards of *GBZ/T 189.10–2007, "Measurement of Physical Agents in the Workplace, Part 10: Classification of Physical Workload"* (33) and *GBZ 2.2-2007, "Occupational Exposure Limits for Hazards in the Workplace, Part 2: Physical Hazards"* (34). Ultimately, G would be classified as harmless (G = 0), mildly hazardous (0 < G ≤ 6), moderately hazardous (6 < G ≤ 24), and severely hazardous (G > 24).

Risk ratio based on risk level conversion

As positions' risk levels under different models were incomparable, they needed to be converted into a kind of homogeneous risk ratio (RR) for quantitative comparisons among different models. Particularly, RR represents the ratio between a certain risk level and the total amount of risk classification. It could be classified into four grades: low risk ($0 < RR \leq 0.25$), medium risk ($0.25 < RR \leq 0.5$), high risk ($0.5 < RR \leq 0.75$), and extremely high risk ($0.75 < RR \leq 1$) (35).

Statistical methods

Epidata 3.0 and SPSS 24.0 were utilized for database establishment and statistical analysis. The Kolmogorov-Smirnov test was conducted for normal distribution judgment, in which data that followed the inclusion criteria were presented by mean ± standard deviation (SD), while abnormally distributed data were alternatively presented by M (P_{25}, P_{75}). Comparison differences toward abnormal rates were carried out by the X^2 test, and quantitative data were analyzed by the Student's t-test or the Mann–Whitney U test. *Spearman's* correlation was used to verify the relative correlation between ambient concentration and ventilation effect data. Multivariate *ANOVA* analysis was used to explore possible independent variables that contributed to multi-dependent variables, and the interactive effect between bilateral variables was done through *LSD*. Logistical linear regression analysis was adopted to analyze different contributions to nervous system symptoms from available variables. Statistical significance for two-tailed P-values was defined as $\alpha < 0.05$.

Results

Investigation of technological process

Y was a large-scale PVC factory with an annual production of 800,000 tons/year of PVC and 610,000 tons/year of VCM using the technique of acetylene hydrochlorination. Y could be divided into divisions of ore breaking, acetylene generation, chemical synthesis, steam stripping, outward processing, VCM polymerization, refrigeration, product packaging, and other auxiliary ones. By comparison, Z was a VCM manufacturing factory with an annual production of 500,000 tons/year on VCM and of 400,000 tons/year on 1,2-DCE ($C_2H_4Cl_2$) through the technique of ethylene oxychlorination. It mainly contained sectors such as material storage, splitting decomposition, chemical reactions, oxychlorination, material recycling, field sampling, central control, maintenance, and public engineering. On average, workers in Y and Z worked a 12 h/d shift with 42 h per week. They usually wore anti-poison or anti-dust respirators with earplugs, safety helmets, and uniforms. Reportedly, they also complied with occupational health management disciplines and attended a safety training program held regularly to intensify the awareness of occupational health.

Introduction of the acetylene hydrochlorination technique

As Figure 1A indicated, the acetylene hydrochlorination technique could be described as a first-order chemical reaction between calcium carbide and water to generate acetylene (C_2H_2) and calcium hydroxide Ca $(OH)_2$, and then, a second-order chemical reaction was initiated with the precondition of a heated environment between purified acetylene (C_2H_2) and hydrogen chloride (HCl) with the acceleration effect of mercury chloride ($HgCl_2$) to catalyze vinyl chloride gas (VCM) and then aggregated into polyvinyl chloride (PVC) under high temperature, and products went through the combined lines of hand-packing and automation after centrifugation and desiccation, with all reactions presented in Equations (11) and (12) (36):

$$CaC_2 + H_2O \rightarrow C_2H_2 + Ca(OH)_2 \tag{11}$$

$$CH = CH + HCl \xrightarrow{HgCl_2} CH_2 = CHCl \tag{12}$$

Introduction of the ethylene oxychlorination technique

The ethylene oxychlorination technique was operated in three phases, as shown in Figure 1B: (1) the material of chloride (Cl_2) reacted with ethylene (C_2H_4) at a relatively lower temperature environment with the catalysis of ferric trichloride ($FeCl_3$) to generate 1, 2-DCE ($C_2H_4Cl_2$), and then a portion of the qualified 1, 2-DCE would be purified for intermediate products, while the rest would be recycled and steamed out and transmitted into a second step for disintegration. (2) The 1, 2-DCE would be split into VCM gas and HCl at a high reaction temperature inside a sealed cracking furnace. (3) VCM, 1, 2-DCE, and HCl were distinctively isolated through temperature-controlled screening in quench converters, and the purified VCM would be steam-stripped and distributed to the downstream division for polymerization. Chemical reactions are exhibited in Equations (13) and (14) (37):

$$Cl_2 + C_2H_4 \xrightarrow{FeCl_3} C_2H_4Cl_2 \tag{13}$$

$$C_2H_4Cl_2 \rightarrow C_2H_3Cl + HCl \tag{14}$$

Questionnaire analysis

As Table 2 indicated, significant differences in the constituent ratio involved were found on the following parameters: age, length of employment, weekly exposure time, smoking status, alcohol consumption, and sleeping quality between Y and Z before improvement took place in 2020 ($P < 0.05$ or $P < 0.001$). Population distribution by gender

TABLE 2 Comparison results of questionnaires between Y and Z in 2020.

Parameters	Y ($n = 408$)		Z ($n = 349$)		X^2, P-value
Gender	**Number**	**%**	**Number**	**%**	
Male	341	83.6	275	78.8	2.84, 0.090
Female	67	16.4	74	21.2	
Age (years)					
−35	89	21.8	128	36.7	23.65, <0.001**
−45	207	50.7	126	36.1	
−55	112	27.5	95	27.2	
Length of employment (years)					
−5	58	14.2	112	32.1	89.14, <0.001**
−20	182	44.6	195	55.9	
−35	168	41.2	42	12.0	
Working shift system					
8 h day-shift	49	12.0	62	17.8	9.194, 0.010
8 h shift	221	54.2	199	57.0	
12 h night-shift	138	33.8	88	25.2	
Weekly working time (h)					
−40	14	3.4	21	6.0	2.85, 0.091
−60	394	96.6	328	94.0	
Weekly exposure time (h)					
−20	96	23.5	48	13.8	10.33, 0.001*
−40	312	76.5	301	86.2	
Smoking status					
Yes	225	55.1	145	41.5	13.92, <0.001**
No	183	44.9	204	58.5	
Alcohol consumption					
Yes	262	64.2	93	26.7	106.60, <0.001**
No	146	35.9	256	73.4	
Sleeping duration (h)					
−4	69	16.9	36	10.3	10.169, 0.006*
−6	231	56.7	192	55.0	
−8	108	26.5	121	34.7	
Sleeping quality					
Good	149	36.5	283	81.1	152.52, <0.001**
General	214	52.5	55	15.8	
Bad	45	11.0	11	3.2	
Individual protective masks					
Always wearing	336	82.3	288	82.5	3.10, 2.212
Sometimes if necessary	59	14.5	42	12.0	
Never	13	3.2	19	5.4	
Status of ventilation installment					
Normal operation	102	25.0	114	32.7	5.99, 0.051
Temporary suspension	227	55.6	181	51.9	
Fully broken	79	19.4	54	15.5	

*Presented $P < 0.05$ and **presented $P < 0.001$ as parameters between Y and Z were compared.

between Y and Z was largely homogeneous, as the sex ratio of men to women in Y and Z were 5:1 (341 vs. 67) and 3.7:1 (275 vs. 74), respectively, without significant differences ($X^2 = 2.84$, $P > 0.05$). Next, they were slightly different in age and length of employment, as ∼78.2% of workers in Y were middle-aged men (50.7% were 36–45 years old, and 27.5% were 46–55 years old), while nearly 36.7% of workers in Z were young ones under 35 years. Specifically, statistical differences of age and gender were observed neither between men (44.65 ± 9.40 years) in Y and men (43.65 ± 8.43 years) in Z ($t = 3.23$, $P > 0.05$), nor were they observed between women (44.53 ± 9.21 years) in Y and women (41.17 ± 6.04)] in Z ($t = 2.27$, $P > 0.05$). Occupationally, the percentage toward the length of employment for workers in Y and Z mainly concentrated on a subgroup of 6–20 years, and significant differences were observed between men (18.91 ± 6.67 years) in Y and men (14.46 ± 8.50 years) in Z ($t = 11.46$, $P < 0.001$) and between women (17.2 ± 9.41 years) in Y and women (13.95 ± 4.73 years) in Z ($t = 9.01$, $P < 0.001$). Further, it is worth mentioning that workers under both techniques were under a huge amount of workload with high intensity and density, which might be potentially harmful to their physical health. In addition, it could be noted that the proportion of 54.2% workers in Y were on the 8-h shift and another 33.8% ones were in their 12-h shift pattern respectively, which accounted for a total of 96.6% of laborers in Y working longer than 40 h per week and nearly 73.5% of them sleeping shorter than 6 h per day (56.6% on the 4–6 h and 16.9% on the 0–4-h shift), while the same situation persisted in Z, as shown in Table 2. In addition, it could be noted that the ventilation effect in Y might need to be improved based on the practical experiences or witness as 55.6% of workers argued part of ventilation facilities were temporarily suspended and approximately 19.4% other ones identified fully broken, while 51.9% of workers and 15.5% of others in Z stated the similar statuses.

Ambient concentration detection

As Table 3 presented, in 2020, positions in Y of ore breaking ($C_{TWA} = 28.4$ mg·m^{-3}) and acetylene generation ($C_{TWA} = 13.5$ mg·m^{-3}) that were exposed to CaC_2 dust and steam stripping ($C_{TWA} = 11.7$ mg·m^{-3}), outward processing ($C_{TWA} = 15.2$ mg·m^{-3}), welding maintenance ($C_{TWA} = 11.2$ mg·m^{-3}) that mainly exposed to VCM were disqualified as compared to OEL. No disqualification results were found in Z. Comparatively, those who were disqualified in Y in 2020 declined to qualify in 2021. Correspondingly, comparison results of C_{TWA} toward VCM, PVC dust, CaC_2 dust, and so on between 2020 and 2021 presented that significant differences were observed in Y ($t = 2.847$, $P = 0.016$, 95% CI = 1.36–10.6) and Z ($t = 2.40$, $P = 0.030$, 95% CI = 0.08–1.27).

Fresh air requirement and ventilation air changing rate

Room volumes and vent areas remained the same before and after the improvement. As Table 4 showed, indoor wind speed in Y significantly increased to 15.21 (14.24, 15.89) m/s in 2021 from 6.04 (5.21, 6.40) m/s in 2020 ($Z = -12.59$, $P < 0.001$). Fresh air requirements in Y significantly increased to 30,693.60 (28,602.00, 32,486.40) [m^3/(people·h)] in 2021 from 10,631.52 (9,216.00, 13,413.60) [m^3/(people·h)] in 2020 ($Z = -15.59$, $P < 0.001$). Ventilation air changing rates increased to 15.56 (13.30, 16.72) t/h in 2021 from ones of 5.76 (4.66, 6.82) t/h in 2020 ($Z = -13.77$, $P < 0.001$), with statistical differences sequentially. Meanwhile, indicators in Z enhanced to 15.98 ± 0.85 m/s ($Z = -11.70$, $P < 0.001$), 28,925.17 ± 1,317.04 [m^3/(people·h)] ($Z = -13.12$ $P < 0.001$), and 13.78 ± 0.41 t/h ($Z = -17.25$, $P < 0.001$) in 2021 from 5.39 (4.65, 6.17) m/s, 9,072.00 (8,566.20, 11,315.70) [m^3/(people·h)] and 4.51 (4.24, 5.29) t/h in 2020 with significant differences.

Correlation analysis

As Table 5 demonstrated, ambient concentration (C_{STE} or C_M) in Y connected to fresh air requirement ($r = -0.48$, $P = 0.032$) and ventilation air changing rate ($r = -0.49$, $P = 0.029$) with a moderate negative correlation in 2020 and converted into a much stronger one in 2021 ($r = -0.76$, $P = 0.015$; $r = -0.81$, $P = 0.011$). In the meantime, ambient concentration in Z did not show much negative correlation with fresh air requirements and ventilation air changing rate in 2020 but revealed a weak correlation in 2021 ($r = -0.27$, $P = 0.044$; $r = -0.24$, $P = 0.042$). It could be assumed that improvements in fresh air requirements and ventilation air changing rates significantly correlated to concentration decline in Y as the majority of positions made activities at indoor plants, while these factors did not seem to be the decisive factor in impacting ambient concentration in Z as its intensive facilities with hazards were placed outdoors, and general ventilation was also involved.

Occupational health risk assessment

Semi-quantitative comprehensive index model

The risk (R) of the semi-quantitative comprehensive index model was determined by HR and ER. In that regard, HR was classified to level 5 as VCM was an IARC group 1 carcinogen (G1), and NaOH, HCl, Cl_2, H_2S, and manganese and inorganic compounds were classified into level 4 due to corrosive chemical reagents, poisonous gases of irritation and suffocation, or proved to be mutagenic to humans based on limited animal experiments. HR of NH_3, 1, 2-DCE, welding fume, PVC dust, and CaC_2 dust were in level 3 for irritating

TABLE 3 Results of hazards detection before and after improvements in protective measures.

Positions	Cumulative exposure time (h)	Hazards	2020			2021		
			C_{STE}/C_M	C_{TWA}	Judgment of results	C_{STE}/C_M	C_{TWA}	Judgment of results
Ore breaking	5	CaC_2 dust	45.4 (18.1–72.7)	28.4 (11.3–45.4)	Disqualified[a]	6.5 (1.7–11.2)	4.1 (1.1–7.0)	Qualified
Acetylene generation	6	CaC_2 dust	18.0 (2.2–33.8)	13.5 (1.7–25.3)	Disqualified[a]	6.6 (0.4–6.2)	2.5 (0.3–4.7)	Qualified
Chemical synthesis	3	VCM	<0.9	<0.9	qualified	<0.9	<0.9	Qualified
	1	NaOH	<0.016	—	qualified	<0.016	—	Qualified
Steam stripping	3	VCM	29.2 (4.3–54.1)	11.7 (1.6–20.3)	Disqualified[a]	11.3 (2.5–20.0)	4.5 (1.5–7.5)	Qualified
Outward processing	3	VCM	40.4 (7.5–73.3)	15.2 (2.8–27.5)	Disqualified[a]	6.2 (0.4–12.0)	2.3 (0.2–4.5)	Qualified
VCM polymerization	3	VCM	23.9 (4.0–43.7)	8.9 (1.5–16.4)	Qualified	6.5 (0.2–12.7)	4.9 (0.08–4.8)	Qualified
refrigeration	3	NH_3	2.9 (2.7–3.0)	1.1 (1.0–1.1)	Qualified	0.3 (0.2–0.4)	0.1 (0.08–0.2)	Qualified
Product packaging	6	PVC dust	3.5 (0.4–6.5)	2.6 (0.3–4.9)	qualified	1.3 (0.2–1.1)	0.3 (0.1–0.4)	Qualified
Welding and repairing	6	VCM	14.9 (1.3–28.5)	11.2 (1.0–21.4)	Disqualified[a]	4.7 (0.3–9.1)	3.5 (0.2–6.8)	Qualified
	3	Welding fume	1.1 (0.2–1.9)	0.8 (0.2–1.4)	Qualified	0.7 (0.2–1.2)	0.6 (0.2–0.9)	Qualified
	3	manganese and inorganic compounds	<0.02	<0.02	Qualified	<0.02	<0.02	Qualified
	3	O_3	<0.02	—	Qualified	<0.02	—	Qualified
Laboratory testing	5	VCM	3.5(1.1–5.8)	2.2(0.7–3.6)	Qualified	1.5 (0.2–2.8)	1.0 (0.1–1.8)	Qualified
	1	Cl_2	<0.2	—	Qualified	<0.2	—	Qualified
	1.5	HCl	<0.027	—	Qualified	<0.027	—	Qualified
	1.5	NaOH	<0.016	—	Qualified	<0.016	—	Qualified
Sewage cleaning	5	VCM	<0.9	<0.9	Qualified	<0.9	<0.9	Qualified
	1.5	H_2S	<0.53	—	Qualified	<0.53	—	Qualified
Material storage	3	VCM	<0.9	<0.9	Qualified	<0.9	<0.9	Qualified
	3	1,2-DCE	<0.56	<0.56	Qualified	<0.56	<0.56	Qualified
	1	HCl	<0.027	—	Qualified	<0.027	—	Qualified
	1	Cl_2	<0.2	—	Qualified	<0.2	—	Qualified
Splitting decomposition	6	VCM	<0.9	<0.9	Qualified	<0.9	<0.9	Qualified
	3	1,2-DCE	<0.56	<0.56	Qualified	<0.56	<0.56	Qualified
	1	HCl	<0.027	—	Qualified	<0.027	—	Qualified

(Continued)

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TABLE 3 (Continued)

Positions	Cumulative exposure time (h)	Hazards	2020			2021		
			C_{STE}/C_M	C_{TWA}	Judgment of results	C_{STE}/C_M	C_{TWA}	Judgment of results
	1	Cl_2	<0.2	—	Qualified	<0.2	—	Qualified
Chemical reaction	6	1,2-DCE	2.9 (2.4–3.3)	2.2 (1.8–2.5)	Qualified	1.4 (0.2–2.6)	1.1 (0.2–2.0)	Qualified
	1	Cl_2	<0.2	—	Qualified	<0.2	—	Qualified
	1	NaOH	<0.016	—	Qualified	<0.016	—	Qualified
Oxychlorination	4	1,2-DCE	1.6 (1.0–2.2)	0.8 (0.5–1.1)	Qualified	1.1 (0.5–1.8)	0.6 (0.3–0.9)	Qualified
	4	VCM	<0.9	<0.9	Qualified	<0.9	<0.9	Qualified
	1	Cl_2	<0.2	—	Qualified	<0.2	—	Qualified
Material recycling	6	1,2-DCE	6.3 (2.1–10.4)	4.7 (1.6–7.8)	Qualified	4.8 (1.1–8.5)	3.6 (0.8–6.4)	Qualified
	6	VCM	3.3 (0.7–5.9)	2.5 (0.5–4.4)	Qualified	2.4 (0.3–4.5)	1.8 (0.2–3.4)	Qualified
	1.5	HCl	<0.027	—	Qualified	<0.027	—	Qualified
Field sampling	7	1,2-DCE	6.7 (1.1–12.3)	5.9 (1.0–10.8)	Qualified	2.1 (0.6–3.6)	1.6 (0.5–2.7)	Qualified
	7	VCM	1.8 (0.7–2.9)	1.6 (0.6–2.5)	Qualified	1.4 (0.5–2.3)	1.2 (0.4–2.0)	Qualified
Central controlling	6	VCM	<0.9	<0.9	Qualified	<0.9	<0.9	Qualified
Maintenance	6	VCM	2.9 (2.7–3.0)	2.2 (2.0–2.3)	Qualified	1.6 (0.2–3.0)	1.0 (0.1–0.9)	qualified
	6	1,2-DCE	3.1 (0.3–5.9)	2.3 (0.2–4.4)	Qualified	0.6 (0.2–1.0)	0.5 (0.1–0.8)	Qualified
Public engineering	6	VCM	<0.9	<0.9	Qualified	<0.9	<0.9	Qualified
	6	1,2-DCE	<0.56	<0.56	Qualified	<0.56	<0.56	Qualified

[a]Presented to disqualified results as compared to OEL of certain hazards in manner of C_M or C_{STE}.

TABLE 4 Comparison results of wind speed, fresh air requirement and ventilation air changing rate.

Factories	Worksites	2020			2021			*Z*, *P*-value
		Wind speed[a] (m/s)	Fresh air requirement[b] [m^3/(people·h)]	Ventilation air changing rate[c] (t/h)	Wind speed[d] (m/s)	Fresh air requirement [m^3/(people·h)][e]	Ventilation air changing rate[f] (t/h)	
Y	Crushing plant	6.42	10,631.52	5.76	14.42	23,879.52	12.93	1–4: −12.59, <0.001* 2–5: −15.59, <0.001* 3–6: −13.77, <0.001*
	Generating plant	6.40	9,216.00	3.75	22.40	32,256.00	13.14	
	1# Compressor plant	5.21	9,378.00	4.74	15.21	27,378.00	13.85	
	1#Converter plant	5.89	10,602.00	5.36	15.89	28,602.00	14.46	
	2#Material filling plant	4.09	7,362.00	3.38	16.09	28,962.00	13.30	
	1# Polymerization plant	7.54	16,829.28	8.66	13.54	30,221.28	15.56	
	1#Stripping plant	6.32	14,106.24	7.18	15.32	34,194.24	17.40	
	2# Polymerization plant	6.04	13,046.40	6.72	15.04	32,486.40	16.72	
	2#Stripping plant	6.21	13,413.60	6.82	14.21	30,693.60	15.62	
	3#Polymerization plant	5.28	11,404.80	5.87	15.28	33,004.80	16.99	
	3#Stripping plant	4.24	9,158.40	4.66	14.24	30,758.40	15.65	
	Refrigeration plant	6.08	9,849.60	5.03	16.08	26,049.60	13.31	
	Package plant	6.26	10,141.20	5.54	14.26	23,101.20	12.62	
	Maintenance plant	5.91	8,510.40	3.02	25.91	37,310.40	13.26	
	Testing laboratory	7.33	11,874.60	6.17	15.33	24,834.60	12.91	
	Sewage treatment plant	5.39	8,731.80	4.42	15.39	24,931.80	12.61	
Z	Storage plant	6.89	14,882.40	7.69	14.89	32,162.40	16.62	1–4: −11.70, <0.001* 2–5: −13.12, <0.001* 3–6: −17.25, <0.001*
	Chlorination plant	4.93	8,874.00	4.51	14.93	26,874.00	13.67	
	Controlling room	4.98	10,756.80	4.29	14.98	32,356.80	12.92	
	Cracking plant	4.46	8,028.00	4.11	14.46	26,028.00	13.32	
		4.79	8,622.00	4.84	14.79	26,622.00	14.94	
	Reacting plant	4.51	8,118.00	4.19	14.51	26,118.00	13.49	
	Repair plant	6.04	13,046.40	4.43	17.04	36,806.40	12.50	
	Storage zone	4.20	9,072.00	4.70	15.20	32,832.00	17.00	

[a–c]Referred to wind speed (m/s), fresh air requirement [m^3/(people·h)], and ventilation air changing rate (t/h) in 2020; [d–f]referred to wind speed (m/s), fresh air requirement [m^3/(people·h)], and ventilation air changing rate (t/h) in 2021.*$P < 0.001$ as [a]compared with [d], [b]compared with [e], [c]compared with [f].

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TABLE 5 Correlation analysis among ambient concentration, fresh air requirement, and ventilation air changing rate in Y and Z.

Factories	Factors	2020			2021		
		Ambient concentration	Fresh air requirement	Ventilation air changing rate	Ambient concentration	Fresh air requirement	Ventilation air changing rate
Y	Ambient concentration	1.000	—	—	1.000	—	—
	Fresh air requirement	-0.48^{a*}	1.000	—	-0.76^{a*}	1.000	—
	Ventilation air changing rate	-0.49^{b*}	0.84^{c*}	1.000	-0.81^{b*}	0.87^{c*}	1.000
Z	Ambient concentration	1.000	—	—	1.000	—	—
	Fresh air requirement	−0.21	1.000	—	−0.27	1.000	—
	Ventilation air changing rate	−0.23	0.78^{c*}	1.000	−0.24	0.84^{c*}	1.000

Ambient concentration indicated to C_{STE} or C_M of Identified occupational hazards at workplaces in Y and Z. [a]indicated the comparison of fresh air requirement with ambient concentration; [b]indicated the comparison of ambient concentration with ventilation air changing rate; [c]indicated to the comparison of fresh air requirement with ventilation air changing rate. $^*P < 0.05$.

substances (pH = 8–12), possible human carcinogens (G2B), or hazardous substances to humans or animals with limited evidence. O_3 would fall into level 2 due to possible irritation threats to the eyes, nose, and throat.

By contrast, ER was calculated through the corresponding assignment of EI. For instance, vapor pressures (EI_1) of VCM, 1, 2-DCE, NH_3, HCl, and NaOH were assigned to 5 as they were at 5.5×10^7 Pa (25°C), 1.3×10^6 Pa (20–25°C), 3.8×10^4 Pa (90°C), 3.2×10^4 Pa (20–25°C), 3.9×10^4 Pa, respectively, which exceeded the highest range of vapor pressure (>13,300 Pa), while O_3, H_2S, Cl_2 were assigned to 4 as the standard atmospheric pressure of 101,325 Pa. Next, particle sizes of PVC dust, welding fume, manganese, and inorganic compounds, CaC_2 dust were assigned to 4, as they were concentrated within a range of 10–50 μm (dry particulate within a range of 10–100 μm). Weekly usage amount (EI_2) to materials by-products or products such as CaC_2 dust, VCM, PVC dust, NaOH, HCl, 1, 2-DCE, NH_3, and Cl_2 were approximately one hundred thousand tons per year, so their EI would be assigned to five (>1,000 kg or >1,000 L), welding fume, manganese, inorganic compounds, O_3, and H_2S would be assigned to one (almost negligible usage amount < 1 kg/ < 1L). Further, the worker's weekly contact time (EI_3) to NaOH, HCl, H_2S, Cl_2, and H_2S was assigned to 1 (<8 h), as it was relatively short, as much as 3.5 h, while other hazards were assigned to 2 (≥8 h, <16 h) or to 3(≥16 h, <24 h), as it ranged from 10.5 to 24.5 h. Hazard control measures were, respectively assigned to relevant values in terms of the on-site survey. (5) The ratio of $E/(OEL \times f)$ (EI_9) was assigned to certain values based on C_{TWA} or C_M.

Comparative results in Y showed that while positions such as steam stripping, outward processing, VCM polymerization, welding, and repairing declined to medium risk in 2021 from high risk in 2020, ore breaking and acetylene generation decreased to low risk in 2021 from medium ones in 2020, other positions like chemical reaction (medium), refrigeration (low), product packaging (low), the laboratory technician (medium), or sewage cleaning (medium) remained unchanged, even though risk levels affected by Cl_2, HCl, NaOH, and H_2S were reduced to low risks in 2021. Vertically, it should be noted that significant differences in risk levels were observed at positions in Y ($Z = 1.62$, $P = 0.011$) between 2020 and 2021, while no such alteration was found in Z ($P > 0.05$), as Tables 6, 7 showed.

Implementation of the ICMM model

Hazard consequence (C) was based on the severity of harm or damage that occurred at workplaces. In this case, C caused by CaC_2 dust, PVC dust, welding fume, VCM, HCl, NaOH, 1, 2-DCE, and manganese, and inorganic compounds would cause major disabilities (C = 50), NH_3 and O_3 might cause serious illness or be absent for longer than 14 days (C = 15), and Cl_2 and H_2S were hazardous gases that would cause one or more fatalities (C = 100) even at a minimum concentration. U was determined to be certain (U = 1) throughout the hazards exposed by workers from Y and Z, before and after improvement.

Furthermore, PrE of HCl, NaOH, and Cl_2 was assigned to the grade "conceivable" but "very unlikely" or "only remotely possible" (PrE = 0.5 or 1) as hazards like these were auxiliary materials in catalysis or neutralization reactions or were frequently used in a laboratory test. Meanwhile, PrE of CaC_2 dust and VCM would be assigned to "continuously exceeding" (PrE = 10) as C_{TWA} had exceeded the relevant OEL, and PrE of other hazards would be assigned to "unusual but possible or intermittently" (PrE = 3 or 6). PeE of different hazards would be assigned in terms of the exposure period.

The only risk level for oxychlorination changed from an intolerable one in 2020 to a very high one in 2020, while other positions remained unchanged at very high or intolerable risks, respectively. In addition, positions would be at high or very high risk when exposed to strong acids, alkalis, or highly toxic substances, such as Cl_2, HCl, NaOH, NH_3, and

TABLE 6 Comparison results among three risk assessment models in 2020.

Positions	Hazards	Semi-quantitative comprehensive index model				ICMM quantitative model						Model of occupational hazards classification at workplaces				
		HR	ER	R	Rank	C	PrE	PeE	U	R	Rank	W_M/W_D	W_B	W_L	G	Rank
Ore breaking	CaC_2 dust	3	3	3	Medium	50	10	6	1	3,000	Intolerable	1	3.5	2	7	Moderate harm
Acetylene generation	CaC_2 dust	3	3	3	Medium	50	10	10	1	5,000	Intolerable	1	1	2	2	Mild harm
Chemical synthesis	VCM	5	2	3	Medium	50	3	6	1	900	Intolerable	8	0	1.5	0	Relatively harmless
	NaOH	4	2	3	Medium	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless
Steam stripping	VCM	5	3	4	High	50	10	6	1	3,000	Intolerable	8	1.2	1.5	14	Moderate harm
Outward processing	VCM	5	3	4	High	50	10	6	1	3,000	Intolerable	8	1.5	1.5	18	Moderate harm
VCM polymerization	VCM	5	3	4	High	50	6	6	1	1,800	Intolerable	8	0	1.5	0	Relatively harmless
Refrigeration	NH_3	3	2	2	Low	15	3	6	1	270	Very high	8	0	1.5	0	Relatively harmless
Product packaging	PVC dust	3	2	2	Low	50	6	10	1	3,000	Intolerable	1	0	1.5	0	Relatively harmless
Welding and repairing	VCM	5	3	4	High	50	6	10	1	3,000	Intolerable	8	1.1	1.5	13	Moderate harm
	Welding fume	3	2	2	Low	50	3	6	1	900	Intolerable	1	0	1.5	0	Relatively harmless
	manganese and inorganic compounds	3	2	2	Low	50	3	6	1	900	Intolerable	8	0	1.5	0	Relatively harmless
	O_3	3	2	2	Low	15	3	6	1	270	Very high	1	0	1.5	0	Relatively harmless
Laboratory technician	VCM	5	2	3	Medium	50	6	6	1	1,800	Intolerable	8	0	1	0	Relatively harmless
	Cl_2	4	2	3	Medium	100	0.5	3	1	150	High	8	0	1	0	Relatively harmless
	HCl	4	2	3	Medium	50	1	3	1	150	High	4	0	1	0	Relatively harmless
	NaOH	4	2	3	Medium	50	1	3	1	150	High	4	0	1	0	Relatively harmless
Sewage cleaning	VCM	5	2	3	Medium	50	3	6	1	900	Intolerable	8	0	1.5	0	Relatively harmless
	H_2S	4	2	3	Medium	100	1	3	1	300	Very high	8	0	1.5	0	Relatively harmless
Material storage	VCM	5	2	3	Medium	50	1	6	1	300	Very high	8	0	1.5	0	Relatively harmless
	1, 2-DCE	3	2	2	Low	50	1	6	1	300	Very high	3	0	1.5	0	Relatively harmless
	HCl	4	2	3	Medium	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless
	Cl_2	4	2	3	Medium	100	0.5	3	1	150	High	8	0	1.5	0	Relatively harmless
Splitting decomposition	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	1, 2-DCE	3	2	2	Low	50	3	6	1	900	Intolerable	3	0	1.5	0	Relatively harmless
	HCl	4	2	3	Medium	50	0.5	3	1	150	High	4	0	1.5	0	Relatively harmless
	Cl_2	4	2	3	Medium	100	0.5	3	1	150	High	8	0	1.5	0	Relatively harmless
Chemical reaction	1, 2-DCE	3	2	2	Low	50	3	10	1	1,500	Intolerable	3	0	1.5	0	Relatively harmless
	Cl_2	4	2	3	Medium	100	0.5	3	1	150	High	8	0	1.5	0	Relatively harmless
	NaOH	4	2	3	Medium	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless

(Continued)

TABLE 6 (Continued)

Positions	Hazards	Semi-quantitative comprehensive index model				ICMM quantitative model						Model of occupational hazards classification at workplaces				
		HR	ER	R	Rank	C	PrE	PeE	U	R	Rank	W_M/W_D	W_B	W_L	G	Rank
Oxychlorination	1, 2-DCE	3	2	2	Low	50	3	6	1	900	Intolerable	3	0	1	0	Relatively harmless
	VCM	5	2	3	Medium	50	3	6	1	900	Intolerable	8	0	1	0	Relatively harmless
	Cl_2	4	2	3	Medium	100	0.5	3	1	150	High	8	0	1	0	Relatively harmless
Material Recycling	1, 2-DCE	3	2	2	Low	50	6	10	1	3,000	Intolerable	3	0	1.5	0	Relatively harmless
	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	HCl	4	2	3	Medium	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless
Field sampling	1, 2-DCE	3	2	2	Low	50	6	10	1	3,000	Intolerable	3	0	1.5	0	Relatively harmless
	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
Central controlling	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1	0	Relatively harmless
Maintenance	VCM	5	2	3	Medium	50	6	10	1	3,000	Intolerable	8	0	1.5	0	Relatively harmless
	1, 2-DCE	3	2	2	Low	50	6	10	1	3,000	Intolerable	3	0	1.5	0	Relatively harmless
Public engineering	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	1, 2-DCE	3	2	2	Low	50	3	10	1	1,500	Intolerable	3	0	1.5	0	Relatively harmless
	RR [median (range)]*	0.6 (0.4–0.8)[a]				0.9 (0.6–1)[b]						0.3 (0.25–0.75)[c]				

The RR [median (range)] indicated the certain risk level and the total amount of risk classification with the classification of 4 grades, as low risk ($0 < RR \leq 0.25$), medium risk ($0.25 < RR \leq 0.5$), high risk ($0.5 < RR \leq 0.75$), and extremely high risk ($0.75 < RR \leq 1$), [a]presented to 0.6 (0.4–0.8), [b]presented to 0.9 (0.6–1), [c]presented to 0.3 (0.25–0.75), *$P < 0.001$.

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TABLE 7 Comparison results among three risk assessment models in 2021.

Positions	Hazards	Semi-quantitative comprehensive index model				ICMM quantitative model						Model of occupational hazards classification at workplaces				
		HR	ER	R	Rank	C	PrE	PeE	U	R	Rank	W_M/W_D	W_B	W_L	G	Rank
Ore breaking	CaC_2 dust	3	2	2	Low	50	6	6	1	1,800	Intolerable	1	0	2	0	Relatively harmless
Acetylene generation	CaC_2 dust	3	2	2	Low	50	6	10	1	3,000	Intolerable	1	0	2	0	Relatively harmless
Chemical synthesis	VCM	5	2	3	Medium	50	3	6	1	900	Intolerable	8	0	1.5	0	Relatively harmless
	NaOH	4	1	2	Low	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless
Steam stripping	VCM	5	2	3	Medium	50	6	6	1	1,800	Intolerable	8	0	1.5	0	Relatively harmless
Outward processing	VCM	5	2	3	Medium	50	6	6	1	1,800	Intolerable	8	0	1.5	0	Relatively harmless
VCM polymerization	VCM	5	2	3	Medium	50	3	6	1	900	Intolerable	8	0	1.5	0	Relatively harmless
Refrigeration	NH_3	3	1	2	Low	15	3	6	1	270	Very high	8	0	1.5	0	Relatively harmless
Product packaging	PVC dust	3	2	2	Low	50	1	10	1	500	Intolerable	1	0	1.5	0	Relatively harmless
Welding and repairing	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	Welding fume	3	1	2	Low	50	3	6	1	900	Intolerable	1	0	1.5	0	Relatively harmless
	manganese and inorganic compounds	3	1	2	Low	50	3	6	1	900	Intolerable	8	0	1.5	0	Relatively harmless
	O_3	3	1	2	Low	15	3	6	1	270	Very high	1	0	1.5	0	Relatively harmless
Laboratory technician	VCM	5	2	3	Medium	50	3	6	1	900	Intolerable	8	0	1	0	Relatively harmless
	Cl_2	4	1	2	Low	100	0.5	3	1	150	High	8	0	1	0	Relatively harmless
	HCl	4	1	2	Low	50	1	3	1	150	High	4	0	1	0	Relatively harmless
	NaOH	4	1	2	Low	50	1	3	1	150	High	4	0	1	0	Relatively harmless
Sewage cleaning	VCM	5	2	3	Medium	50	3	6	1	900	Intolerable	8	0	1.5	0	Relatively harmless
	H_2S	4	1	2	Low	100	1	3	1	300	Very high	8	0	1.5	0	Relatively harmless
Material storage	VCM	5	2	3	Medium	50	1	6	1	300	Very high	8	0	1.5	0	Relatively harmless
	1,2-DCE	3	2	2	Low	50	1	6	1	300	Very high	3	0	1.5	0	Relatively harmless
	HCl	4	1	2	Low	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless
	Cl_2	4	1	2	Low	100	0.5	3	1	150	High	8	0	1.5	0	Relatively harmless
Splitting decomposition	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	1,2-DCE	3	2	2	Low	50	3	6	1	900	Intolerable	3	0	1.5	0	Relatively harmless
	HCl	4	1	2	Low	50	1	3	1	150	High	4	0	1.5	0	Relatively harmless
	Cl_2	4	1	2	Low	100	0.5	3	1	150	High	8	0	1.5	0	Relatively harmless
Chemical reaction	1,2-DCE	3	2	2	Low	50	3	10	1	1,500	Intolerable	3	0	1.5	0	Relatively harmless
	Cl_2	4	1	2	Low	100	0.5	3	1	150	High	8	0	1.5	0	Relatively harmless
	NaOH	4	1	2	Low	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless

(Continued)

TABLE 7 (Continued)

Positions	Hazards	Semi-quantitative comprehensive index model				ICMM quantitative model						Model of occupational hazards classification at workplaces				
		HR	ER	R	Rank	C	PrE	PeE	U	R	Rank	W_M/W_D	W_B	W_L	G	Rank
Oxychlorination	1,2-DCE	3	2	2	Low	50	1	6	1	300	Very high	3	0	1	0	Relatively harmless
	VCM	5	2	3	Medium	50	1	6	1	300	Very high	8	0	1	0	Relatively harmless
	Cl_2	4	1	2	Low	100	0.5	3	1	150	High	8	0	1	0	Relatively harmless
Material recycling	1,2-DCE	3	2	2	Low	50	3	10	1	1,500	Intolerable	3	0	1.5	0	Relatively harmless
	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	HCl	4	1	2	Low	50	0.5	3	1	75	High	4	0	1.5	0	Relatively harmless
Field sampling	1,2-DCE	3	2	2	Low	50	3	10	1	1,500	Intolerable	3	0	1.5	0	Relatively harmless
	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
Central controlling	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1	0	Relatively harmless
Maintenance	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	1,2-DCE	3	2	2	Low	50	3	10	1	1,500	Intolerable	3	0	1.5	0	Relatively harmless
Public engineering	VCM	5	2	3	Medium	50	3	10	1	1,500	Intolerable	8	0	1.5	0	Relatively harmless
	1,2-DCE	3	2	2	Low	50	3	10	1	1,500	Intolerable	3	0	1.5	0	Relatively harmless
	RR [median (range)]*			0.5 (0.4–0.6)[a]					0.9 (0.6–1)[b]					0.25[c]		

The RR [median (range)] indicated the certain risk level and the total amount of risk classification with the classification of 4 grades, as low risk ($0 < RR \leq 0.25$), medium risk ($0.25 < RR \leq 0.5$), high risk ($0.5 < RR \leq 0.75$), and extremely high risk ($0.75 < RR \leq 1$), [a]presented to 0.5 (0.4–0.6), [b]presented to 0.9 (0.6–1), [c]presented to 0.25, *$P < 0.001$.

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H_2S concurrently or any of them alternatively. No significant difference in risk levels among positions in Y or Z was found before and after improvement ($P > 0.05$) using the ICMM model, as shown in Tables 6, 7.

Classification of occupational hazards at workplaces

According to a previous survey, the crystalline free silica content (M%) of CaC_2 dust, PVC dust, and welding fume were estimated to be lower than 10%, as they did not contain many silicates; thus, their $W_M$would be assigned to level 1(M < 10%). As regards chemical agents, the hazardous toxicant index (THI) of O_3 was at mild harm (THI < 35) in terms of the calculation equation in GBZ 230-2010; therefore, the $W_D$would also be assigned to level 1 (mild harm). Then Cl_2, NH_3, H_2S, VCM, manganese, and inorganic compounds were all hazards on the *Catalogue of Highly Toxic Substances (2003)* (38), *and* their $W_D$would be assigned to 8 (extreme harm); HCl and NaOH would be assigned to 4 (severe harm), as their THI was in the range of severe harm (50 ≤ THI < 65). In addition, $W_B$and $W_L$were, respectively, assigned according to CM or CTWA and manual labor intensity. Positions included ore breaking, acetylene generation, steam stripping, outward processing, welding, and repairing, which were adjusted to relatively harmless in 2021 from mild or moderate harm in 2020. No significant difference in risk classification for positions throughout Y or Z was found between 2020 and 2021 ($P > 0.05$), as Tables 6, 7 show.

Comparison results of different models

The ICMM quantitative model achieved the highest RR of 0.9 (0.6–1.0) in both 2020 and 2021, followed by the semi-quantitative comprehensive index model of 0.6 (0.4–0.8) and 0.5 (0.4–0.6); subsequently, the model of occupational hazards classification at workplaces was at the lowest at 0.3 (0.25–0.75) and 0.25. Significant differences in RR among models in 2020 ($Z = 19.21$, $P < 0.001$) and 2021 ($Z = 16.01$, $P < 0.001$) were observed, respectively. It could be observed that the risk levels using the ICMM model could be frequently elevated to very high or intolerable levels, leading to an overestimated evaluation that would exaggerate the real risk points (39), as indicated in Figure 2.

Analysis of physical examination results

Abnormal rate analysis for liver ultrasound

Given that risk assessment levels toward several positions in Y and Z were found to be different before and after improvements in protective measures from 2020 to 2021. How this effect could be related to physical health status in terms of liver function remains unknown yet. To discover possible alterations toward fatty liver and other hepatic symptoms in liver ultrasound results between 2020 and 2021, abnormal rates (%) were visualized in Figures 3A,B, and data were compared in Tables 8–10. Primarily, it should be noted that the majority of positions in Y and Z showed alterations toward abnormal rates to a different extent. However, significant differences containing fatty liver and other hepatic symptoms were only found in Y ($X^2 = 10.19$, $P < 0.001$) between 2020 and 2021, and no such changes were ever discovered under a bilateral interaction for year and position categories ($P > 0.05$).

And then, in Y, positions referring to increased abnormal rates of fatty liver from 2020 to 2021 touched on acetylene generation (31.1%), welding and repairing (21.2%), or breaking (9.9%), chemical synthesis (7.9%), and steam stripping (2.9%), while sewage cleaning (18.0%), product packaging (7.9%), refrigeration (6.2%), VCM polymerization (5.1%), and outward processing (2.3%) exhibited a decreased tendency, and the laboratory technician (a 0.2% decrease) remained roughly unchanged. With regard to other hepatic symptoms, abnormal rates of most positions in Y exhibited a declining trend except ore breaking (a 0.3% increase) and acetylene generation (0.0%), as Figure 3A presented.

By contrast, in Z, positions of maintenance (25.0%), central control (21.9%), material recycling (17.2%), field sampling (5.9%), and public engineering (1.9%) maintained an increasing trend in abnormal rates toward the fatty liver, while chemical reaction (20.0%), splitting decomposition (15.8%), oxychlorination (11.9%), as well as material storage (7.4%), were in an opposite orientation. As for other hepatic symptoms, material storage (5.9%), a chemical reaction (5.0%), splitting decomposition (2.6%), oxychlorination (2.4%), and central control (2.3%) revealed a slightly dropped tendency, while field sampling presented a slight increase of 2.9%, while others like material recycling (0.0%), maintenance (0.0%), and public engineering (0.4%) kept unchanged, as Figure 3B shows.

Analysis of multiple linear regression

This part is intended to evaluate independent variables that might contribute to fatty liver and other hepatic symptoms in both 2020 and 2021 by using multiple linear regression analysis. In Tables 8–10, the variable for males made a straight contribution to fatty liver and other hepatic symptoms in Y and Z for 2 years. Concretely, it played a role in the fatty liver [($Exp(B) = 3.052$, 95% CI = 1.396–6.669, $P = 0.005$) in 2020, ($Exp(B) = 3.574$, 95%CI = 2.718–5.568, $P < 0.001$) in 2021] and to other hepatic symptoms [($Exp(B) = 6.055$, 95% CI = 1.620–12.627, $P = 0.007$) in 2020, ($Exp(B) = 3.276$, 95% CI = 0.987–5.026, $P = 0.004$) in 2021] in Y as compared to women; in Z, a similar effect to the fatty liver [($Exp(B) = 1.248$, 95% CI = 0.372–1.505, $P = 0.006$) in 2020, ($Exp(B) = 1.570$, 95% CI = 0.331–1.699, $P = 0.004$) in 2021] and other hepatic

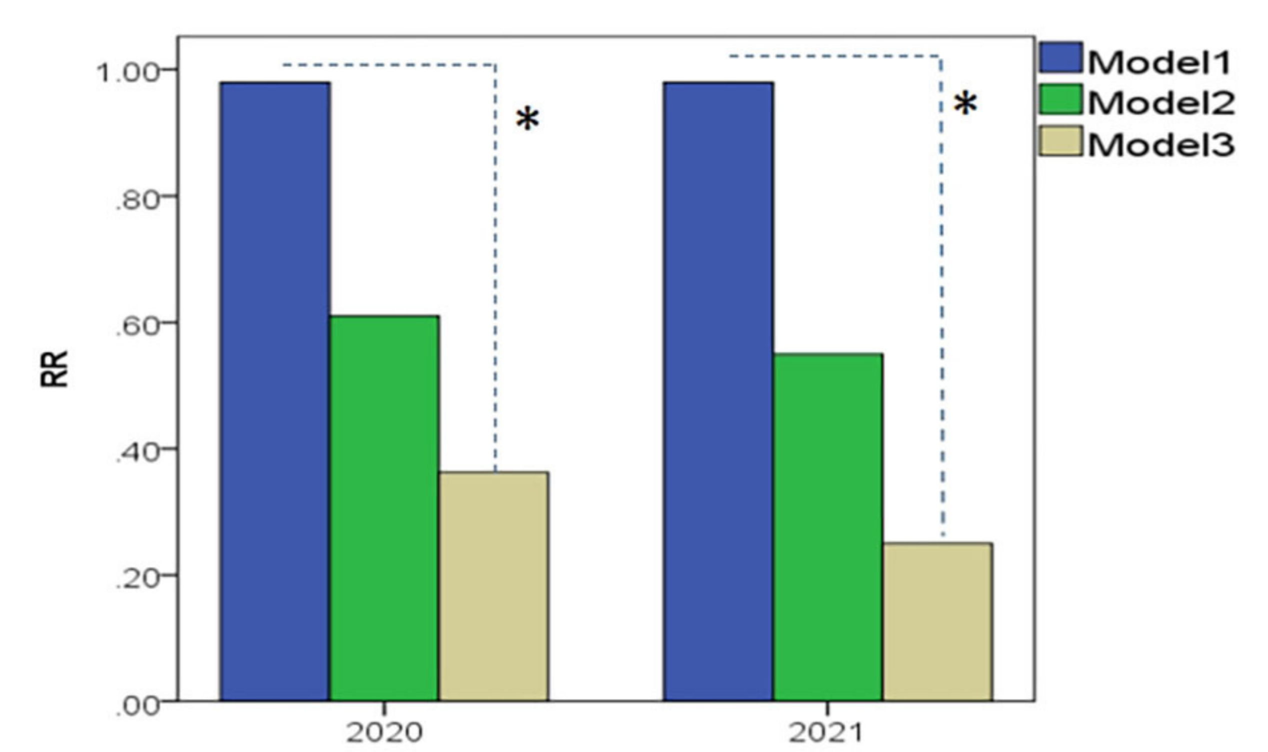

FIGURE 2
Comparison results of RR among Model 1–3, as they, respectively, represented to ICMM quantitative model, the semi-quantitative comprehensive index model, and the model of occupational hazards classification at workplaces (industrial dust and chemical agents). Model 1: The ICMM quantitative model achieved the highest RR of 0.9 (0.6–1.0) in both 2020 and in 2021; Model 2: RR toward the semi-quantitative comprehensive index model went to 0.6 (0.4–0.8) in 2020 and 0.5 (0.4–0.6) in 2021, respectively; Model 3: the model of occupational hazards classification at workplaces left to the lowest of 0.3 (0.25–0.75) and 0.25. $^{*}P < 0.001$ as significant differences of RR among models were compared.

symptoms [(*Exp(B)* = 1.440, 95% CI = 0.204–1.950, $P = 0.007$) in 2020 (*Exp(B)* = 1.937, 95% CI = 0.352–2.495, $P = 0.006$) in 2021] was observed as compared to women.

In Y, variables such as ALT, AST, GGT, TG, and TC were influential factors that contributed to fatty liver in 2020, and in left-handed males, TG and TC had a similar effect in 2021. In the meantime, variables such as ALT, AST, and GGT contributed to other hepatic symptoms in 2020, and no such effect was spotted in 2021 anymore. In Z, only the variables TG and TC contributed to the fatty liver, while ALT and AST contributed to other hepatic symptoms, and these indicators lasted through 2020 and 2021. Next, not surprisingly, variables TG and TC were only found to contribute to fatty liver in Y and Z in both 2020 and 2021, and no such effect was found on other hepatic symptoms. In particular, variables such as ALT, AST, and GGT in Y were observed to contribute to the fatty liver [ALT (*Exp(B)* = 1.159, 95% CI = 1.050–1.278, $P = 0.003$); AST (*Exp(B)* = 0.878, 95% CI = 0.790–0.977, $P = 0.017$); GGT (*Exp(B)* = 1.010, 95% CI = 1.013–1.047, $P = 0.021$)] and to other hepatic symptoms [ALT (*Exp(B)* = 1.187, *95%CI* = 1.070-1.318, $P = 0.001$); AST (*Exp(B)* = 1.153, 95% CI = 0.754–1.965, $P = 0.012$); GGT (*Exp(B)* = 1.022, 95% CI = 1.003–1.040, $P = 0.019$)] in 2020. In contrast, ALT and AST played an important role in Z only for other hepatic symptoms in both 2020 [ALT (*Exp(B)* = 1.012, 95% CI = 0.906–1.063, $P = 0.025$); AST(*Exp(B)* = 1.033, 95% CI = 0.925–1.153, $P = 0.036$)] and 2021 [ALT(*Exp(B)* = 1.084, 95% CI = 0.966–1.199, $P = 0.040$); AST (*Exp(B)* = 1.006, 95% CI = 0.978–1.034, $P = 0.025$)].

Analysis of liver function indicators

As the results above show, indicators such as ALT, AST, GGT, TG, and TC played pivotal roles in contributing to fatty liver and other hepatic symptoms. These differences still needed to be discovered in terms of what positions they could significantly affect. The box charts in Figures 4A,C,E,G,I, 5A,C,E,G illustrate the quantitative distribution differences of indicators toward positions in Y and Z between 2020 and 2021. In that regard, significant disparity toward ALT, AST, and GGT in Y involved ore breaking, steam stripping, VCM polymerization, outward processing, product packaging, welding, and repairing, while similar discrepancy toward ALT and AST in Z referred to material storage, chemical reactions, field sampling, oxychlorination, material recycling, and

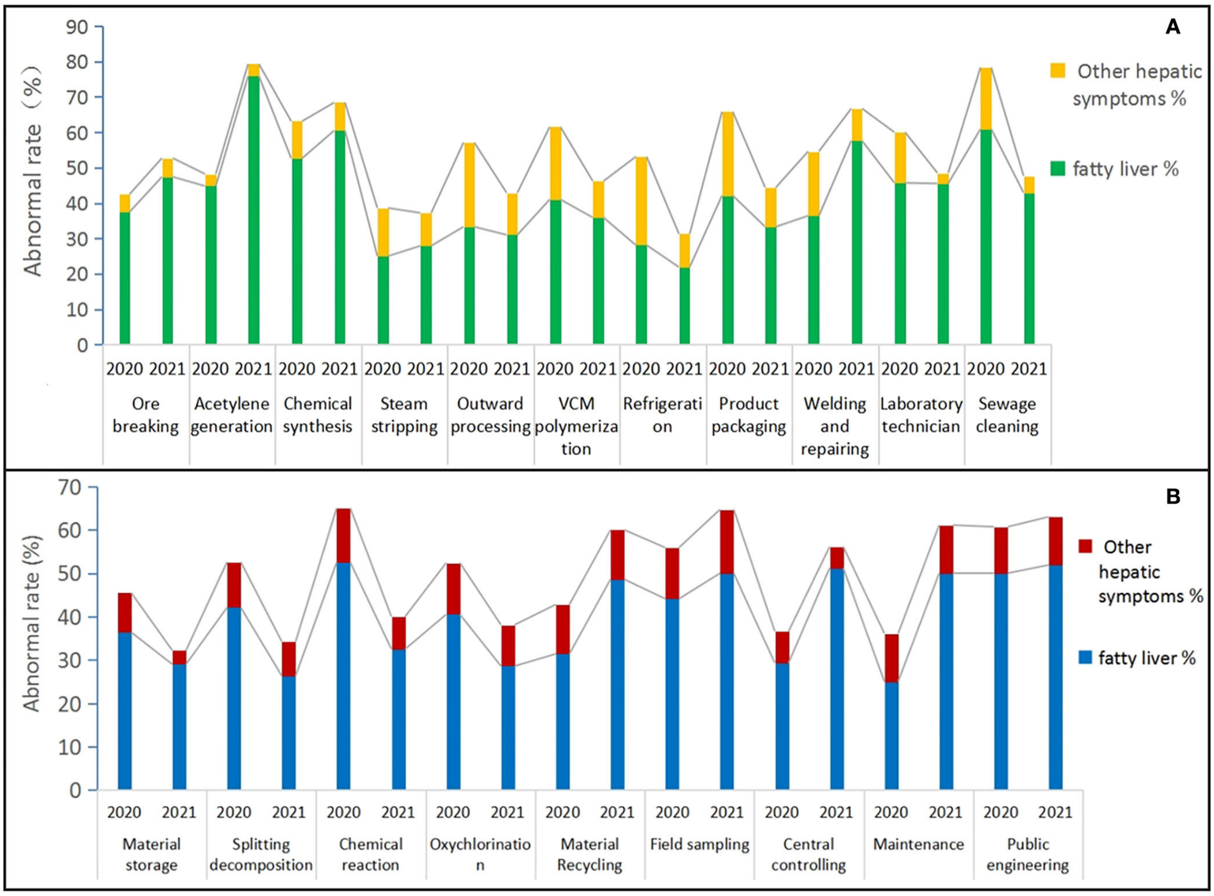

FIGURE 3
Abnormal rates of alteration toward fatty liver and the other hepatic symptoms among all positions throughout Y and Z between 2020 and 2021 were visualized in histograms **(A,B)**. That chart **(A)** described the distribution of abnormal rates of fatty liver (green) and the other hepatic symptoms (yellow) for 11 positions in Y; Chart **(B)** presented the distribution of abnormal rates of fatty liver (blue) and the other hepatic symptoms (red) for nine positions in Z. Abnormal rates (%) for each position were, respectively, calculated through dividing the abnormal person-time of fatty liver or other hepatic symptoms to the total number of each relevant position.

maintenance. Furthermore, by utilizing analysis of multivariate ANOVA analysis, we observed significant differences among variables such as ALT ($F = 5.12$, $P < 0.001$), AST ($F = 3.31$, $P < 0.001$), and GGT ($F = 4.42$, $P < 0.001$) in Y using a bilateral interaction for a year and position categories, but no such influence was found in TG ($F = 0.68$, $P > 0.05$) or TC ($F = 0.80$, $P > 0.05$). Specifically, the *LSD* test further indicated that positions of outward processing ($P = 0.002$, $P = 0.026$, $P = 0.003$), VCM polymerization ($P = 0.011$, $P = 0.026$, $P = 0.020$), steam stripping ($P = 0.020$, $P = 0.010$, $P = 0.016$), and product packaging ($P = 0.027$, $P = 0.028$, $P = 0.011$) demonstrated differences on ALT, AST, and GGT at the same time as compared to others, as shown in Figures 4B,D,F,H,J.

In contrast, this bilateral interaction in Z presented significant differences in ALT ($F = 7.50$, $P < 0.001$) and AST ($F = 4.04$, $P < 0.001$), and no such effect was found in TG ($F = 0.64$, $P > 0.05$) and TC ($F = 0.58$, $P > 0.05$). Positions of material storage ($P = 0.004$, $P = 0.002$), field sampling ($P = 0.011$, $P = 0.004$), oxychlorination ($P = 0.003$, $P = 0.011$), maintenance ($P = 0.008$, $P = 0.033$), and material recycling ($P = 0.003$, $P = 0.009$) were displayed simultaneous differences in ALT and AST as compared to other positions, as Figures 5B,D,F,H present.

Overall, it could be inferred that positions such as steam stripping, outward processing, VCM polymerization, and product packaging in Y had abnormal rate alterations in fatty liver and other hepatic symptoms that significantly differed in ALT, AST, and GGT simultaneously and that these positions also indicated a reduced risk assessment level alteration using the semi-quantitative comprehensive index model. By comparison, positions of material storage, oxychlorination, material recycling, and field sampling in Z significantly differed in ALT and AST with similar changes, as positions were not in line with risk assessment levels, as no significant changes were

TABLE 8 Results of multiple linear regression analysis for physical exam data in Y in 2020 and 2021.

Liver ultrasound	Factors	2020 ($n = 393$)						2021 ($n = 384$)					
		B	*SE*	*Wald* X^2	*P*	*Exp(B)*	*95% CI*	*B*	*SE*	*Wald* X^2	*P*	*Exp(B)*	95% CI
Fatty liver	Male	1.116	0.399	7.823	0.005*	3.052	1.396–6.669	1.274	0.253	25.404	0.000**	3.574	2.178–5.568
	Female	0.123	0.054	0.839	0.360	1.131	0.390–3.281	0.470	0.072	0.468	0.206	1.600	1.142–2.242
	Age	0.056	0.017	0.974	0.201	1.058	1.023–1.093	0.004	0.013	0.073	0.787	1.004	0.978–1.030
	ALT	0.147	0.050	8.630	0.003*	1.159	1.050–1.278	−0.005	0.016	0.113	0.737	0.995	0.964–1.027
	AST	−0.130	0.054	5.728	0.017*	0.878	0.790–0.977	0.007	0.009	0.599	0.439	1.007	0.989–1.025
	GGT	0.030	0.008	4.495	0.021*	1.010	1.013–1.047	0.000	0.008	0.001	0.975	1.000	0.984–1.016
	ALP	0.011	0.007	2.407	0.121	1.011	0.997–1.025	−0.018	0.021	0.699	0.403	0.982	0.942–1.024
	TBIL	−0.012	0.021	0.329	0.566	0.988	0.947–1.030	0.174	0.234	4.100	0.143	1.206	1.015–2.541
	TG	0.590	0.286	4.253	0.009*	1.803	1.030–3.159	0.546	0.328	4.223	0.016*	1.216	0.529–1.912
	TC	0.440	0.160	3.761	0.018*	1.250	0.840–1.574	0.340	0.127	2.362	0.021*	1.244	0.921–1.631
Other hepatic symptoms	Male	1.801	0.673	7.169	0.007*	6.055	1.620–12.627	1.116	0.009	0.248	0.004*	3.276	0.987–3.026
	Female	0.084	0.588	0.416	0.519	1.373	0.524–3.596	−0.005	0.024	0.049	0.825	0.995	0.950–1.042
	Age	0.029	0.022	2.530	0.346	1.127	1.079–1.177	0.012	0.020	0.362	0.548	1.012	0.973–1.053
	ALT	0.172	0.053	10.368	0.001*	1.187	1.070–1.318	0.024	0.074	5.548	0.119	3.052	1.206–7.724
	AST	−0.159	0.063	6.359	0.012*	0.853	0.754–0.965	0.019	0.057	3.839	0.136	1.521	0.620–3.725
	GGT	0.021	0.009	5.476	0.019*	1.022	1.003–1.040	0.002	0.015	0.010	0.920	1.002	0.972–1.032
	ALP	−0.002	0.012	0.036	0.849	0.998	0.982–1.015	0.003	0.018	0.014	0.906	1.010	0.968–1.037
	TBIL	0.002	0.027	0.006	0.940	1.002	0.951–1.055	0.005	0.010	0.247	0.620	1.005	0.985–1.026
	TG	0.177	0.347	0.259	0.611	1.193	0.604–2.356	0.222	0.409	0.295	0.587	1.249	0.561–2.781
	TC	−0.024	0.201	0.015	0.904	0.976	0.658–1.448	0.134	0.202	0.345	0.198	1.202	0.918–2.142

*Presented to $P < 0.05$, **presented to $P < 0.001$.

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TABLE 9 Results of multiple linear regression analysis for physical exam data in Z in 2020 and 2021.

Liver ultrasound	Factors	2020 ($n = 327$)						2021 ($n = 324$)					
		B	*SE*	*Wald* X^2	*P*	*Exp(B)*	*95% CI*	*B*	*SE*	*Wald* X^2	*P*	*Exp (B)*	95% CI
Fatty liver	Male	−0.290	0.356	5.662	0.006*	1.248	0.372–1.505	−0.287	0.417	4.474	0.004*	1.570	0.331–1.699
	Female	−0.049	0.125	0.489	0.312	0.637	0.442–1.291	−0.026	0.043	0.396	0.412	0.787	0.641–1.184
	Age	−0.055	0.019	2.230	0.212	0.937	0.902–0.973	−0.041	0.018	1.081	0.124	0.960	0.927–0.995
	ALT	0.013	0.028	0.221	0.638	1.013	0.959–1.071	−0.028	0.008	3.979	0.064	0.962	0.958–0.987
	AST	0.006	0.039	0.020	0.886	1.006	0.931–1.086	0.019	0.012	2.589	0.108	1.020	0.996–1.044
	GGT	−0.002	0.008	0.038	0.846	0.998	0.983–1.014	−0.012	0.008	2.244	0.134	0.988	0.972–1.004
	ALP	0.004	0.007	0.336	0.562	1.004	0.991–1.018	0.011	0.007	2.458	0.117	1.011	0.997–1.026
	TBIL	0.010	0.035	0.082	0.774	1.010	0.944–1.081	0.012	0.035	0.123	0.725	1.012	0.946–1.083
	TG	0.651	0.179	9.415	0.002*	1.734	1.220–2.465	0.462	0.174	7.006	0.008*	1.587	1.127–2.234
	TC	0.512	0.267	3.605	0.035*	1.336	0.891–1.715	0.382	0.168	6.826	0.033*	1.526	0.954–1.843
Other hepatic symptoms	Male	−0.020	0.392	4.372	0.007*	1.440	0.204–1.950	−0.066	0.500	4.017	0.006*	1.937	0.352–2.495
	Female	−0.019	0.028	0.429	0.310	0.882	0.735–1.008	−0.022	0.019	0.513	0.329	0.871	0.632–1.278
	Age	−0.033	0.023	2.093	0.148	0.967	0.925–1.012	−0.010	0.021	0.220	0.639	0.990	0.950–1.032
	ALT	−0.049	0.041	4.206	0.025*	1.012	0.906–1.063	−0.018	0.009	4.237	0.040*	1.084	0.966–1.199
	AST	0.032	0.056	3.329	0.036*	1.033	0.925–1.153	0.036	0.014	4.165	0.025*	1.006	0.978–1.034
	GGT	0.000	0.010	0.000	0.983	1.000	0.981–1.019	−0.015	0.010	2.298	0.130	0.985	0.967–1.004
	ALP	−0.009	0.008	1.125	0.289	0.991	0.975–1.008	0.006	0.008	0.520	0.471	1.006	0.990–1.022
	TBIL	0.018	0.040	0.209	0.648	1.018	0.941–1.012	0.018	0.040	0.199	0.656	1.018	0.941–1.102
	TG	0.369	0.200	3.415	0.065	1.447	0.978–2.141	0.297	0.195	2.323	0.127	1.345	0.919–1.970
	TC	0.290	0.193	2.263	0.133	1.336	0.916–1.949	0.358	0.191	3.501	0.061	1.430	0.983–2.080

*Presented to $P < 0.05$.

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TABLE 10 Results of liver ultrasound analysis in Y and Z between 2020 and 2021.

Factories	Positions	2020					2021					X^2, *P*-value
		n	Fatty liver		Other hepatic symptoms		*n*	Fatty liver		Other hepatic symptoms		
			Abnormal[a]	%	Abnormal[b]	%		Abnormal[c]	%	Abnormal[d]	%	
Y2020($n = 393$);2021($n = 384$)	Ore breaking	40	15	37.5	2	5.0	38	18	47.4	2	5.3	0.03, 0.86
	Acetylene generation	29	13	44.8	1	3.4	29	22	75.9	1	3.4	0.13, 0.72
	Chemical synthesis	38	20	52.6	4	10.5	38	23	60.5	3	7.9	0.27, 0.60
	Steam stripping	44	11	25.0	6	13.6	43	12	27.9	4	9.3	0.41, 0.52
	Outward processing	42	14	33.3	10	23.8	42	13	31.0	5	11.9	0.86, 0.35
	VCM polymerization	39	16	41.0	8	20.5	39	14	35.9	4	10.3	0.62, 0.43
	Refrigeration	32	9	28.1	8	25.0	32	7	21.9	3	9.4	0.76, 0.38
	Product packaging	38	16	42.1	9	23.7	36	12	33.3	4	11.1	0.55, 0.46
	Welding and repairing	33	12	36.4	6	18.2	33	19	57.6	3	9.1	2.20, 0.13
	Laboratory technician	35	16	45.7	5	14.3	33	15	45.5	1	3.0	2.06, 0.15
	Sewage cleaning	23	14	60.9	4	17.4	21	9	42.9	1	4.8	0.66, 0.42
	Total	393	156	39.7	64	16.3	384	164	42.7	31	8.1	10.19, < 0.001*
Z2020($n = 327$);2021($n = 324$)	Material storage	33	12	36.4	3	9.1	31	9	29.0	1	3.2	0.45, 0.50
	Splitting decomposition	38	16	42.1	4	10.5	38	10	26.3	3	7.9	0.05, 0.83
	Chemical reaction	40	21	52.5	5	12.5	40	14	32.5	3	7.5	0.02, 0.90
	Oxychlorination	42	17	40.5	5	11.9	42	12	28.6	4	9.5	0.03, 0.87
	Material Recycling	35	11	31.4	4	11.4	35	16	48.6	4	11.4	0.22, 0.64
	Field sampling	34	15	44.1	4	11.8	34	17	50.0	5	14.7	0.02, 0.90
	Central controlling	41	12	29.3	3	7.3	41	21	51.2	2	4.9	1.02, 0.31
	Maintenance	36	10	25.0	4	11.1	36	18	50.0	4	11.1	0.73, 0.49
	Public engineering	28	13	50.0	3	10.7	27	14	51.9	3	11.1	0.01, 0.94
	Total	327	127	38.8	35	10.7	324	131	40.4	29	9.0	0.61, 0.43

*Referred to $P < 0.001$ as compared to abnormal rates of fatty liver and other hepatic symptoms between 2020 and 2021, [a]indicated the abnormal number of fatty liver among positions in 2020, [b]indicated the abnormal number of other hepatic symptoms among positions in 2020; [c]indicated to the abnormal number of fatty liver among positions in 2021, and [d]indicated to the abnormal number of other hepatic symptoms among positions in 2021.

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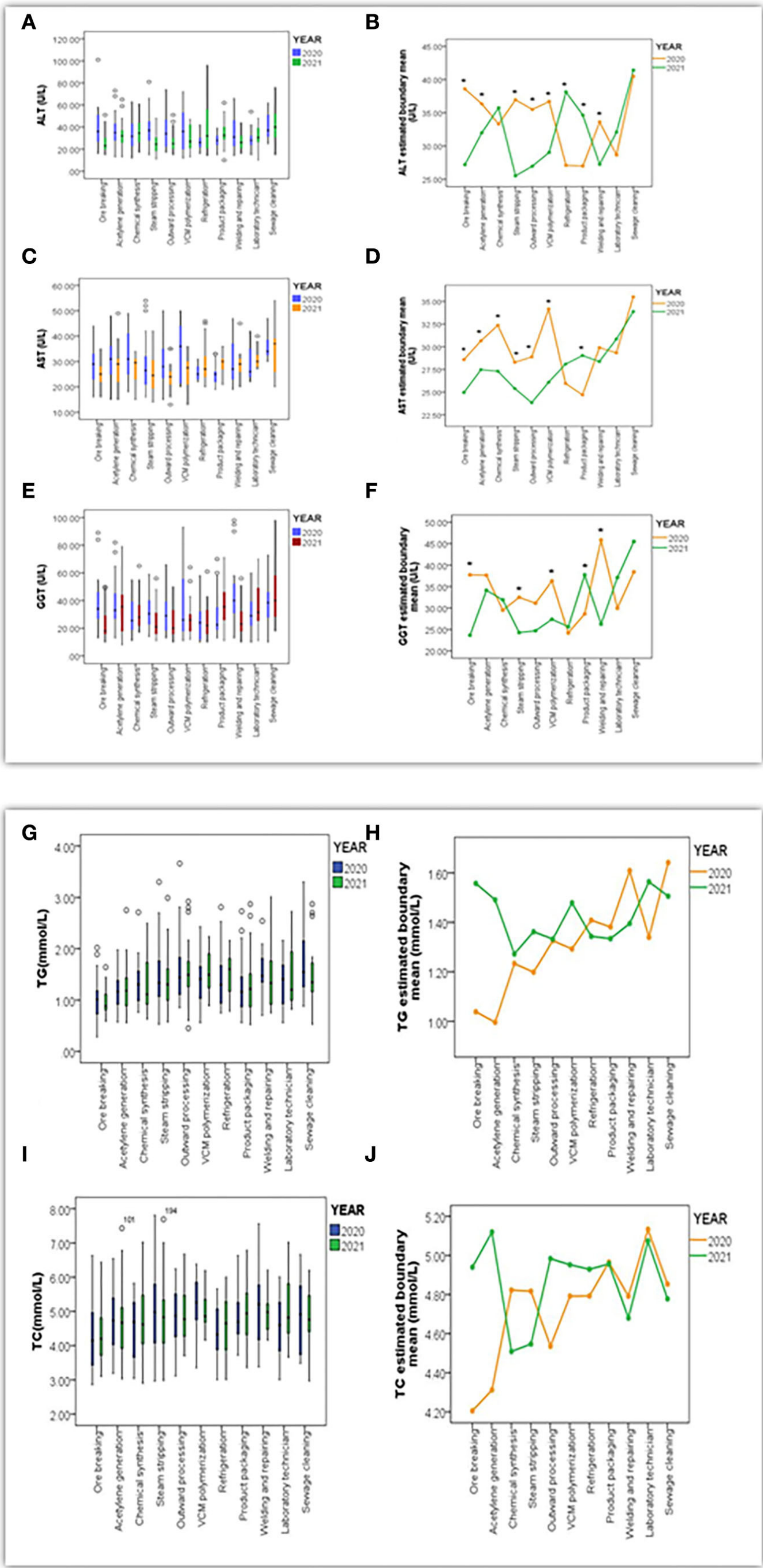

FIGURE 4
Box charts **(A,C,E,G,I)** presented the quantitative distribution extent of variables in ALT (U/L), AST (U/L), GGT (U/L), TG (mmol/L) and TC (mmol/L) throughout positions in Y between 2020 and 2021; Line Charts **(B,D,F,H,J)** indicated differentiation of estimated boundary mean for ALT, AST, GGT, TG, and TC under the bilateral interaction effect between year and position (*referred to $P < 0.05$ when differences of variables were significant).

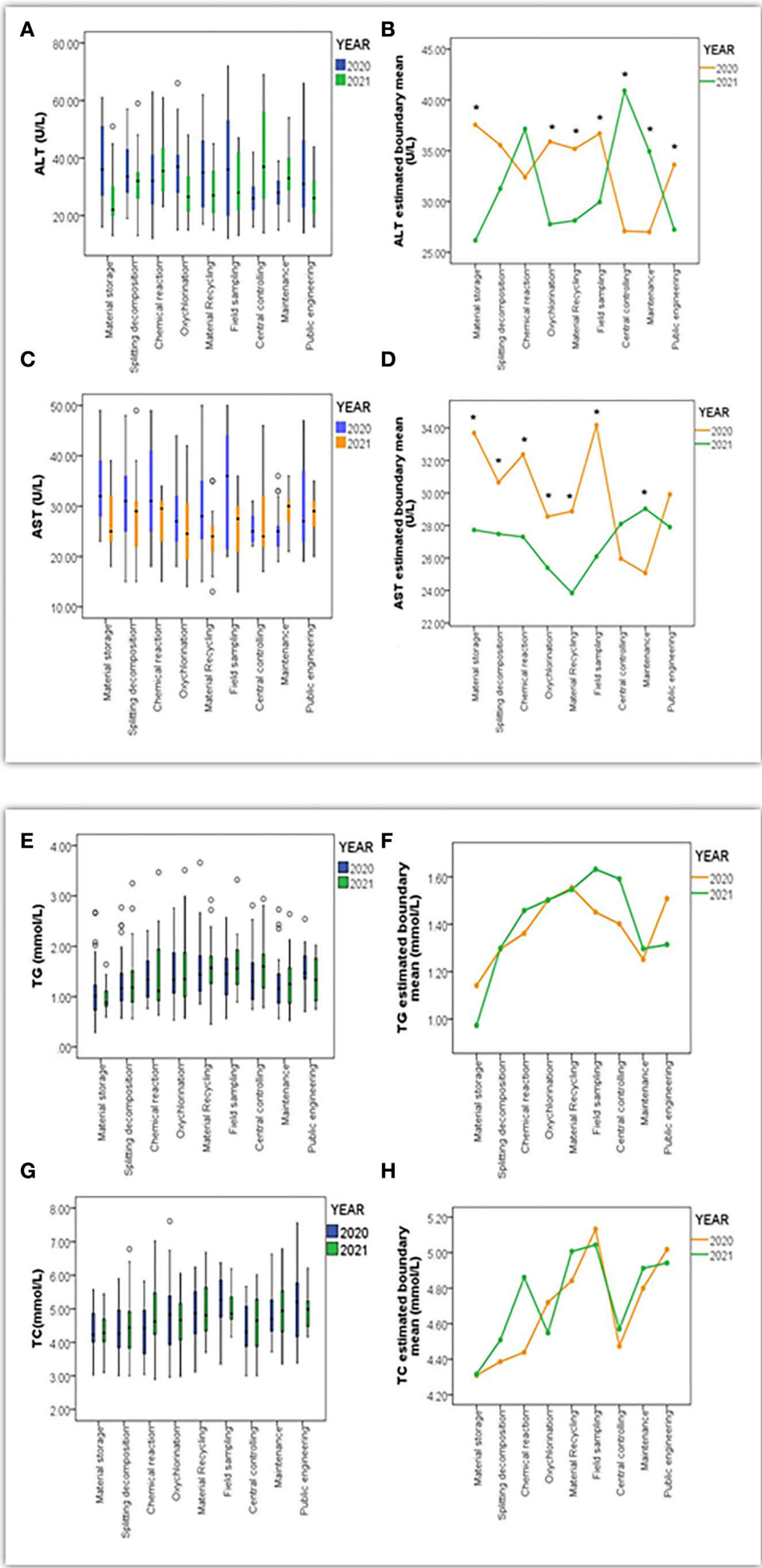

FIGURE 5
Box charts **(A,C,E,G)** presented the quantitative distribution extent of variables in ALT (U/L) and AST (U/L), TG (mmol/L), and TC (mmol/L) throughout positions in Z between 2020 and 2021. Line Chart **(B,D,F,H)** indicated differentiation of estimated boundary mean for ALT, AST, TG, and TC under a bilateral interaction effect between year and position (*referred to $P < 0.05$ when differences among variables were significant).

found before and after improvement. Besides, TG and TC were not critical variables to affect the fatty liver, especially when differences were statistically analyzed simultaneously under year and position classification.

Discussion

Nowadays, techniques of acetylene hydrochlorination are still the predominant processes for VCM synthesis and PVC production, with the advantages of abundant resources, low investment, and high return. However, the replacement of ethylene oxychlorination has been overwhelming because of the disadvantages of high energy consumption and heavy contamination of the environment. The technique of ethylene oxychlorination still has a long way to go before it can substitute for the former one, given the requirement of high-tech equipment and enormous amounts of imported ethylene as the raw material (40). Under these circumstances, improvements in protective measures and technology upgrades are urgently required to facilitate development, innovation, environmental protection, and labor health. Thus, we were interested to discover whether improvement implementation could work effectively on positions' risk assessment levels and liver health status.

According to the studies at home or abroad, VCM and PVC dust were major hazards from others that imposed adverse effects on workers' health, and the correlation of eternal concentration with the related incidence of ASL and HCC has already been linked. For example, Pirastu, R (41) found that inhaled PVC dust (particularly with an aerodynamic diameter of <5 mm) may remain in the pulmonary interstitium for years and gradually release residual VCM, which may account for the neoplastic transformation of an epithelial cell. Facciolà et al. (42) discovered that some laboratory studies revealed the pathogenic role of PVC and revealed the link between exposure to PVC dust and both non-malignant and malignant lung disease. Despite the low reactivity, the number of surface area atoms per unit mass was high for PVC dust, greatly enhancing the surface area for chemical reactions with bodily fluids and tissue in direct contact, resulting in persistent inflammation that led to pulmonary fibrosis or even carcinogenesis. In an Italian cohort of 1,658 workers from a VCM/PVC plant in Porto Marghera (Venice, Veneto Region, Italy), Ugo Fedeli and Paolo Girardi found an increased risk of stomach cancer (SMR 1.53, CI 1.06–2.19) and a high rate of liver cancer (57 observed deaths; SMR 2.30, CI 1.78–2.99). Mortality from liver cancer was consistently increased through the follow-up: SMRs were 2.09 (1.33–3.27), 2.80 (1.79–4.39), and 2.15 (1.37–3.36) across subsequent calendar periods (1973–1999, 2000–2007, 2008–2017, with 19 observed liver cancer deaths in each period. Besides, out of 56 deaths from all causes observed among workers with cumulative exposure above 5,188 ppm-years, 12 (21%) were identified as primary liver cancer with clinical or histological confirmation, reporting six HCC and six ASL cases. The SMR for lung cancer was 1.73 (90% confidence interval 0.93–3.21) among "only baggers"; the ratio between the SMR for "only baggers" and that for "never baggers" was 2.31 (90% CI: 1.15–4.61) (43). In a re-analysis of mortality data from the same plant, with respect to the reference group (technicians and clerks), the lung cancer rate ratio was 3.13 (95% CI 0.96–10.28) in PVC baggers. In another case-control study nested in the same Porto Marghera cohort, 38 patients with a histological lung cancer diagnosis were compared with 224 controls without cancer. A logistic regression analysis showed an increase of 20% (odds ratio: 1.20; 95% CI: 1.07–1.35) in the risk of lung cancer for each additional year of work as a PVC packer, taking into account age and smoking. By excluding a potentially important source of bias, the adjustment for smoking strengthened the results of previous studies showing an increased risk for lung cancer among PVC baggers. Long-term exposure to high levels of PVC dust might cause pulmonary carcinogenesis through persistent alveolar inflammation, alveolar macrophage activation, and the release of growth factors (44).

Next, the demographic and occupational information in Y and Z indicated that the population distribution by gender between Y and Z was largely homogeneous, and VCM-exposed workers were under a heavy workload. Factors like long weekly working periods, frequent shift systems, sleep deprivation, or disorders might be potentially hazardous factors affecting physical health. The operation status of ventilation facilities had not reached its maximum, as temporary suspensions or fully broken systems were witnessed or described by workers on duty. It could be inferred that improving protective measures, especially the ventilation facilities, was necessary and urgent.

Afterward, improvements in protective measures in Y were implemented in 2021, mainly through the enhancement of ventilation and collection facilities as fresh air requirements and ventilation air changing rates at local plants was intensified so that ambient concentrations for VCM, PVC dust, and others were found to be declining, which could be a result of a stronger negative correlation between ventilation effects and ambient concentration in Y. On the contrary, the hazards of VCM, 1, 2DCE, and others in Z slightly declined due to improvements in sealing and airtight measures, but the magnitude of the correlation was not as significant as it was in Y. It could be inferred that improvements in protective measures in Y effectively limited hazard concentration levels, while that effect in Z was not prominent as natural ventilation was another main confounding factor that impacted air motion at workplaces.

However, it did not result in deleterious consequences from low-concentration VCM exposure, which could be ignored even if the ambient concentration was successfully reduced. More research found that low-concentration VCM exposure would induce health issues. For example, in a US cohort, based on 32 cases of HCC identified from death certificates, mortality rates did not increase, except for the highest quintile of cumulative exposure (≥2,271 ppm-years). However, after exposures were lagged by 30 years, HCC mortality significantly increased already in the 865–2,271 ppm-years class (45). In the European cohort of vinyl chloride workers, increased liver cancer risk (all types) with increasing exposure was confirmed in analyses restricted to subjects with cumulative exposure < 1,500 ppm-years. In an Italian cohort, an approach based on non-parametric regression was adopted to model in continuous form the relationship between exposure and mortality, considering 31 confirmed HCC cases; HCC mortality rates were found to increase with cumulative VCM exposure already in the range below 2,000 ppm-years (43).

Moreover, for the sake of screening out typical positions that could encounter health risks under different techniques and discovering whether differences in risk levels before and after improvements in protective measures might exist, three semi-quantitative risk assessment models were applied. The results showed that the semi-quantitative comprehensive index model significantly differed in risk level alterations before and after improvements in Y ($Z = 1.62$, $P = 0.011$), and no such alterations were ever observed from models of ICMM and occupational hazards classification at workplaces. In that, assessment levels concerning ore breaking and acetylene generation declined to low risk in 2021 from medium risk in 2020, the risk of steam stripping, outward processing, VCM polymerization, welding, and repairing dropped to medium risk from high risk in 2020, and others like refrigeration (low), product packaging (low), and the laboratory technician (medium) remained unchanged before and after improvement, even if risk levels under exposure to Cl_2, HCl, NaOH, and H_2S all reduced to low risk in 2021 from medium ones in 2020. These may stem from models' advantages and limitations in terms of methodological principles. Concretely, the semi-quantitative comprehensive index model was originally converted from the risk assessment of Singapore model from OHRA and incorporated into the Chinese national guideline for occupational health risk assessment (GBZ 298-2017) with adjusted modifications. More than that, it developed its own comprehensive advantages by taking ambient concentration, protective measures, emergency rescue measures, and other semi-quantitative factors into account, which made risk levels more tightly bound with practical situations and more subjected to present alteration once hardware improvements or innovative changes were operated.

Moreover, the ICMM model was mainly evaluated through professional knowledge and working experience when determining hazard levels, leading to subjectivity and justification bias in the methodology (46). Thus, risks would usually be overestimated as long as workers were exposed to hazards that would cause severe harm under a longer working period. Conversely, the classification of occupational hazards (dust and chemical agents) at workplaces usually would be underestimated only if B assignments that referred to C_{TWA}/OEL or C_M/OEL were lower than 1 ($B < 1$), then risk classifications turned out to be relatively harmless no matter what differences other weight factors could affect (47). Furthermore, their RR sequence among the three models was ordered from RR ICMM > RR semi-quantitative comprehensive index model > RR classification of occupational hazards at workplaces (dust and chemical agents) in China ($P < 0.05$). These results were supported by a similar study from Qiu liang Xu's (48) research, which stated that the EPA model achieved the highest RR [0.8 (0.2–1.0)], respectively, followed by the COSHH model [0.6 (0.6–1.0)], the Singaporean model [0.4 (0.2–0.8)], the Australian model [0.4 (0.2–0.6)]. The Romanian model [0.3 (0.3–0.4)] and the ICMM model [0.2 (0.2–0.8)] had the lowest RR. The order of RR among the six models was as follows: RR EPA > RR COSHH > RR Singaporean > RR Australian > RR Romanian > RR ICMM ($P < 0.05$), The Singaporean model was positively correlated with the other five models ($P < 0.01$), and their correlation coefficients were relatively greater than others, which could be attributed to its characteristics of compensating for shortcomings in quantitative and qualitative methods and giving relatively practical results by combining investigation data and standardized judgment. Above all, the semi-quantitative comprehensive index model was the most appropriate one among the two others for improvements in protective measures in a self-contrast pattern.

Subsequently, physical examination data between 2020 and 2021 were analyzed to discover whether differences among liver function indicators could be found. In fact, significant differences toward abnormal rates of fatty liver and other hepatic symptoms were only found in Y ($X^2 = 10.19$, $P < 0.001$) between years, and no such effect was discovered among positions ($P > 0.05$), which indicated that there were changes in abnormal rates among positions before and after improvements on protective measures, but the low sample size for individual positions caused insignificance. Particularly, the majority of positions in Y and Z demonstrated a declining tendency on abnormal rates toward other hepatic symptoms from 2020 to 2021, in which the ones with relatively higher reduction rates involved in outward processing, product packaging, sewage cleaning, VCM polymerization, refrigeration, steam stripping in Y and material storage, chemical reactions, and splitting decomposition in Z, and no such apparent trend on the fatty liver was observed. It should be noted that the number of people in every position has mostly stayed the same from 2020 to 2021. It was unlikely to witness a significant alleviation of a series of organic liver lesions, such as hepatic cysts, intrahepatic calcification, and thickened intrahepatic echo, in a short interval phase of 1 year, unless there were new patients enrolled to substitute for the individuals with hepatic symptoms. They were further arranged for recuperation and position switching. In addition, to explore whether improvements in protective measures in Y and Z played a role in the reduction of abnormal rates of fatty liver and other hepatic symptoms, analyses of multiple linear regression and multivariate ANOVA were performed.

Results showed that in Y, the variable for males, ALT, AST, GGT, TG, and TC were factors contributing to fatty liver in Y in 2020. A similar effect was only seen in males, TG, and TC in 2021, and then variables of men, ALT, AST, and GGT were found to be essential to other hepatic symptoms, with only men left in effect in 2021. Meanwhile, in Z, the variables for men, TG and TC, which contained fatty liver, while males ALT and AST affected other hepatic symptoms in both 2020 and 2021. In addition, the male variable was the most significant factor among others to play a critical role in alterations toward liver ultrasound as demographic proportions in Y and Z were approximately five-fold and three-fold higher in men than in women. It was undeniable that the overwhelming proportion of males made a great contribution. TG and TC were critical variables to affect the fatty liver, but they were not when differences using a bilateral interaction between years and positions were analyzed. Combined with charts from Figures 3A,B, it is worth mentioning that positions such as steam stripping, outward processing, VCM polymerization, and product packaging in Y were ones with alterations toward abnormal rates in fatty liver and other hepatic symptoms that significantly differed in ALT, AST, and GGT at the same time, while material storage, oxychlorination, material recycling, and field sampling in Z were ones with similar changes that differed in ALT and AST simultaneously.

It could be inferred that, after improvements in protective measures (2021), variables such as ALT, AST, and GGT were no longer critical indicators to affect the fatty liver and other hepatic symptoms. When combined with the results of the on-site survey, it was possible to assume that the protective measures had improved in Y and Z and that those changes may have contributed to the positions' health improvement by practically reducing the disadvantages. However, no such alteration was seen from TG and TC to fatty liver, and it appeared that this improvement had no obvious influence on abnormal liver health in Z as indicators of TG, TC, ALT, and AST. For instance, ALT and AST normally exist within hepatocytes. They would be released into the bloodstream once impairment or cell death occurred. The ratio of AST/ALT was a common indicator to signify liver cell damage within normal ranges. The extent of damage could be judged to be mild when the ratio was lower than 1. It might uncover a much more serious level involved in severe hepatitis, cirrhosis, and even HCC when the ratio exceeds 1. It also would be helpful to diagnose alcoholic liver disease, especially when the ratio was extremely higher than 2. Serum transaminases might be partially related to nonalcoholic fatty liver disease (NAFLD), which may eventually progress to liver fibrosis, cirrhosis, and cancer (49). For instance, Lang et al.'s (50) studies also found that joint action between VCM and HFD significantly enhanced liver disease and further resulted in some inflammatory foci and alterations of ALT and AST in circular blood, which were sufficient to exacerbate experimental NAFLD, as VCM did cause the liver to be more susceptible to damage from a secondary insult by decreasing mitochondrial function. Notably, serum transaminases of those with non-alcoholic steatohepatitis (TASH) were not altered with respect to healthy chemical workers. The consequences of current high VCM exposures may not always be reversible after exposure has been withdrawn and may further evolve into progressive liver injury and fibrosis (51, 52). The study conducted on clinical data and biological specimens from Louisville, Kentucky, demonstrated the prevalence of TASH, a liver pathology, in highly exposed VCM plant workers because of its noncancerous pathophysiology. TASH is a progressive form of nonalcoholic fatty liver disease (NAFLD). NAFLD is a spectrum of liver disorders ranging from lipid accumulation (steatosis) and hepatic inflammation (steatohepatitis) to the presence of fibrosis and cirrhosis (53, 54).

In this regard, it could be inferred that alterations toward fatty liver and other hepatic symptoms among positions before and after improvements in protective measures could be partially caused by corresponding changes of ALT, AST, and GGT in typical positions in Y and Z, but their evidence for specific significance to fatty liver and other hepatic symptoms and relationship with improvements in protective measures in Y and Z needs further exploration.

Limitation

Several limitations prevented us from conducting systematic research on the relationship between improvements in protective measures and the health problems caused by VCM and other hazards. (1) This research could not connect health indicators with position classification for failure on collection of position's classification from the physical examination process for consecutive years, the available data are not enough to verify the relationship between improvement on protective measures and liver health status. (2) In addition to the ventilation effect at indoor plants, we missed the effect of the natural ventilation requirement on ambient concentration alterations as numerous devices or facilities were placed outdoors; (3) General maintenance for sealing and airtight devices, valves, pipes, or sampling facilities were found to be improved in 2021, which radically inhibited evaporation and effusion of organic solvents or industrial dust, but we failed to verify their enhancement through the collection of quantitative data; (4) The very important catalyst $HgCl_2$ failed to be brought into detection as it existed in a solid pattern during the production process, and mercury-containing wastewater was not our primary purpose.

Conclusion

This study selected two factories with different techniques for VCM and PVC synthesis to evaluate the effect of improving protective measures in 2020 on alterations of health risk levels and liver function indicators. Severe conclusions could be drawn from the following: (1) Improvements in protective measures in Y and Z contributed to the reduction of ambient concentration at workplaces through the promotion of local ventilation effects and sealing airtight measures; (2) the semi-quantitative comprehensive index model is appropriate for evaluating risk level alterations before and after improvements on measures in a self-contrast pattern; and (3) alterations toward fatty liver and other hepatic symptoms among positions before and after improvements in protective measures could be partially caused by corresponding changes in ALT, AST, and GGT.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Medical Ethical Review Committee of National Institute for Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

Writing for original draft preparation: YD. Conception or design of the work: YD, XingW, WH, and MY. On-site survey or field investigation work: YD, XingW, WH, HB, XinW, NK, FH, and SZ. Questionnaire, data acquisition, analysis, or interpretation of data for the work: YD, HB, XinW, NK, FH, and SZ. Revising critically for important intellectual content: MY. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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An interdisciplinary framework for derivation of occupational exposure limits

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Protecting the health and safety of workers in industrial operations is a top priority. One of the resources used in industry to ensure worker safety is the occupational exposure limit (OEL). OELs are derived from the assessment and interpretation of empirical data from animal and/or human studies. There are various guidelines for the derivation and implementation of OELs globally, with a range of stakeholders (including regulatory bodies, governmental agencies, expert groups and others). The purpose of this manuscript is to supplement existing guidance with learnings from a multidisciplinary team approach within an industry setting. The framework we present is similar in construct to other risk assessment frameworks and includes: (1) problem formulation, (2) literature review, (3) weight of evidence considerations, (4) point of departure selection/derivation, (5) application of assessment factors, and the final step, (6) derivation of the OEL. Within each step are descriptions and examples to consider when incorporating data from various disciplines such as toxicology, epidemiology, and exposure science. This manuscript describes a technical framework by which available data relevant for occupational exposures is compiled, analyzed, and utilized to inform safety threshold derivation applicable to OELs.

KEYWORDS

risk assessment, problem formulation, literature review, weight of evidence (WOE), point of departure (POD), assessment factors (AFs)

Introduction

Maintaining safe operations and protecting worker health is a clear priority in industrial settings. For select chemicals and industrial processes, OELs have been established by multiple stakeholders, including (but not limited to) regulatory bodies, governmental agencies, and expert groups and may apply on a global scale. Most notable are the American Conference of Government Industrial Hygienists (ACGIH®) Threshold Limit Values (TLVs), the Occupational Alliance for Risk Assessment (OARS) Workplace Environmental Exposure Levels (WEELs), and other national and regional OEL regulatory bodies.

Local regulatory limits should be the primary source for occupational exposure limits. However, some published OELs may lack the inclusion of the most recent relevant data. Also, for some chemicals and industrial processes, OELs have not been established or published by these stakeholders. In these cases, industry may need to develop their own internal OEL. Given that there are complexities in developing an OEL, including data integration, analysis and interpretation, transparency of the scientific process is important.

As a petrochemical company, we use a multidisciplinary framework which incorporates expertise in toxicology, epidemiology, exposure science, and/or industrial hygiene. The process begins with a review of published values such as the ACGIH® TLVs, OARS WEELS, and national and regional OEL regulatory bodies, where applicable. Generally these values are adopted. An exception may be in cases where the scientific derivation of these published limits are not aligned with current scientific evidence; in this case, an internal OEL may be established. In the event that an OEL does not exist or is not supported by current science, we maintain a formal procedure for setting OELs that augment advisory and regulatory health limits to protect worker health. Where the science supports a more stringent limit, we adhere to the more stringent limit.

OEL reviews and development are triggered by several scenarios: (1) new products or manufacturing processes, (2) ACGIH Notice of Intended Change (NIC) to an existing TLV [Time Weighted Average (TWA) and/or Short-Term Exposure Limit (STEL)], (3) new or evolving science that suggests potential occupational health impacts, (4) business line, worker, or customer concerns or (5) periodic scheduled reviews of existing OELs. OEL review and development begins with assembling a multidisciplinary technical work team, followed by data assimilation and technical expert analysis where scientific expertise and principles of risk assessment are brought to bear.

A special issue on the state of the science of OEL development was published in 2015 in the Journal of Occupational and Environmental Hygiene, which put forward contemporary advances in methodology and analysis of data relevant to OEL development, as well as a call for the use and implementation of advanced methods for OEL development [for e.g., (1–3)]. Advances in evaluation methods and emerging technologies continue to be published in this area [for e.g., (4, 5)]. The purpose of this manuscript is to share our learnings from this multidisciplinary approach to the collective OEL derivation process, starting with problem formulation and ending with uncertainty analysis. The technical assessment that is foundational to the development of a scientifically-derived OEL follows a sequence of steps which align with risk assessment frameworks (Figure 1). In this manuscript we discuss the technical attributes of each step: (1) problem formulation (define the scope of the question), (2) literature review (curate, sort, and evaluate all relevant data), (3) weight of evidence considerations (identify and gauge relative impact of key studies), (4) point of departure (PoD) selection/derivation (select the most sensitive adverse effect for hazard identification), (5) application of assessment factors (appropriately identify and quantify uncertainty related to PoD/key study), technical considerations (data quality, database uncertainty, integration of epidemiological and toxicological data), and the practical applicability of available information in the context of occupational settings.

We recognize that different organizations/industries may apply a range of inputs/problem formulations and scope to specifically address their needs. Regardless of these inputs, clear and sufficiently detailed documentation of decisions and rationale are central to transparency and reproducibility of the OEL process. Outside the scope of this manuscript is the comparison of approaches to OEL derivation globally; this has recently been undertaken by the OECD and the report is publicly available (6) and this type of comparison have been recently published, for example, Schneider et al. (4).

Problem formulation for OEL development

Problem formulation is a critical first step in conducting any human health risk assessment (7–11). Problem formulation addresses the fundamental questions of "what do you need to know?" and/or "what decision do you need to make?" (10). First developed for ecological risk assessment (12), the problem formulation step establishes purpose, scope, and plan for collecting and evaluating information to guide effective use of resources at each stage of the assessment process and guards against collecting data with no clear sense of how they will be used. Additionally, by first focusing on describing and evaluating the specific problem to be solved, there is less tendency to immediately jump to all possible solutions, many of which may be inappropriate for the decision at hand.

Specific considerations to guide problem formulation have been tabulated (7) (Table 1). A more general framework to guide problem formulation (11), applicable to a wide range of assessment scenarios, can also be utilized. Explicit definition of these considerations promotes a flexible approach that allows a fit-for-purpose application of risk assessment methods. For example, comprehensive literature reviews on toxicity may not be necessary when the salient health effects are well-recognized, as is the case with benzene and hematological effects (however, as a best practice, periodic evaluations of the literature to identify new potential health hazards, as well as monitor advances in characterizing the dose response curve should be employed). As such, the scope of the problem can be refined when the health effects are well understood.

The primary purpose of the problem formulation step is to adequately define what is in scope and what is out of scope to ensure appropriate resources and expertise are engaged to solve the defined problem. In the context of setting OELs, a problem formulation statement would include

FIGURE 1
Overview of basic risk assessment steps involved in OEL derivation.

TABLE 1 Problem formulation considerations[a].

Element	Description	OEL considerations
Scenario	Describes the occurrence and/or use of a chemical, biological, or physical agent	• Physical form of the substance • Monitoring method availability, limit of detection, and selectivity
Existing knowledge	Assembly and evaluation of all relevant information (chemical, physical and biological), including knowledge of chemical class and hypothesized modes of action	• All human and animal data on the substance • Alternative sources of data (e.g., read across, *in vitro*, *in silico*)
Context	Describes the conditions under which exposure may occur	• Operations (tasks and processes) associated with the substance(s) or chemical(s) • Co-exposures are generally out of scope [b]
	Describes the population to whom exposure may be associated	Individuals/populations who would be exposed, and exposure routes (e.g., inhalation, dermal) associated with the defined tasks and processes
Statement of the purpose of the assessment (e.g., priority setting, evaluation of a new use of an existing product, assessment of combined exposures)	• Determine decision point [e.g., target margin of exposure (MOE)] • Review available regulatory options (if applicable)	• Set an inhalation exposure limit that is measurable and health protective for most workers over a working lifetime (i.e., 40 years; adults ages 18–70; 8–12 h/day, 5 days/week) • Assess need for a STEL • Assess potential for skin sensitization

[a] As adapted from Embry et al. (7).
[b] An example of an exception to the consideration of co-exposures is the reciprocal calculation approach used to set OELs for hydrocarbon solvents, where "group guidance values" are assigned to similar constituents due to the similar toxicological properties and additive effects demonstrated in toxicological studies (13).

relevant information on the scope of the OEL, such as new products or manufacturing processes or new or evolving science that suggests potential occupational health impacts. The OEL process aims to set an inhalation exposure limit that is measurable and health protective for most workers over a working lifetime (i.e., 40 years; adults ages 18–70; 8–12 h/day, 5 days/week), while also assessing the need for a STEL, importance of dermal routes of exposure, and skin sensitization concerns.

OELs are frequently communicated as 8 h TWA, 15 mins STEL, or both. TWA typically applies where there is a health effect from repeated exposures to a relatively continuous exposure concentration (i.e., not solely peak or intermittently high exposures). The TWA is more frequently associated with observed effects following repeated exposures, where effects are thought to be primarily time- and concentration-driven (as opposed to solely concentration-dependent). STEL typically applies where there is a health effect resulting from a single exposure or peak exposures may result in effects not observed following relatively continuous exposure concentrations. The STEL is more frequently associated with effects such as respiratory irritation, where effects are thought to be primarily concentration-driven (as opposed to both time- and concentration-dependent) or dose rate-dependent toxic effects (i.e., narcosis of sufficient degree to increase the likelihood of accidental injury, impaired self-rescue, or reduced work efficiency). Thus, the problem formulation step includes consideration of the nature of the health effects and if those effects justify a TWA and/or STEL. It may be important to recognize that even if the key effect justifies only a TWA, a secondary effect may justify a STEL recommendation. For example, if liver injury is the key effect and a TWA is derived, but an exposure only marginally higher would result in respiratory irritation, a STEL might also be recommended.

Recommendation for a STEL only (no TWA recommended) may be considered when available information supports potential solely for acute effects and repeat exposure effects are secondary to the acute effect. Respiratory irritants can be an example of this scenario. If a chemical's mode of action for repeat exposure effects is dependent on repeated irritation to the lung, but a STEL will prevent lung irritation, then the STEL could be appropriate to consider for the OEL. Where there is a TWA only (no STEL), an excursion limit, similar to the ACGIH Peak Exposures guidance of three times the TWA, is recommended to limit short-term high exposures.

Another factor to consider during problem formulation is the nature of potential exposure in the workplace to ensure that the assumptions used to derive the OEL align with the exposure scenarios of interest. Such consideration may include characterization of the exposed population (i.e., worker groups), as well as the work environment (e.g., operating conditions) and tasks performed, which inform the source and form of the substance in the workplace and the primary route(s) of exposure. If the exposures in the workplace are sufficiently different from that of the science behind the derived limit, the OEL might not be relevant (e.g., ACGIH TLV for chromium; see discussion for details) and may lead to inappropriate risk management decisions.

Literature review

Literature reviews and literature-based data synthesis is the second key step in OEL development (Figure 2). Though some of the elements of a systematic review (14, 15) are used to identify and evaluate potentially relevant studies in this context, the literature review in developing new and reviewing existing OELs is considered broader in scope. This is because a clearly specified research objective, which is usually defined in a Population-Exposure-Comparator-Outcome (PECO) statement, is not typically included. Here we outline the methods for conducting a literature review and synthesis for two OEL development scenarios (Figure 2). Software-assisted approaches for large bodies of literature are highly recommended to improve efficiency in time, resources and documentation. Elements of the workflow can also be adapted to be fit-for-purpose, and depends on the body of literature at hand.

In terms of search strategy, literature searches for OEL derivation may be conducted in the context of (1) *de novo* OEL development or (2) periodic scheduled review cycles. For *de novo* OELs, a search strategy is developed by a multidisciplinary team, ideally in collaboration with an information specialist. For the periodic reviews, previous OEL documentation can inform search terms, together with review and modification of the search strategy if appropriate. Once a search strategy has been established, an information specialist conducts the literature search in appropriate databases (e.g., PubMed, ProQuest, internal company archives). If multiple databases are used, duplicate entries should be excluded using reference management software, such as Endnote. Once duplicate references have been removed, the EndNote library can be exported as a Research Information Systems file (.ris). RIS file formats can be imported to various bibliographic software and are compatible with other text-mining tools, including SWIFT Active Screener (SWIFT is an acronym for "Sciome Workbench for Interactive computer-Facilitated Text-mining") (16), and Health Assessment Workspace Collaborative (HAWC) (17, 18).

Because manual curation for a large number of search returns is labor- and resource-intensive, content management using software tools in combination with subject matter expert screening is strongly recommended. As an example, two web-based, collaborative software tools may be useful: SWIFT-Active Screener and HAWC.

1. SWIFT-Active Screener (16): SWIFT-Active Screener (https://www.sciome.com/swift-activescreener/) is a commercial web-based platform designed to facilitate literature prioritization for unscreened articles based on screened articles that were included or excluded using an underlying statistical model. The .ris file exported from EndNote can be imported into Active Screener. After screening, results can be exported in standard data formats compatible with another content management tool, HAWC.
2. HAWC (17, 18): HAWC (https://hawcproject.org) is a freely-available, web-application and content management tool designed to support the systematic review process, including search hit categorization, content extraction, risk of bias analysis, and data visualization. HAWC therefore provides a convenient platform used to capture key study data.

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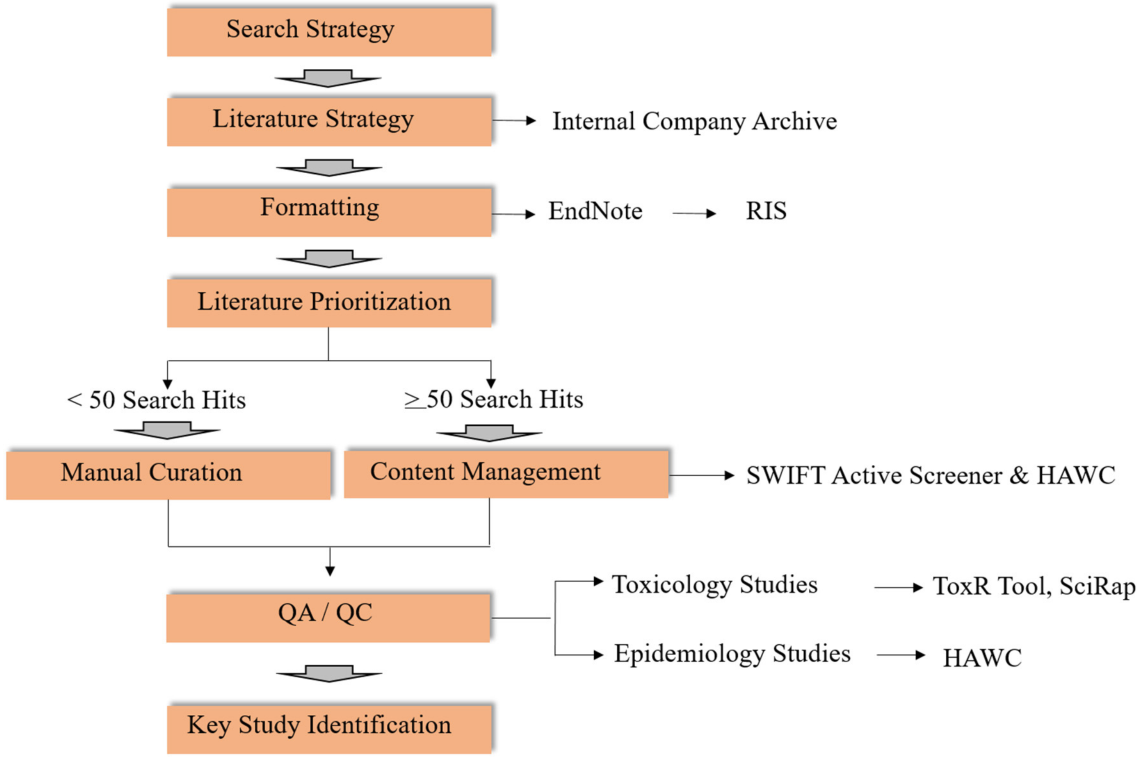

FIGURE 2
Workflow for literature review for activities related to OELs (RIS, Research Information Systems; SWIFT, Sciome Workbench for Interactive computer-Facilitated Text-mining; HAWC, Health Assessment Workspace Collaborative; SciRap, Science in Risk Assessment and Policy; QA/QC, Quality Assessment/Quality Control).

For the development of new OELs in particular, it is recommended to start with compendium documents (e.g., ACGIH and/or NIC documentation, SCOEL, systematic reviews, etc.) to facilitate rapid identification of the highest quality studies, regardless of the software tools being used to organize the results of the literature search. Although compendium and other summary documents will help to expedite the literature review process by narrowing scope and clarifying the most sensitive health endpoints associated with a compound, review of the original paper(s) referenced in the compendium document(s) is still essential. Outdated compendium documents should be utilized with caution and underscore the importance of evaluating the most relevant and informative studies identified in the literature search.

Weight of evidence

After the relevant literature has been identified, the next step in the hazard assessment and OEL derivation process is synthesis of the available lines of evidence (LOE), which often include diverse and not readily comparable types of data (e.g., animal studies, epidemiological studies, *in vitro* mechanistic studies, physical-chemical properties) in order to make a single, health-protective decision. The integration and critical weighting of all suitable, available studies using predefined, scientifically justified criteria for both quality and relevance to the problem formulation is known as a weight of evidence (WOE) assessment. Several regulatory agencies have recently published frameworks or perspectives on approaches to integrate and weight different LOE in hazard identification, including EFSA, Health Canada, and the National Toxicology Program (19–21). Although each organization has slight nuances, each includes the following three steps: establishing the LOE (including selection of relevant studies and assessing the quality of the studies), assessing confidence in the LOE, and integrating the LOE to express a single WOE hazard conclusion. The following sections highlight key considerations for each of these processes.

Establishing LOE

A critical part of establishing the LOE is a clear and transparent process to select individual studies to make up the body of evidence. Without clear criteria, a WOE assessment tends to rely on expert judgement, resulting in variable

TABLE 2 A practical example to an approach to the systematic and transparent documentation of a WOE assessment[a].

Step 1. Establish the LOE, including quality assessment of the individual studies per LOE.

Step 2: Assign confidence rating to each hazard endpoint per LOE

LOE	Considerations informing confidence[b]	Confidence description	Confidence rating
Hazard endpoint 1/Animal data	• Clear dose response • Large magnitude of effect/meets UN GHS classification criteria[c] • Consistency across disparate study designs • Mode of action considerations	High confidence that additional studies and/or data are unlikely to change the understanding of the exposure/effect relationship	High
Hazard endpoint 2/Animal data Hazard endpoint 3/Animal data, Etc.	• Lack of dose-responsiveness • Small magnitude of effect • Indirect measurement of effect • Inconsistent findings across animal models/species/study designs	Low confidence in accurate representation of the exposure/effect relationship; new data likely to change the representation	Low
	No studies identified	No studies identified	No data
Hazard endpoint 1/Epidemiological data	• Quantitative/measured exposure data • Clearly described exposure history, including shape of the exposure distribution • Repeated air sampling • Accounts for co-exposures and/or confounders • Study population sizes with substantial effect observations (e.g., >5 cases) • Diverse study populations or meta-analyses	High confidence that additional studies and/or data are unlikely to change the understanding of the exposure/effect relationship	High
Hazard endpoint 2/Epidemiological data Hazard endpoint 3/Epidemiological data, etc.	• Case reports, accidents, intentional misuse, etc. • Qualitative exposure metrics • General population studies • Exposure to other stressors (e.g., excessive smoking, alcohol/drug use) • Small or non-diverse study populations	Low confidence in accurate representation of the exposure/effect relationship; new data likely to change the representation	Low
	No studies identified	No studies identified	No data

Step 3. Translate the confidence ratings into the level of evidence

Effects observed?	Confidence rating	Level of evidence for effect
Yes	High	High potential
Yes	Low	Moderate potential
No	High	Low potential
No	Low	Low potential
No data	Low	Note: in an absence of data, adjustment factors for database quality should reflect the increased uncertainty or potential underestimation of effect

[a] Process adapted from Rooney et al. (21).
[b] Considerations adapted from Rooney et al. (21) and (25). For more detail on epidemiological considerations that may influence confidence, (see Appendix).
[c] United Nations (UN) Globally Harmonized System of Classification and Labelling of Chemicals (GHS): Eighth Revised Edition (2019). https://unece.org/ghs-rev8-2019.

conclusions with little insight into the underlying reasons for the variability. For the purposes of setting OELs, inclusion criteria may be defined as direct assessment of a hazard endpoint (e.g., acute toxicity, irritation, sensitization, genetic toxicity, carcinogenicity, reproductive or developmental toxicity) in either animals or human subjects or assessment of mechanistic information. Such mechanistic studies may identify previously unknown adverse effects or change previous conclusions on relationships between exposure and effect levels. Additionally, mechanistic data can inform as to the human relevance of findings observed in animals (22).

For the studies considered relevant (i.e., meet the inclusion criteria described above), a quality assessment may be conducted to determine the impact of study design on the validity of the link between effect and exposure, following the National Toxicology Program's (NTP) Office of Health Assessment and Translation's (OHAT) Risk of Bias tool (23). The intent of this step is to identify limitations that could potentially introduce a systematic bias that would threaten the validity of the study's findings. The Risk of Bias tool asks a series of questions to address various types of bias (selection, confounding, performance, attrition/exclusion, detection, and selective reporting), with different considerations per study type (human controlled trial, cohort, case-control, cross-sectional, and case series/case report, experimental animal studies). As an example, confounding bias is the major threat to an observational study's validity, as occupational epidemiology studies often do not adjust for co-exposures and lifestyle issues such as smoking (24).

Assessing confidence in LOE

The overall confidence in the body of evidence provides an indication of the likelihood that the available study findings provide an accurate representation of the association between exposure and effect. Characterizing confidence in the evidence takes into account both the amount of data available and professional judgement on the consistency, relevance of study design to directly and/or precisely measure the effect, etc. It is recognized that this step in the process requires scientific judgment; however, a transparent, systematic process to include all relevant data and to document the rationale for exclusion and confidence decisions provides a foundation for further discussion as needed. As noted above, organizations may use varied processes to assess confidence; the critical element is that the process followed is clearly communicated. Table 2 provides an example of how confidence decisions may be documented in a systematic manner.

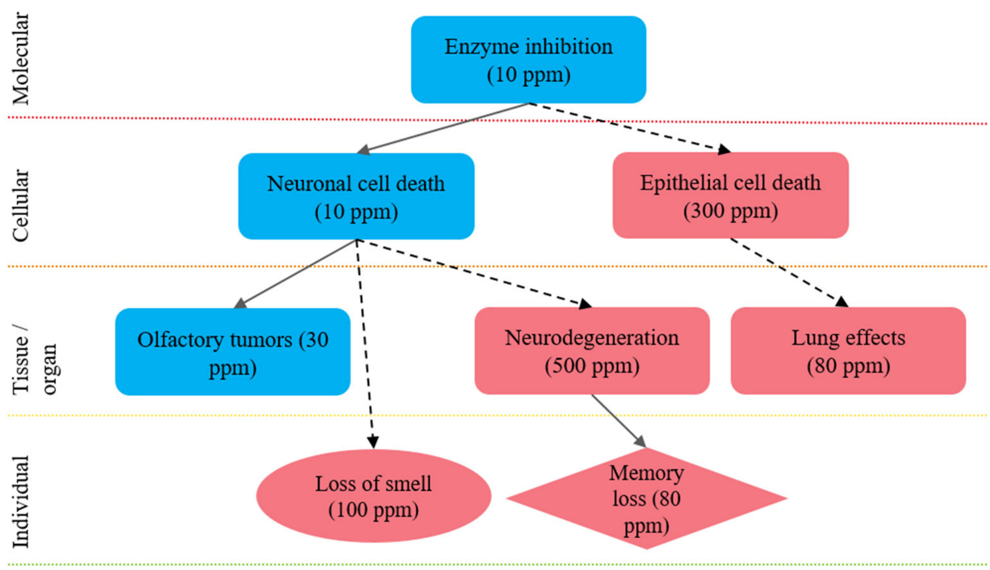

FIGURE 3
Integration of health effects into a biological pathway network to inform future selection of a point of departure: example biological pathway network approach to integrate health effect data derived from distinct LOEs to inform selection of a health-protective POD. The key events shown here are proposed to lead to hallmark effects associated with hydrogen sulfide exposure: nasal tissue outcomes; neurological tissue outcomes and pulmonary tissue outcomes. The shape of each key event indicates the LOE: rectangle, animal data; circle, epidemiological data; and diamond, both animal and epidemiological data. The level of evidence supporting linkages between key events is shown by the arrows: solid arrows, quantitative evidence; dotted arrows, qualitative evidence. The color of each shape reflects a relative distinction between high- and low-dose effects, where effects observed at <30 ppm are considered low dose effects (blue) and effects observed at >30 ppm are considered high-dose effects (red). Figure adapted from Goyak and Lewis (26).

Integrating LOE

Different approaches can be taken to integrate effects information obtained in separate LOE. Most commonly, all effects (including animal effects and human health effects) are shown together in tabular format, and endpoints with an effect deemed to have a high level of evidence (i.e., high potential) are considered as potential points of departure for OEL derivation.

Ideally, a biological-pathway approach should be considered to integrate both the animal and human LOE, as well as to put mechanistic information into the context of the apical outcomes derived from observational animal and human studies. In this approach, the effects observed at a molecular or tissue level, obtained in *in vitro* or animal studies, are linked to apical outcomes, often observed in animal or epidemiological studies. In this way, observations across distinct LOE can be assessed for both dose- and temporal-concordance and consistency across species. For example, an agent characterized as being particularly toxic to a specified organ system *via* toxicology studies paired with unadjusted epidemiologic results might suggest that, whatever level of confounding might reasonably exist, the epidemiologic findings are reasonably valid.

To demonstrate the organization of effects into biological pathways, (see Figure 3), which summarizes effects observed after exposure to hydrogen sulfide in mechanistic studies (e.g., enzyme inhibition), animal studies (e.g., nasal lesions, lung effects, memory impairment), and epidemiological studies and/or human case reports (e.g., loss of sense of smell, memory impairment). See Goyak and Lewis (26) for more detailed discussion of this example biological pathway network. Integration of the effects data obtained from different LOEs can increase the overall confidence in the body of evidence. For example, through demonstration of consistency in effect across disparate study designs, by highlighting the distinction between low- and high-dose effects, and by showing dose- and/or temporal-concordance across the entire pathway.

Regardless of the method, the overall goal of integrating the LOE is to characterize the evidence base and assess confidence in each possible outcome, in order to inform subsequent steps in the OEL derivation process. Specifically, the confidence descriptors are used to inform both PoD selection (e.g., an endpoint with low confidence is likely not an appropriate candidate for the point of departure) and application of assessment factors (e.g., an endpoint with no supporting data indicates low confidence and usage of additional assessment factors may be considered).

Point of departure selection

A point of departure (PoD) refers to a dose (either measured empirically or modeled using dose-response data) at which an adverse effect occurs as a result of a specific exposure. The International Programme on Chemical Safety's (IPCS) definition of adversity is helpful in PoD selection (27):

"Change in the morphology, physiology, growth, development, reproduction, or life span of an organism, system, or (sub) population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences."

Utilizing a PoD which reflects an accurate and holistic scenario for occupational exposures is a critical aspect of an OEL determination. This section details approaches to PoD selection which consider unique aspects of human and animal datasets, as well as scientific criteria which aid in the selection of a PoD relevant for an occupational exposure to that substance. Because considerations for PoD selection can vary based on study design, underlying assumptions, extrapolation potential, the human and animal considerations are separated in this section. However, it is best practice to consider all available data together in a WOE approach to select the most appropriate study for the PoD.

PoD selection based on human data

If an adverse health effect is identified, a PoD can be selected. In cases where a reported human health effect(s) is unsuitable for determining an OEL, the available animal toxicity data to select the PoD should be considered. If there are no available animal toxicity data for the substance, read across data is in scope to select a PoD.

It may be challenging to identify a PoD or threshold of effect from human data, because in many cases the study was not designed to allow the dose-response relationship to be characterized quantitatively or a threshold of effect to be identified. A dose/concentration level which corresponds to a no or low effect level is selected as the PoD, the starting point for low dose extrapolations (28). The PoD can be the no-observed-adverse-effect level (NOAEL), the lowest-observed-adverse effect level (LOAEL), or derived using dose/concentration-response modeling, e.g., the benchmark dose (BMD).

In selecting the PoD from human data, consider the following features of the PoD regarding irritation as an endpoint. For human studies, with only subjective symptoms, such as irritation, reported for local effects, consider selecting the concentration associated with clear to moderate irritation as the PoD (since very slight to slight discomfort subjective irritation is often reported at near zero exposure) (29). If human data are limited to chemosensory irritation (trigeminal nerve stimulation, reported as burning, stinging, headache, discomfort), the assessor may consider using animal Alarie data to support the human-derived PoD because the Alarie data provides an objective measure of irritation. Alarie data refers to the historical use of an animal bioassay to predict sensory irritants in humans (30). The correlation drawn from this animal bioassay still has practical application to OELs in this context, to support conclusions on human data when the human data is of lower quality or potentially ambiguous interpretation.

Categorical exposure assessment is frequently used in environmental or occupational epidemiology studies. The descriptive statistics for exposure categories (mean, median, upper or lower limits for range in exposure categories) are potential quantitative inputs for PoDs in human studies. The central tendency of individual exposure categories may be preferred if the category interval is not large, but if the interval between the upper and lower bound of a category is large it may be preferable to adopt the upper or lower bound of the interval as the PoD, depending on whether the exposure category would be considered a NOAEL or LOAEL. Consideration of the quality of the exposure assessment method may also be appropriate in informing the scientific confidence in exposure categories.

In some cases a regression model may be available for predicting the endpoint of interest. It may be possible to use a regression model similarly to a BMD. In this scenario, the assessor may identify a specific effect size on the critical endpoint (i.e., the amount of risk to be used), then calculate the corresponding exposure concentration from the regression model to identify a PoD. The rationale for the selected effect size should be documented in the OEL. If this approach is considered, consultation with a statistician may be required to understand the underlying model constraints and resultant uncertainties that may be introduced into the PoD selection.

Approaches to PoD selection from animal studies

Two approaches to PoD selection are common in OEL development from animal studies, NOAEL/LOAEL and BMD approaches. The approach selection is likely dependent on the available study design (for considerations on applicability of adverse effect and study design to OEL development, see Figure 4). Primary considerations useful in guiding selection of an approach are the number of dose groups, group sizes, dose spacing, and approximated dose-response inflection point.

NOAEL/LOAEL approach

A NOAEL/LOAEL approach has been traditionally applied in toxicology. It commonly relies on one or more pair-wise comparisons of a control group to exposed group(s). When an adverse effect is observed, the NOAEL is the **highest** dose where a statistically significant difference does **not** exist between the control and exposed groups. The LOAEL is the **lowest** dose where an adverse effect shows a statistically significant difference from the control group. In this context, both statistical and biological significance should be considered. Some expert judgment may need to be applied when statistical comparisons are borderline significant **or** when effects are statistically significant, but not biologically significant or relevant to humans when considering the animal model used in the study design. The NOAEL/LOAEL approach may be preferred if there are a limited number of experimental groups. A NOAEL/LOAEL approach is the only realistic approach if there are two dose groups, as there is insufficient information in such a design to permit dose response assessment.

Two primary weaknesses of a NOAEL/LOAEL approach is that it can become strongly dependent on the statistical power for comparisons between groups and the spacing of the dose groups. In a study design with low statistical power, the NOAEL/LOAEL approach may be prone to misestimating the true NOAEL/LOAEL because a true effect may not be observed as statistically significant (due to limited sample size or chance). A scenario in which one additional study subject would have changed a result to be statistically significant is distinctly different from needing to triple the group sizes. With sample sizes of five to ten animals per group, the influence of variability, random effects, and multiple comparisons may increase the chance that a true effect is not statistically significant. The spacing of dose groups can also be a weakness. Because the NOAEL/LOAEL approach requires the selected PoD to be one of the test concentrations, wide intervals between doses or tests performed well above the NOAEL can occur. Wide dose spacing may obscure the true threshold, leading to selection of a NOAEL that is far below the true PoD. In studies where adverse effects occur in all exposed groups, there can be substantial uncertainty about where the true PoD is.

When applying a NOAEL/LOAEL approach in OEL development, consideration of how statistical power may influence NOAEL/LOAEL determination should be deliberately assessed. Consideration of the historical control range for a specific lab and strain of animal model can be helpful in assessing results that are not statistically significant, but may be biologically significant. Consideration of dose spacing can also be a consideration in the assessment factor for LOAEL to NOAEL extrapolation, as wide dose spacing could introduce uncertainty in the true NOAEL.

BMD approach

The BMD approach addresses several weaknesses of NOAEL/LOAEL approach, but is not without its' own weaknesses. In BMD modeling, multiple statistical models are fit to the observed data in an effort to identify the model that best represents the observed data. The modeler identifies a Benchmark Response (BMR) that is consistent with a non-adverse effect, and the dose corresponding to that BMR is identified as the BMD. All the statistical models have some uncertainty with regard to the precise location of the true BMD, thus the 95th percentile lower confidence limit (BMDL) is generally selected as the PoD for a selected BMR (31).

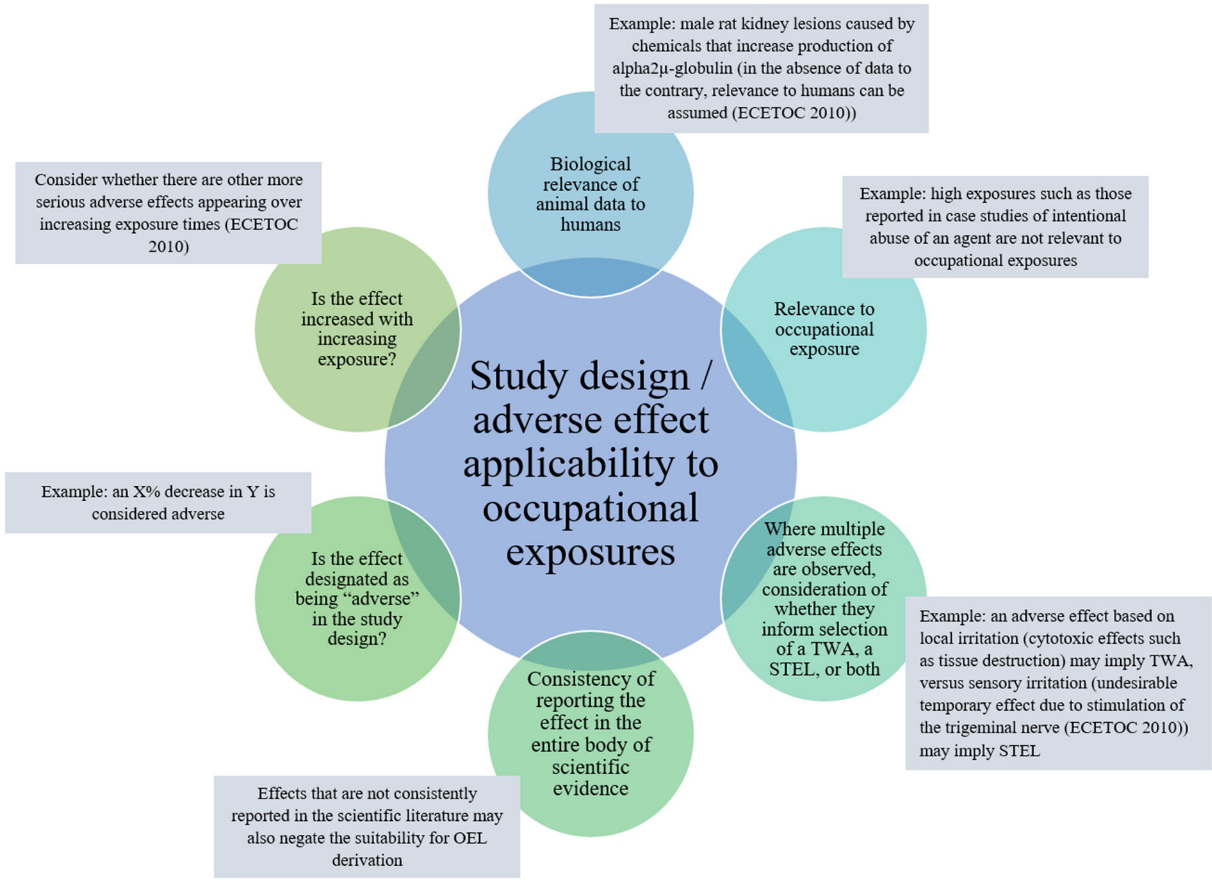

FIGURE 4
Key adverse health effect: effect and study design features to consider regarding applicability to OEL development.

Model selection when multiple appropriately fitting statistical models are available is one of the challenges of BMD analysis. In selection of a single statistical model the assessor may introduce a "model selection error." US EPA (31) and EFSA Scientific Committee et al. (32) have articulated guidance on model selection, both of which consider model fits but compare by different measures. The risk of model selection error may be decreased by applying model averaging techniques (33). US EPA BMDS has integrated model averaging for some statistical models, and web-based tools for deriving a model average BMD are also available (34). In documenting the BMD analysis the rationale for selected model should be provided by the assessor. As an additional consideration, model averaging does not mean using individual BMD or BMDL estimates from different models to calculate a mean (sometimes called an average BMD or BMDL), but instead using whole dose response models with different mathematical weights to calculate a model average. A discussion of model averaging methods is beyond the scope of this summary information.

One additional element to keep in mind for the BMD approach, the BMD software offers the analyst a choice for risk type: added risk or extra risk. Both are different approaches to handling the background incidence of an effect. When the background incidence is zero there is no difference, but if the background incidence is high it can create a major difference in the calculated BMR. As background incidence increases, the calculated risk will increase linearly. The result of the higher calculated risk will be a lower BMD and BMDL. If background incidence of the response is high (80–90%) the calculated BMD and BMDL will differ substantially based on the selected risk type, with the Extra Risk value being lower. Because of the calculation method Extra Risk will always be equal or more conservative than Added Risk. When using BMD software for a quantal (dichotomous) endpoint measurement it is desirable to document values using both approaches to risk.

Adjustments to PoD—inhalation exposure

If the key study used to identify a PoD is based on inhalation there may be additional considerations that cause an assessor to adjust the PoD because breathing rates and particle depositions can differ between laboratory animals and humans. The PoD value identified following adjustment based on respiratory differences has historically been called the "Human Equivalent Concentration" in some documentation. For further discussion and guidance on the Human Equivalent Concentration, consult the EPA Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (35). The complexity of inhalation dosimetry can lead to some confusion with regards to the appropriateness of applying allometric scaling in route to route extrapolation (see next paragraph on allometric scaling). ECHA (36) provides a flow chart for extrapolating an oral exposure to an inhalation exposure for both the general public (Example R.8-1, p. 58) and for an occupational exposure (Example R.8-2, p. 59). These flow charts describe approaches to allometric scaling within the context of route-to-route extrapolation to inhalation, and under which circumstances allometric scaling should explicitly be performed, or whether it has been implicitly addressed in other aspects of the extrapolation procedure.

Briefly, an interspecies allometric scaling assessment factor is *not* applied if a PoD adjustment for inhalation is applied. Inhalation scales nearly allometrically, so adjusting the PoD based on intraspecies differences in inhalation replaces allometric scaling (i.e., do not adjust breathing rates *and* apply allometric scaling). Route-to-route extrapolations, where an oral exposure in rodents is extrapolated to an inhalation scenario, are likely to apply allometric scaling [see examples R.8-1 and R.8-2 (36)]. Where a rodent inhalation exposure is extrapolated to a human inhalation scenario, the breathing rates are more likely to be applied. Adjustment in breathing rate differences for resting animals compared to working humans can be included in the PoD adjustment. Because allometric scaling pertains to resting energy use, adjustment for the difference between resting and working breathing rates is appropriate even when allometric scaling has been applied. Most rodent inhalation studies are performed with animals at rest, resulting in a comparatively smaller volume of air consumed compared to that of a physically active worker. If the adjustment is performed in PoD adjustment the calculation, and source for breathing rate data, should be identified in the documentation.

For particle exposures (aerosol, dust, mist) the comparative deposition fraction can be calculated from common laboratory animal species and humans if particle size and distribution information are available. The comparative deposition fraction can be used to adjust anticipated dose. The Multiple-Path Particle Dosimetry model (https://www.ara.com/products/multiple-path-particle-dosimetry-model-mppd-v-304) can be used for calculation (37, 38). Assessors using Multiple-Path Particle Dosimetry model for PoD adjustment should document the parameters and source of the parameters used for modeling.

Assessment factor (AF) application

The principles underpinning the selection of the PoD (e.g., study quality, route of exposure, animal or human study as key study, duration of exposure) characterize and inform uncertainties that need to be addressed in further steps to derive the OEL. These uncertainties are addressed by applying assessment factors, which introduce quantitative conservativism to the PoD. These AFs are based on physiological differences between human populations as well as animal models and humans, extrapolations for exposure route and duration, and the quality of the overall database on the substance.

This section introduces the application of appropriate AFs to a key study from which the PoD has been derived. Scientifically justifiable AF selection is a critical component of the OEL derivation process, as it accounts for the uncertainty around aspects of the key study. An aim of this section is to articulate assignment of appropriate ranges or values to use when assigning an AF, in addition to when uncertainties in the dataset may require additional expert judgement.

Human datasets and animal datasets are inherently different. There are two primary sources of human data from which an OEL may be derived: (1) observational studies and (2) experimental/intentional exposure. In general, observational studies are well suited for studying chronic, long-term endpoints, including cancer; studies often involve worker populations of sufficient size to validly estimate risk. Experimental human studies are generally conducted to examine a focused set of acute, transient heath endpoints. Sample sizes are often small, and study subjects are generally younger and healthier relative to the workforce.

When developing the rationale for AFs, there are five main areas to account for: (1) interspecies extrapolation, (2) intraspecies adjustment, (3) exposure duration of the study, (4) dose-response extrapolation, and (5) database quality. There are publicly available guidance documents which detail considerations for application of assessment factors (29, 36, 39). Each of these guidance documents utilizes scientific principles which often, but not always, agree on recommendations for appropriate AF selection and application. For a comprehensive table comparing the recommended ranges for each AF between ECHA and ECETOC, (see Table 1) in the ECETOC guidance (29).

Route to route extrapolation

The route to route extrapolation factor accounts for uncertainties when the key study uses a route of exposure which is different from the exposure meant to be understood in the workplace. Where a route to route extrapolation is applied, the assessor should document their rationale for all factors used (even if the factor is 1, which necessitates the justification for why a chemical's disposition would not vary among exposure routes). As outlined in their guidance on deriving AFs for human health risk assessment (39), the consideration of the following factors for specific chemicals may lead the assessor to recommend an AF for route to route extrapolation:

As an illustration of route to route extrapolation, consider three examples*:

1. Extrapolation from a rat oral gavage study to an inhalation OEL, where available toxicokinetic information indicates oral absorption is 90%. The daily exposure at the PoD was 100 mg/kg/d. The nominal dose is adjusted for oral absorption to 90 mg/kg/d (100 mg/kg/d * 90% absorption = 90 mg/kg/d absorbed dose). No additional adjustment for route to route extrapolation is suggested.
2. Extrapolation from a rat dermal study to an inhalation OEL, where available toxicokinetic information indicates dermal absorption is 5%. The daily exposure at the PoD was 100 mg/kg/d. The nominal dose is adjusted for dermal absorption to 5 mg/kg/d (100 mg/kg/d * 5% absorption = 5 mg/kg/d absorbed dose). No additional adjustment for route to route extrapolation is suggested.
3. Extrapolation from a rat oral gavage study, where an acceptable toxicokinetic model (may be one, two, or many [PBPK] compartment) is available. The daily exposure at the PoD was 100 mg/kg/d, resulting in a model predicted time-weighted blood concentration (AUC_{0-24h} = 7,000 µg h/ml). Using the model, the same AUC_{0-24h} is achieved with a 30 mg/m^3 for 8 h exposure, which is then utilized as the PoD. No further adjustment for route to route extrapolation is suggested.

*These examples do not take into account any chemical-specific knowledge on ability to extrapolate between exposures in air and exposures to the skin; assessor should consider these and other aspects of ADME dynamics which are chemical-specific when doing route-to-route extrapolations.

Interspecies

The interspecies AF accounts for the extrapolation between the average study animal and the average human. This extrapolation is primarily based on differences in metabolism between the animal species utilized in the study and humans, and accounts for toxicokinetic and toxicodynamic differences. In the absence of substance or species-specific data, ECETOC guidance recommends using allometric scaling factors to inform the interspecies AF under certain conditions (39). Allometric scaling is defined as biological changes in an organism related to proportional changes in body size. In the context of the interspecies AF, the principle of allometric scaling is used to account for differences in basal metabolic rate between animals and humans. Most toxicokinetic differences can be explained by differences in the basal metabolic rates between species—this is based on the principle that metabolic rates of smaller animals are faster than that of humans. This difference means that humans "would less effectively detoxify and/or excrete xenobiotics than laboratory animals and thus are more vulnerable" (29). If toxicity is expected to be independent of basic metabolic rate (e.g., skin corrosion resulting from direct chemical reactivity), then allometric scaling is not appropriate.

Systemic effects

Allometric scaling factor recommendations are based on calculations accounting for differences in each species' body size in relation to humans. Suggested allometric scaling factors by ECETOC align with ECHA's recommendations (36) (for other species, consult Table R.8-3 in the ECHA guidance). While this approach is generally appropriate to account for interspecies differences, it should be modified if additional data on the substance or the species is known. It should be noted that this approach is appropriate for systemic toxicity following oral or dermal administration. It doesn't apply to direct local effects (i.e., skin or gastrointestinal irritation/corrosion), inhalation effects (local *or* systemic), or for doses in oral animal studies from the diet or in drinking water expressed as concentration in media (i.e., ppm in diet, mg/L in drinking water; dietary or drinking water exposures expressed in mg/kg/d would still apply allometric scaling). The rationale for the inhalation and oral dietary or drinking water concentration studies as exceptions to allometric scaling are justified in other guidance (29) (p. 23; for additional physiologically-driven restrictions on the use of allometric scaling, see p. 24–28).

For inhalation studies resulting in a systemic effect, no AF application is recommended where the principles of allometric scaling apply (note the limitations discussed in the above paragraph and in the PoD section) because breathing rates are anticipated to scale allometrically. However, owing to differences in experimental study design and occupational environments, it is appropriate to adjust for: (1) breathing rate differences between the test species (usually resting) and humans in the workplace (usually lightly respiring) and (2) number of days/hours the study includes compared to the average work week someone will experience in an occupational setting. These derivations are explained in full on page 8 of the ECETOC guidance (29), and are discussed in the PoD chapter of this guidance document.

REACH guidance suggests the use of an additional safety factor of 2.5 to account for any remaining interspecies differences in addition to the allometric scaling factor (36);

ECETOC concludes that this additional variability is likely due to intraspecies differences that were inherent to the experimental design, and was therefore not recommended by ECETOC.

Local effects

Allometric scaling should not be applied since local effects (e.g., irritation) are not dependent upon metabolic rate (recommended interspecies AF of 1). For more information on the scientific basis and rationale to be considered for this type of effect, see ECETOC [(29), p. 28–29].

Intraspecies

The intraspecies AF accounts for uncertainty resulting from differences in the underlying characteristics of the study population (e.g., age, gender, health status) compared to the diverse working population for whom the OEL is intended to protect. Size and composition of the study population are the two primary considerations when evaluating intraspecies uncertainty, with smaller, more homogenous studies requiring adjustment due to concerns that the average variability in the study population does not adequately represent the many unmeasured or unknown factors that affect human response in the target worker population.

For the purposes of OELs, ECETOC recommends an AF of 3 for worker populations (29), whereas ECHA recommends an AF of 5 (36), as an OEL is an exposure limit specifically pertaining to workplace exposures [for further explanation on this recommended difference, see Table 1 (29)]. This recommendation is held true for both systemic and local effects. The factor of 3 is expected to account for variability across a healthy population of working age, and is lower than the factor one would use if the effects observed in the key study were being applied to the general population (which inherently contains a higher degree of inter-individual variability). If there is reason to believe the working population would be uniquely susceptible to effects of exposure to the chemical/substance being evaluated, a higher AF may be considered and proposed, if substantiated with evidence.

For compounds studied using very large, diverse cohorts, or large meta-analyses, an assessment factor of 1 is considered appropriate. An AF of 1 may also be appropriate for study populations where sensitivity is well-defined and sensitive individuals are adequately represented in the study population. In addition, an intraspecies factor of 1–1.5 is generally a good starting point for intentional exposure studies of immediate, transient effects, such as irritation, which are usually associated with less inter-individual (i.e., intra-species) variation in response. However, because experimental studies are also relatively small (e.g., 10–20) and volunteers are usually younger and healthier than the average workplace population, the range of human variability may not be fully tested, necessitating a small intra-species AF.

Exposure duration

The exposure duration AF accounts for extrapolation from a study design of shorter duration to a chronic exposure. This is important because an OEL needs to account for exposure across a number of years over a human's working lifespan, and the majority of animal studies occur within a much shorter time span. Because of this, an exposure duration AF is applied to account for any uncertainty in the extrapolation from a shorter term study in animals to longer term effects in humans. Essentially, the recommendation for the exposure duration AF is the same for both systemic and local effects. Scientific reasoning behind considerations for systemic and local effects, and why they are the same, can be found for the exposure duration AF in the ECETOC guidance (29). The table below details recommended ranges for default exposure duration study AFs (where subacute equates to a 28 day study, subchronic to a 90 day study, and chronic is a 1.5 year to lifetime study in a standard rodent assay):

There are instances where exposure duration AFs would need to account for not just the extrapolation of exposure duration based on study design, but additional aspects of the endpoint of interest itself as well. For example, expert judgement would need to be exercised in selecting the AF value if the NOAEL would decrease when an effect would be expected to become more severe with increasing exposure time, or if it would be expected that new effects would be likely if the study were extended out to a chronic exposure paradigm. For specific examples on what would drive these decisions and more information on where expert judgement should be applied, consult the ECETOC guidance document (29).

For human studies, the exposure AF generally accounts for uncertainty in one or more of the following: (1) insufficient exposure duration, (2) insufficient follow-up time, especially for long-latency endpoints such as most cancers, and/or (3) errors in exposure measurement/assessment and/or classification.

Uncertainty around insufficient exposure and/or follow up time are handled similarly. In the context of human data, ECETOC (26) recommended an AF of 2 where "sub/semi chronic effects are observed such as depression of blood counts or transitional chromosome aberrations following days/weeks of exposure, i.e., they are observable effects of possible pre-clinical significance and serve as a surrogate measure for frank effects". However, to the extent possible, determination of an exposure AF should be data-driven. For example, if data exists that show that an exposure's effects increases by 40% after 20 years of exposure, due to an extremely long half-life, it could be reasonable to predict another 40% increase of this effect had exposure been extended out to 40 years, the maximum exposure time of a worker in the OEL setting. Thus, a data-derived AF of 1.4, which incorporates existing data, could be considered.

At least some degree of exposure measurement error and/or misclassification is present in virtually all epidemiologic studies and the uncertainty this source of error imparts into establishing a protective OEL derivation should be taken into consideration. Measurement error can occur as a result of either poor or inappropriate IH collection methods and procedures or limited retrospective exposure estimation. Measurement error can lead to exposure misclassification when individuals are assigned to categories of exposure (e.g., high, medium, low) that do not accurately reflect their true exposure level. Depending on how and when IH measurements were taken and how well those measurements correlate with actual individual level exposure (e.g., excursions, emergency response, maintenance), the direction of the error could lead to either an under- or over-estimation. If the health endpoint observed in the key study is attributed to an over-estimated exposure concentration, an AF greater than 1 is justified. Conversely, if effect estimates are associated with exposures that were under-estimated the AF should be <1. To the extent possible, a data-driven approach to identifying empirically derived AF are encouraged.

Where available, biomonitoring information can be helpful in assessing potential for under- and over-estimation of exposure from air measurements, especially in cases where respiratory protection was used (i.e., air monitoring data is not representative of the person's actual exposure) or where other routes of exposure are significant (e.g., dermal exposure which is often not quantitatively assessed). Biomonitoring may help reflect the total exposure, and in cases where correlations between biomonitoring values and air equivalent exposures are available, may be a more robust indicator of exposure depending on the specific chemical being considered.

Dose-response (NOAEL-LOAEL extrapolation)

The dose-response AF takes into account potential differences in the dose response curve observed in the population under study to the dose response curve that is applicable to the target (working) population. Common complexities unique to the epidemiologic literature can complicate clear LOAEL/NOAEL identification and characterization of the dose-response curve, creating uncertainty around the selected PoD. In particular, continuous exposure data may preclude accurate identification of the concentration at which point risk increases above background. Wide and open-ended exposure categories may also limit clear identification of NOAEL/LOAEL. In addition, lack of monotonicity, whereby risk increases with each incremental dose or exposure category, creates further uncertainty about the robustness of observed associations.

For most well-designed toxicological studies, an AF of 3 will account for extrapolation from a LOAEL to a NOAEL [(29), Table 1; for further justification, see Table 1 (39); 7 studies are cited which detail ranges of the ratio of LOAEL/NOAEL for differing study durations and designs which substantiate the use of an AF of 3]. ECHA recommends a range of 1–10 for this AF (36). If the PoD from the key study is a NOAEL (or a BMDL, as this is considered equivalent to a NOAEL), an AF of 1 is suggested, as there are no adjustments to be made to account for uncertainties related to extrapolating from a LOAEL to a NOAEL. For further scientific evidence supporting the extrapolation AF value of 3 for LOAEL to NOAEL, refer to Section 2.2 of the ECETOC guidance (39). ECETOC states that the maximum value for LOAEL/NOAEL extrapolation generally is 10 but they considered that value as overly conservative; a larger AF should be considered where data indicate that a steep dose-response exists and/or for severe endpoints, thereby accounting for the greater consequence of any error in estimating the LOAEL/NOAEL (39).

Properties of the LOAEL or NOAEL that can influence justification to deviate from the recommended AFs to a higher value include: low study quality (note: different from quality of the whole database discussed in the next section), serious and/or irreversible effects, shallow dose-response curve (in which it's more difficult to determine where the true LOAEL/NOAEL lies), and dose-spacing higher than 2–4 fold (36). Consult the ECETOC 2010 guidance (29) for more detail on properties of the LOAEL or NOAEL that could justify deviation from these defaults, and whether these justifications apply specifically to the key study of interest.

Quality of whole database

The database quality AF assignment includes a combination of a recommended range of acceptable values, and the expectation that expert judgement will be applied when selecting an appropriate AF for the key study.

When deciding whether to use the default AF of 1 for database quality, the following remaining uncertainties should be considered (39) in the potential assignment of a higher value than an AF of 1 (including, but not limited to): (1) completeness of the database, such that all endpoints potentially relevant to the compound of interest, both acute and/or chronic, have been adequately studied, (2) the use of a surrogate compound or compound(s), or the use of Quantitative Structure-Activity Relationship (QSAR)-derived information as a 'read-across' to the substance being assessed, (3) consistency in the direction and magnitude of results across the body of data, (4) study quality (in the design, conduct, analysis, reporting) and (5) causal nature of the relationship, which would include but not be limited to: (a) potential deficiencies in the key study/studies such that confounders or effect modifiers were not adequately measured or analyzed, (b) whether appropriate statistical methods were used, (c) adequacy of sample size and study power, and (d) evaluation of bias, including the healthy worker/healthy worker survivor effect.

Considerations for when to further refine AF based on available data

For substances with the type and/or specificity of toxicological data to deviate from default values recommended by ECHA and ECETOC guidance (29, 36, 39) (i.e., toxicokinetic and toxicodynamic data available), then chemical specific assessment factors (CSAFs) and more precise AFs may be considered. Some recommendations of ranges for AFs have been detailed above. For more information on what would specifically drive considerations for assignment of AFs based on considerable uncertainties, the respective sections of available guidance (29), and available literature, as AF application continues to be an ever-evolving space [for e.g., (5)].

Discussion

Protecting worker health is a clear priority. Integrating information to meet this endeavor is a complex process which requires the combination of existing risk assessment frameworks and guidance as well as expert scientific judgment. Utilizing a multidisciplinary team of experts in epidemiology, toxicology, and exposure allows for a robust scientific process. This cross-disciplinary approach provides for the integration of substance-specific datasets (or read-across substances, when necessary) within the context of existing internationally recognized guidance and expert scientific judgment. The technical evaluation includes the following tenets of risk assessment: (1) problem formulation (2) literature review, (3) weight of evidence considerations, (4) point of departure, (PoD) selection/derivation, (5) application of assessment factors, and ultimately, the derivation of an OEL which is protective of worker health.

For more insight into how the OEL derivation framework could be applied in practice, consider the following example of chromium in specific conditions of use. The OEL derivation for Chromium (VI) [Cr(VI)] for welding and other "hot work" activities (e.g., torch-cutting, arc gouging) serves as a recent example of the applicability of the risk assessment principles detailed within this manuscript. There was a need identified to develop an OEL for Cr(VI) exposure to welders and those engaged in other "hot work" in ExxonMobil operations. While sodium dichromate is entirely hexavalent chromium, it was considered less relevant to the ExxonMobil occupational environment than chromium oxide exposure because it is a soluble form [unlike particulate chromium oxide dust (ACGIH 2017)], thus not expected to be representative of the form of chromium present from welding and thermal cutting/gouging processes. Problem formulation involved defining exposures relevant to welders as being within scope, which greatly limited the applicability of that dataset to the current question. Through the literature review and WoE process, it was determined that the form of Cr(VI) present in exposures during welding activities may be less toxic than during other types of occupational exposures (i.e., chromate production). Animal models exhibited quantitatively different responses as a function of different forms of hexavalent chromium (i.e., sodium dichromate vs. chromium oxide aerosols), and the studies offered limited precision in allowing for direct comparisons between the observed quantitatively different responses among different Cr(VI) forms.

There is sufficient information to support carcinogenic potential for hexavalent chromium in animal models. Observed tumor types appear largely restricted to the portal of entry. Drinking water exposures to sodium dichromate dihydrate resulted in clear evidence for carcinogenicity in both rats and mice (males and females affected similarly), with the tumor sites being the oral cavity (rats) or small intestine (mice). Due to the portal of entry dependence for carcinogenicity of chromium the OEL development focused on inhalation exposures to particulate, insoluble forms of chromium. The OEL recommendation for Cr(VI) is based on a chronic inhalation exposure of male Wistar rats ($n = 18$ exposed and $n = 37$ controls) to a 2:3 mixture of trivalent:hexavalent chromium oxide dust for 22–23 h/day, 7 days/week for 18 months, then monitored for up to 12 additional months (40). Chromium oxide dust was selected as the preferred form on the basis it is more likely to reflect chromium in fume generated from welding and thermal cutting/gouging processes. The measured concentration of Cr(VI) was reported to be 63.3 $\mu g/m^3$ for the single group of rats exposed. No statistically significant effects on carcinogenic measures (number of rats with tumors, total tumor rate [benign or malignant]) were reported. Lung histopathology findings suggest 63.3 $\mu g/m^3$ is a lowest observed adverse effect level (LOAEL) and served as the point of departure for OEL derivation. Applying assessment factors, the calculated value is 0.75 $\mu g/m^3$, which was rounded to 1 $\mu g/m^3$ per the SCOEL rounding guidance (41). Due to the limited nature of reported exposure levels of Cr(VI) and health outcomes among welder cohorts, the key study for this OEL derivation was based on animal data.

There is a need for transparency in the approach to OEL derivation, due to the amount and type of possible outcomes of the use of expert judgment. Utilizing existing risk assessment principles in a fit-for-purpose paradigm for OEL derivation is imperative in the pursuit of reproducibility of the process, especially in terms of the use of new and contemporary applications (e.g., integration of AOPs, literature search automation). These concepts were recently highlighted in a special issue on the state of the science of OEL development put forth in the Journal of Occupational and Environmental Health (42), which detailed contemporary advances in methodology and analysis of data relevant to OEL development, as well as a call for the use and implementation of advanced methods for OEL development. The approach to OEL derivation detailed in this manuscript are intended to integrate risk assessment principles tailored toward the needs of understanding how to utilize data to best protect worker health with state-of-the science approaches to those principles. OEL derivation techniques are evergreen processes which will evolve/modify over time as new operations, analyses/technologies and data emerge.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found referenced in this manuscript: quantitative data and resources are listed as references in the reference list.

Author contributions

LM and KG contributed to conception and design of the manuscript. LM, MA, AB, FG, RL, CN, NW, and KG each wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Conflict of interest

The authors of this paper are or were employed by companies that manufacture petroleum products. The manuscript was written as part of normal employment and was the sole responsibility of the authors. No external funding was obtained for manuscript preparation.

Publisher's note

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Appendix

Additional detail regarding confidence considerations for human health effects

For the LOE consisting of human health effects assessed in observational epidemiology studies, characteristics of studies that decrease confidence include:

- *Case reports*. These are often one-off situations resulting in catastrophic event such as knock-down or an unusual/severe clinical finding. Typically, neither the circumstance nor the level of exposure is relevant to OEL development. Additionally, the lack of a referent/control group represents a serious limitation with regards to inferences about exposure and the apical effects of interest.
- *Qualitative exposure metrics*. Ever/never, exposed/non-exposed, and high/medium/ low without some quantitative distinctions cannot inform an OEL. However, there might be situations in which the author provides a median/mean value for those categories. If those values are relatively close together, they might be useful in finding a NOAEL/LOAEL threshold (a POD). Values which, for example, vary by an order of magnitude are generally not helpful as that threshold/POD might exist anywhere along the broad within-category exposure continuum.
- *Inseparable components of mixtures*. Some types of chemical agents are 'bundled together' when measuring workplace exposures despite significantly different levels of toxicity among sub-types that cannot be teased apart (e.g., benzene, toluene, ethylbenzene, and xylenes). Some authors make adjustments for this using various means, but those can be difficult to successfully execute.
- *Environmental studies (general population studies)*, typically, due to much lower concentrations and different exposure durations. These studies often lack individual-level data, so their utility is significantly limited.
- *Studies in which the study population represented has documented exposures to other stressors that are greater than those expected in the working population* (e.g., excessive smoking, alcohol/drug use). In this case, the study population may be more prone to show effects to the agent in question.

Characteristics of studies, often from the field of analytical epidemiology, that increase confidence include quantitative or measured exposures as a component of the overall exposure estimation, clearly described exposure history (e.g., exposure duration and age, cumulative exposure; average exposure; peak exposures, if available) including shape of the exposure distribution, air sampling that is representative of typical exposures (i.e, more than a single sample or a sample taken during documented IH excursions), short exposure category ranges to facilitate identification of NOAELs/LOAELs, accounts for co-exposures and other potential confounders in the workplace, sufficiently large study population sizes (e.g., large enough to result either in more than 5 expected cases for the key effect in the control/unexposed population or in confidence intervals that cover less than a two-fold range), and diverse study populations (e.g., multi-center trial or a meta-analysis of several studies from different geographical areas) (25).

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Application of multiple occupational health risk assessment models in the prediction of occupational health risks of n-Hexane in the air-conditioned closed workshop

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Background: n-Hexane (NH) poisoning is a common occupational poisoning in the hardware and electronics industries. However, there is few research data on risk assessment of positions using NH in enclosed workshops. It is very important to assess the risk level of these positions and put forward effective measures and suggestions.

Methods: The information of selected companies and air samples were collected through on-site investigation, and data collation and sample testing were carried out according to the requirements of Chinese standards. The Control of Substances Hazardous to Health (COSHH) Essential, the EPA non-carcinogenic risk assessment model, the Singapore exposure index method and the Chinese semi-quantitative risk assessment models were used to assess the risks of NH.

Results: The working hours of the exposure groups, printing groups and packing groups all exceeded 9 h per day, less than 30% of each similar exposure groups (SEG) was equipped with the local exhaust ventilation, and 11.1% of the cleaning group and 8.3% of the printing group had NH concentrations in the air that exceeded the Chinese occupational exposure limit (OEL). In the EPA non-carcinogenic risk assessment model, each SEG was evaluated at high risk. In the Chinese semi-quantitative risk assessment models, all of the work groups of exposure groups, 91.7% of the work groups of printing groups, 77.8% of the work groups of printing groups, and 57.1% of the work groups of printing groups were evaluated at unacceptable risk. More than 40.0% of the work groups of printing groups and cleaning groups and over 20.0% of the work groups of exposure groups and packing groups were evaluated at high risk in the Chinese semi-quantitative risk assessment models.

Conclusions: The Chinese exposure index method and the synthesis index method may have a stronger practicability. Some work groups that use NH in air-conditioned enclosed workshops in China, especially the cleaning groups, are still in a high-risk state. It is necessary to increase protective measures and strengthen occupational hygiene management to reduce risks.

KEYWORDS

occupational health, occupational poisoning, risk assessment, n-Hexane, air-conditioned workshop

Background

NH is a colorless organic compound that belongs to the straight-chain saturated hydrocarbon (1). It is considered a low-boiling chemical that is volatile at room temperature because of its boiling point of 69°C and vapor pressure of 127.5 mmHg at 25°C. It has the advantages of low price and good performance, and thus it is widely used in various production processes. For example, it is used as a cleaning agent and adhesive in printing, hardware and electronic equipment manufacturing industries (2, 3). Workers are exposed to NH at work through inhalation, ingestion and skin contact (4), which is mainly metabolized to 2,5-Hexanedione(2,5-HD) in the body. The concentration of 2,5-HD in urine is often used as a biological monitoring indicator for workers exposed to NH (5). The occupational NH poisoning is mainly chronic or sub-chronic, with clinical manifestations of Polyneuropathy, including bilaterally symmetrical sensory abnormalities, sensory loss and weakness in lower extremities, and neurogenic damage related to electrophysiological changes (6). However, there is no effective treatment for NH poisoning currently. The widespread use of NH in many countries has led to polyperipheral neuropathy, and its poisoning incidents have been reported in China, the United States, Japan, and Italy (6–8). Shenzhen City in Guangdong Province is one of the concentrations of electronic processing industries in China. These manufacturers are dominated by small workshops with high NH use, lack of protection and poor management. Therefore, many cases of NH occupational poisoning have been reported. According to statistics from 2006 to 2011, NH poisoning accounted for 28.2% of the total occupational diseases in Shenzhen (9).

Volatile chemical poisons can exist in the production environment in gaseous form. The chemical poisons in the air are inhaled into the human body through the respiratory tract, and their degree of harm to the human body is closely related to their concentration. Due to the closed structure and lack of natural ventilation, the supply of fresh air and the discharge of polluted air are limited in the closed workshop. This makes the volatile poisons in the workshop easy to accumulate, and high concentrations of poisons in the air can cause poisoning or even death of workers (10). In addition, the closed workshops prefer to be equipped with air conditioners. The air-conditioned air is discharged after the indoor air is circulated and cooled, which cannot remove toxic chemicals in the air. Therefore, the air circulated in the workshop can promote the process of chemical accumulation in the air and the closed air-conditioned workshops are more prone to occupational poisoning than other types of workshops.

The occurrence of NH occupational poisoning associated with various factors, including long exposure duration, enclosed working environment, poor ventilation or low efficiency of the air circulation system, and insufficient protective measures (4, 11). The Occupational Health Risk Assessment (OHRA) model has been proposed as a tool to predict and control the health risks of occupational hazards, which predicts the possibility and extent of hazards by qualitative, quantitative and semi-quantitative methods, and proposes corresponding preventive and control measures (12). Currently, the U.S. Environmental Protection Agency (EPA), Singaporean, Australian, Romanian, International Council on Mining and Metals (ICMM), and UK Control of Substances Hazardous to Health (COSHH) Essential models are considered as the six most common OHRA models (13). Previous studies have analyzed the advantages and limitations of each model (14). Quantitative, semi-quantitative and qualitative methods can be used in combination to assess risk levels more accurately. China has issued the occupational health standard, the "Guidelines for occupational health risk assessment of chemicals in the workplace (GBZ/T 298-2017)" (15), which introduced the basic definition, content and specifications for the use of OHRA. The qualitative and quantitative models in the standard are based on the same principles as the COSHH basic model and the EPA model, respectively. The semi-quantitative model in the standard includes three methods: exposure ratio method, exposure index method and synthesis index method. The principle of exposure ratio method is the same as that of the Singapore model, while the exposure index method and comprehensive index method are further developed based on the Singapore model (16).

Given the excellent oil solubility and low price of NH, there are still many small and medium-sized enterprises in China using NH as auxiliary production material, especially in the Pearl River Delta region where the electronics, hardware and printing industries concentrated. Moreover, NH is still used in large quantities in India, Vietnam and other manufacturing-oriented countries. To sum up, Occupational poisoning of NH is still an important occupational health problem. This study aimed to assess the occupational health risk of NH in the electronics, hardware and printing industries in China by multiple OHRA models, and then propose risk control and hazard management measures to reduce the risk of exposure.

Materials and methods

Description of the similar exposure groups

In this study, factors such as the composition of chemicals used, the amount of use, the setting of positions and the number of people in the positions were considered as the inclusion criteria for companies. A total of 36 positions in 28 companies in Shenzhen City of Guangdong Province in China were selected as the research object, mainly in the electronics and printing industries. In these industries, NH chemicals were used as decontamination detergents for cleaning. According to the characteristics of each position and the similarity of the job content, 36 positions were divided into 4 groups. The SEGs included 8 exposure groups, 12 printing groups, 10 cleaning groups, and 6 packing groups. The work of the exposure groups are to use film cleaner to remove stains on the film, which is mainly distributed in the electronic industry. The work of the printing groups are to use ink cleaning agents such as screen washing agent to remove ink, which is mainly distributed in the printing and electronic industries. The work of the cleaning groups are to use cleaning agents such as wiping water to remove surface stains. The work of the packing groups are mainly to use detergent to remove surface stains during packaging and checking. Details including duration of work, usage of NH, exposure duration, the automation level, ventilation, first-aid facilities, personal protective equipment, emergency rescue measures, occupational health management and NH concentration levels in each group were included in the investigation.

Site survey and on-site testing

We collected data through on-site surveys, including the number of workers, working hours, daily use of NH, exposure time and protective equipment, and then recorded the above information in questionnaire. The collection of air samples and the testing of laboratory NH samples were performed according to the methods described in Chinese Standards "Specifications of air sampling for hazardous substances monitoring in the workplace (GBZ159-2004)" (17) and "Determination of alkanes in the air of workplace (GBZ/T 160.38-2007)" (18). The 8-h time-weighted average concentration (C-TWA) and short-term exposure concentration (C-STEL) of NH were tested and compared with the permissible concentration-time weighted average (PC-TWA) and permissible concentration-short term exposure limit (PC-STEL) in the Chinese standard, "Occupational exposure limits for hazardous agents in the workplace Part 1: Chemical hazardous agents (GBZ 2.1-2019)" (19).

Occupational health risk assessment models

The COSHH essential model, EPA non-carcinogenic risk assessment model, Singapore exposure index method and semi-quantitative risk assessment model in China were selected to assess the occupational health risk of NH. The semi-quantitative risk assessment model can be referred to the standard in China, "Guidelines for occupational health risk assessment of chemicals in the workplace (GBZ/T298-2017)" (15).

(1) The COSHH Essential model. This model conducts risk assessment through both health hazards and exposure levels of chemicals. Health hazards were determined by the range of occupational exposure limits (OELs) or by assigning the assessed substance to a hazard band using a Risk-phrase. The exposure level was determined by the physical property, such as volatility, and by the use of substance.
(2) The EPA non-carcinogenic risk assessment model. The non-carcinogenic risk level could be calculated by the following equation: $HQ = EC/RfC$ (HQ = the hazard quotient, which is the value of the non-carcinogenic risk; EC = the exposure concentration for the acute exposure period; RfC = the reference concentration for inhalation toxicity).

In the equation, the RfC value of NH was 2×10^{-3} mg/m^3. EC values were estimated based on the concentration of chemicals in the air, exposure duration and frequency, working age and etc. The HQ value was used to determine the risk level. When the value was greater than or equal to 1, it indicated that the chemical substance might have a high non-carcinogenic risk (unacceptable risk). In addition, when the value is <1, it indicated that the chemical substance might have a low non-carcinogenic risk (acceptable risk).

(3) The Singapore exposure index method. This method is one of the methods of the Singapore model. The risk level can be calculated by the equation: $Risk = \sqrt{HR \times ER}$ (HR = hazard rating; ER = exposure rating).

In the equation, the HR values could be determined by the carcinogenicity classifications established by the American Conference of Government Industrial Hygienists (ACGIH) and the International Agency for Research on Cancer (IARC) or by the median lethal dose (LD50) and the median lethal concentration (LC50) of chemical substances in Material Safety

Data Sheets (MSDS). The ER was calculated using equation: $ER\ \ [EI_1 \times EI_2 \times \cdots EI_n]^{1/n}$ (EI = the exposure index; n = the number of exposure factors, which includes vapor pressure, particle size, hazard control measures, weekly usage of the chemicals, and duration of work per week).

(4) The semi-quantitative risk assessment model in China. The model includes the exposure ratio method, exposure index method and synthesis index method. The risk level was calculated in the same way as the Singapore exposure index method.

In the exposure ratio method, the ER was determined by the ratio of the exposure level (E) and OEL, and the E was calculated using the equation: $E = F \times D \times M/W$ (F = the frequency of exposure per week; M = the magnitude of exposure; W = the average working hours per week; D = the average duration of each exposure). Compared with the Singapore exposure index method, the EI of the Chinese exposure index method takes into account more factors, including first aid facilities, PPE, emergency rescue measures, occupational health management, daily use of chemicals and daily working hours. And in the synthesis index method, the ratio of exposure level to OEL (E/OEL) was added to the EI.

Risk ratio conversion

The risk level was converted into the risk ratio with the equation: RR = R/N (RR = the risk ratio; R = the risk level; N = the number of total levels). In this study, the hazard ratios were divided into 5 ranges and defined as 5 adjusted risk levels (0–−0.2 = level 1; 0.2–0.4 = level 2; 0.4–0.6 = level 3; 0.6–0.8 = level 4; 0.8–1 = level 5).

Statistical analysis

SPSS 22.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. The statistical significance of differences between the groups was determined by one-way analysis of variance (ANOVA), followed by the Tukey *post hoc* test. The consistency of the two occupational health risk assessment models was assessed by Cohen's Kappa ($k \geq 0.75$, indicating good consistency; $0.75 > k \geq 0.40$, indicating average consistency; $k < 0.40$, indicating lack of consistency).

Results

On-site survey and test results

The number of workers per group, working hours, usage of NH, automation level, ventilation measures, first-aid facilities, emergency rescue measures, occupational health management, and NH concentration levels for the SEGs were listed in Table 1. According to the results of the on-site investigation, the production processes were mainly semi-automatic and manual operations. Most of workplaces were set up with comprehensive ventilation system, while the rest of small number of manufacturers were equipped with local ventilation facilities for operating positions only. Most of manufacturers provided personal protective equipment for their employees, however, it was found that some of the PPE were not equipped in accordance with the standard requirements. In addition, most manufacturers had first-aid facilities and emergency rescue measures. The processes in the exposure and printing groups were mainly semi-automatic operations, while those in the cleaning and packaging groups were mainly manual operations. The amount of hexane used in the exposure and printing groups was significantly more than that in the cleaning and packaging groups. The C-TWA for hexane ranged from 4.20 to 70.30 mg/m^3 with an average value of 20.76 mg/m^3 in the exposure group, from 0.50 to 160.44 mg/m^3 with an average value of 31.07 mg/m^3 in the printing group, 0.40 to 100.40 mg/m^3 with an average value of 41.29 mg/m^3 in the cleaning group, and 1.60 to 33.20 mg/m^3 with an average value of 13.79 mg/m^3 in the packing group, The C-STEL of NH for hexane ranged from 4.90 to 82.90 mg/m^3 with an average value of 34.51 mg/m^3 in the exposure group, from 3.08 to 630.80 mg/m^3 with an average value of 82.93 mg/m^3 in the printing group, 0.40 to 265.30 mg/m^3 with an average value of 86.76 mg/m^3 in the cleaning group, and 5.60 to 89.40 mg/m^3 with an average value of 54.61 mg/m^3 in the packing group.

Although the average values of C-TWA and C-STEL were higher in the printing groups and cleaning groups, the numerical differences between the SEGs were not statistically significant. In addition, the results of the survey showed that 8.3% of the printing groups and 11.1% of the cleaning groups had results of C-TWA and C-STEL exceeding the PC-TWA and PC-STEL in the Chinese standard.

Risk assessment results

As shown in Table 2, NH had a risk level of R48, which indicated a risk of serious damage to health through long-term exposure through inhalation, dermal absorption and ingestion, and therefore its hazard class (HR) in the COSHH Essential model was considered to be Level D. Based on the volatility and use of NH in different manufacturers, the exposure rating (ER) of each SEG was grade 2 to 3. Combining the results of HR and ER, the COSHH essential model showed that all groups exposed to NH had a very high risk. Besides, the results of the EPA non-carcinogenic risk assessment model showed that a total of 82.9% of the all work groups had HQs >1, with 100% of the exposure groups, 91.7% of the printing groups, 77.8% of the cleaning groups and 57.1% of the packaging groups

TABLE 1 Survey results of SEGs exposed to n-Hexane.

SEG		Exposure groups	Printing groups	Cleaning groups	Packing groups
Number of groups		7	12	9	7
Number of workers per group		4–53	2–35	1–11	2–8
Duration of work (months)		44.1(17–68)	32.8(6–156)	19.6(5–42)	20.7(6–48)
Daily usage (kg/L)		7.4 (0.2–20)	8.4 (0.1–30)	1.5 (0.25–4)	3.2 (0.005–15)
Weekly usage (kg/L)		44.1 (1.2–120)	48.1 (0.5–180)	8.6 (1.25–24)	18.9 (0.03–90)
Hours of work per day		9.7 (8–10)	9.3 (8–10)	7.0 (2–10)	9.3 (8–10)
Days of work per week		5.7 (5–6)	5.8 (5–6)	5.4 (5–6)	5.9(5–6)
C-TWA (mg/m^3)		20.76 (4.20–70.30)	31.07 (0.50–160.44)	41.29 (0.40–100.40)	13.79 (1.60–33.20)
C-STEL (mg/m^3)		34.51 (4.90–82.90)	82.93 (3.08–630.80)	86.76 (0.40–265.30)	54.61 (5.60–89.40)
E/OEL		0.557 (0.042–1.873)	1.173 (0.067–9.337)	0.935 (0.002–3.925)	0.631 (0.245–1.323)
Result					
	C-TWA disqualified	0 (0/7)	8.3% (1/12)	11.1% (1/9)	0 (0/7)
	C-STEL disqualified	0 (0/7)	8.3% (1/12)	11.1% (1/9)	0 (0/7)
Automation level					
	Full automation	0 (0/7)	0 (0/12)	0 (0/10)	0 (0/7)
	Semi-automation	100.0% (7/7)	66.7% (8/12)	33.3% (3/9)	14.3% (1/7)
	Manual operation	0 (0/7)	33.3% (4/12)	66.7% (6/9)	85.7% (6/7)
Ventilation					
	General ventilation	71.4% (5/7)	83.3% (10/12)	77.8% (7/9)	85.7% (6/7)
	Local exhaust ventilation	28.6% (2/7)	16.7% (2/12)	22.2% (2/9)	14.3% (1/7)
First-aid facility equipped		100% (7/7)	100% (12/12)	100% (9/9)	100% (7/7)
Personal protective equipment					
	Equipped	85.7% (6/7)	83.3% (10/12)	88.9% (8/9)	85.7% (6/7)
	Used or worn	85.7% (6/7)	83.3% (10/12)	88.9% (8/9)	85.7% (6/7)
Emergency rescue measures complete		85.7% (6/7)	58.3% (7/12)	77.8% (7/9)	85.7% (6/7)
Occupational health management					
	Performs well	71.4% (5/7)	75.0% (9/12)	77.8% (7/9)	71.4% (5/7)
	Performs poorly	14.3% (1/7)	25.0% (3/12)	22.2% (2/9)	28.6% (2/7)
	Lack of management	14.3% (1/7)	0 (0/12)	0 (0/9)	0 (0/7)

C-STEL, short-term exposure concentration; C-TWA, 8-h time weighted average concentration; E/OEL, the ratio of exposure concentration to the occupational exposure limit; the results here represent the larger ratios of C-TWA/PC-TWA and C-STEL/PC-STEL. PC-TWA, the permissible concentration-time weighted average; PC-STEL, the permissible concentration-short term exposure limit; SEG, the similar exposure group. $^{*}P < 0.05$ compared to degreasing groups.

TABLE 2 Evaluation results of the COSHH Essential model and the EPA non-carcinogenic risk assessment model of n-Hexane.

SEG	Number of groups	COSHH essential model			EPA non-carcinogenic risk assessment model		
		HR	ER	Risk level	HQ	Unacceptable risk ratio	Acceptable risk ratio
Exposure groups	7	D	2–3	4 (Very high risk)	10.42 (1.93–32.10)	100.0% (7/7)	0
Printing groups	12	D	2–3	4 (Very high risk)	13.51 (0.23–78.49)	91.7% (11/12)	8.3% (1/12)
Cleaning groups	9	D	2–3	4 (Very high risk)	12.14 (0.06–35.10)	77.8% (7/9)	22.2% (2/9)
Packing groups	7	D	2–3	4 (Very high risk)	5.90 (0.10–11.07)	57.1% (4/7)	42.9% (3/7)
Total	35	D	2–3	4 (Very high risk)	10.84 (0.06–78.49)	82.9% (29/35)	17.1% (6/35)

COSHH, UK Control of Substances Hazardous to Health; EPA, U.S. Environmental Protection Agency; ER, exposure rating; HR, hazard rating; HQ, the hazard quotient; SEG, the similar exposure group.

TABLE 3 Evaluation results of semi-quantitative risk assessment models of n-Hexane.

SEG	Number of groups	R	Exposure ratio method	Singapore exposure index method	Chinese exposure index method	Synthesis index method
Exposure groups	7	2	14.3% (1/7)	0	0	0
		3	71.4% (5/7)	100.0% (7/7)	71.4% (5/7)	71.4% (5/7)
		4	14.3% (1/7)	0	28.6% (2/7)	28.6% (2/7)
Printing groups	12	2	16.7% (2/12)	0	0	0
		3	66.6% (8/12)	50% (6/12)	58.3% (7/12)	58.3% (7/12)
		4	16.7% (2/12)	50% (6/12)	41.7% (5/12)	41.7% (5/12)
Cleaning groups	9	2	11.1% (1/9)	0	0	0
		3	66.7% (6/9)	88.9% (8/9)	44.4% (4/9)	55.6% (5/9)
		4	22.2% (2/9)	11.1% (1/9)	55.6% (5/9)	44.4% (4/9)
Packing groups	7	3	85.7% (6/7)	85.7% (6/7)	71.4% (5/7)	71.4% (5/7)
		4	14.3% (1/7)	14.3% (1/7)	28.6% (2/7)	28.6% (2/7)
Total	35	2	11.4% (4/35)	0	0	0
		3	71.4% (25/35)	77.1% (27/35)	60% (21/35)	62.9% (22/35)
		4	17.2% (6/35)	22.9% (8/35)	40% (14/35)	37.1% (13/35)

R, risk level; SEG, the similar exposure group.

were >1. These results indicated that most work groups had high non-carcinogenic risks.

The results of semi-quantitative risk assessment models of NH were listed in Table 3. Four models were used to assess risk levels. The results of the exposure ratio method showed that the risk levels of all work groups were distributed in levels 2–4 with 17.2% of the work groups being at high risk (level 4), which included 14.3% in the exposure group, 16.7% in the printing group, 22.2% in the cleaning group, and 14.3% in the packaging group. In addition, most of the work groups were at medium risk (level 3), with 71.4% in the exposure group, 66.6% in the printing group, 66.7% in the cleaning group, and 85.7% in the packaging group. The results of the Singapore exposure index method showed that the risk levels of all work groups were distributed in levels 3–4 with 22.9% of the work groups being at high risk, which included 50.0% in the printing group, 11.1% in the cleaning group, and 14.3% in the packaging group. There was no exposure group at high risk. The results of the Chinese exposure index method showed that the risk levels of all work groups were distributed in levels 3–4 with 40.0% of the work groups being at high risk, which included 28.6% in the exposure group, 41.7% in the printing group, 55.6% in the cleaning group, and 28.6% in the packaging group. Meanwhile, 60% in the work groups were at medium risk, including 71.4% in the exposure groups, 58.3% in the printing groups, 44.4% in the cleaning groups and 71.4% in the packing groups. The results of the composite index method showed that the risk levels of the work groups were distributed in levels 3–4, and it differed from the results of the Chinese exposure index method only in the distribution of risk levels in the clean group. In the Synthesis index method, 44.4% of the clean group was at high risk and 55.6% was at medium risk.

The Cohen's Kappa is generally used to evaluate the consistency of bidirectional ordinal classification data. However, the COSHH Essential model, the EPA non-carcinogenic risk assessment model and the semi-quantitative model had different classifications of risk levels. In order to make the models comparable, the risk levels of each model were converted into the RR, and further their adjusted risk levels were obtained. Their adjusted risk levels were listed in Table 4. As shown in Table 5, the consistency of risk assessment models was analyzed by the Cohen's Kappa. There was general consistency between the Exposure ratio method and the Singapore exposure index method, the Singapore Exposure Index method and the Chinese Exposure Index method, and the Singapore Exposure Index method and the Synthesis Index method. The Chinese exposure index method had good consistency with the Synthesis index method. The remaining Cohen's Kappa results suggested a lack of consistency.

Discussion

As a major component of cleaning agent, NH has been widely used in the manufacturing industry. Because NH has a high lethal dose (LD50 = 25 g/kg, orally administered in rats), it is considered as a low toxic compound, therefore, manufacturers have paid little attention to its toxicity. However, given the low boiling point of NH, it is readily absorbed at normal temperatures. Under the condition of massive long-term use of NH and improper protection, occupational poisoning is likely to occur, posing a threat to workers' health. This study targeted NH-exposed industries, including electronics, printing and hardware industries. Through on-site investigation and the application of multiple risk assessment models, the risk levels of

TABLE 4 Risk ratio transformation for risk levels of multiple risk assessment models.

SEG	Number of groups	RR	R (adjusted)	COSHH essential model	EPA non-carcinogenic risk assessment model	Exposure ratio method	Singapore exposure index method	Chinese exposure index method	Synthesis index method
Exposure groups	7	0.2–0.4	2	0	0	14.3% (1/7)	0	0	0
		0.4–0.6	3	0	0	71.4% (5/7)	100.0% (7/7)	71.4% (5/7)	71.4% (5/7)
		0.6–0.8	4	42.9% (3/7)	28.6% (2/7)	14.3% (1/7)	0	28.6% (2/7)	28.6% (2/7)
		0.8–1	5	57.1% (4/7)	71.4% (5/7)	0	0	0	0
Printing groups	12	0.2–0.4	2	0	8.3% (1/12)	16.7% (2/12)	0	0	0
		0.4–0.6	3	0	0	66.6% (8/12)	50% (6/12)	58.3% (7/12)	58.3% (7/12)
		0.6–0.8	4	83.3% (10/12)	41.7% (5/12)	16.7% (2/12)	50% (6/12)	41.7% (5/12)	41.7% (5/12)
		0.8–1	5	16.7% (2/12)	50% (6/12)	0	0	0	0
Cleaning groups	9	0–0.2	1	0	11.1% (1/9)	0	0	0	0
		0.2–0.4	2	0	11.1% (1/9)	11.1% (1/9)	0	0	0
		0.4–0.6	3	0	0	66.7% (6/9)	88.9% (8/9)	44.4% (4/9)	55.6% (5/9)
		0.6–0.8	4	88.9% (8/9)	0	22.2% (2/9)	11.1% (1/9)	55.6% (5/9)	44.4% (4/9)
		0.8–1	5	11.1% (1/9)	77.8% (7/9)	0	0	0	0
Packing groups	7	0.2–0.4	2	0	14.3% (1/7)	0	0	0	0
		0.4–0.6	3	0	28.6% (2/7)	85.7% (6/7)	85.7% (6/7)	71.4% (5/7)	71.4% (5/7)
		0.6–0.8	4	85.7% (6/7)	14.3% (1/7)	14.3% (1/7)	14.3% (1/7)	28.6% (2/7)	28.6% (2/7)
		0.8–1	5	14.3% (1/7)	42.9% (3/7)	0	0	0	0
Total	35	0–0.2	1	0	2.9% (1/35)	0	0	0	0
		0.2–0.4	2	0	8.6% (3/35)	11.4% (4/35)	0	0	0
		0.4–0.6	3	0	5.7% (2/35)	71.4% (25/35)	77.1% (27/35)	60% (21/35)	62.9% (22/35)
		0.6–0.8	4	77.1% (27/35)	22.9% (8/35)	17.2% (6/35)	22.9% (8/35)	40% (14/35)	37.1% (13/35)
		0.8–1	5	22.9% (8/35)	60% (21/35)	0	0	0	0

RR, risk ratio; R, risk level; COSHH, UK Control of Substances Hazardous to Health; EPA, U.S. Environmental Protection Agency; SEG, the similar exposure group.

TABLE 5 Cohen's Kappa results of risk assessment models of n-Hexane.

Cohen's Kappa (A Vs. B)	Value	Approx. Sig.
Exposure ratio method vs. Singapore exposure index method	0.582	0.000
Exposure ratio method vs. Chinese exposure index method	0.318	0.012
Exposure ratio method vs. Synthesis index method	0.355	0.006
Exposure ratio method vs. COSHH Essential model	0.012	0.692
Exposure ratio method vs. EPA non-carcinogenic risk assessment model	0.058	0.155
Singapore exposure index method vs. Chinese exposure index method	0.615	0.000
Singapore exposure index method vs. Synthesis index method	0.668	0.000
Singapore exposure index method vs. COSHH essential model	-0.006	0.869
Singapore exposure index method vs. EPA non-carcinogenic risk assessment model	-0.043	0.276
Chinese exposure index method vs. synthesis index method	0.940	0.000
Chinese exposure index method vs. COSHH Essential model	0.050	0.324
Chinese exposure index method vs. EPA non-carcinogenic risk assessment model	-0.078	0.102
Synthesis index method vs. COSHH essential model	0.039	0.418
Synthesis index method vs. EPA non-carcinogenic risk assessment model	-0.072	0.124
COSHH Essential model vs. EPA non-carcinogenic risk assessment model	0.001	0.989

different job positions were determined to provide a basis for risk management.

The results of the field survey showed that although the mean values of C-TWA and C-STEL of NH were the highest in the cleaning group with 41.29 and 86.76 mg/m^3, respectively, the average usage were very small. This may be due to the fact that 66.7% of the workers in the cleaning group may have been directly exposed to chemicals containing NH during manual handling, resulting in more severe exposure. In the packaging group, 85.7% of the production processes required manual operation, but the average values of C-TWA and C-STEL in this group were only 18.9 and 45.09 mg/m^3, respectively. Therefore, it can be speculated that most of the products may have been cleaned before the packaging process, reducing the NH exposure of packaging workers. In addition, the average NH use was higher in the exposure group and printing group but with normal results of C-TWA and C-STEL for each group, which could be accounted for the higher automated process level and fully equipped ventilation facilities. Only 8.3% of the printing groups and 11.1% of the cleaning groups had exposure concentrations higher than the Chinese occupational exposure limit, which may relate to the characteristics of the production process, automation level and the effectiveness of ventilation facilities.

We evaluated the occupational health risk of NH using three methods, namely COSHH Essential model, EPA non-carcinogenic risk assessment model and semi-quantitative risk assessment model (i.e., Singapore model and three semi-quantitative risk assessment models in China.) The result of COSHH Essential model showed that all the SEGs were at very high risk. According to COSHH Essential model, Since HR of NH was D, when the volatility was considered moderate, the ER of work groups were grade 2–3 with the risk levels 3–4. We took the highest risk level value as the outcome (very high risk). COSHH Essential model is relatively simple and easy to understand, but the drawbacks are obvious too, such as overestimation of the results and influence of subjectivity on judgement of liquid volatility. The EPA non-carcinogenic model is a quantitative assessment model, which can comprehensively evaluate the non-carcinogenic and carcinogenic risks of chemicals, but NH is non-carcinogenic and we do not need to access its carcinogenic risk. Compared to the COSHH Essential model, the EPA models is more reliable because the EPA model assesses risk level by adopting highly-weighted parameters, which tend to show a higher risk level (20). In the EPA's non-carcinogenic risk assessment model, the risk level is determined by the EC and the RfC of the toxicant. The RfC represents the reference concentration of continuous inhalation that does not cause some health risk over a lifetime. Even if both the RfC of NH and its concentration in air are low (<0.5 OEL), the risk level is still high. In addition, the COSHH Essential model may overestimate the levels of risk from NH exposure in work groups because this model highly depends on the physicochemical property and exposure level of the substance but ignores the factors such as automation level, ventilation settlement, emergent rescue measures, management and utilization rate. Therefore, focus on workers' exposure to NH in the above manufacturers may not be sufficient. Nevertheless, the EPA non-carcinogenic risk assessment model can only classify risk level as high and low, leading it unable to distinguish different risk levels well.

Nonetheless, the EPA non-carcinogenic risk assessment models can only classify risk levels as high and low, resulting in a

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TABLE 6 An overview of the application of risk assessment methods relevant to this study.

Classification	Model	Parameter	Equation	Advantage	Disadvantage
Qualitative model	COSHH essential model	health hazard; *exposure levels.	Matrix method	① The usage and nature of chemicals are considered. ② Simple and easy to implement	① Protection measures and management measures are not considered; ② The results may be overestimated; ③ The results may be influenced by subjectivity on judgement of usage of chemicals.
Quantitative model	① EPA non-carcinogenic risk assessment model	*EC = the exposure concentration for the acute exposure period; RfC = the reference concentration for inhalation toxicity	$HQ = EC/RfC$ (HQ ≥ 1, unacceptable risk; HQ < 1, acceptable risk)	① Quantitative data can be well used, including the exposure concentration; ② The non-carcinogenic and carcinogenic risks of chemicals can be adequately assessed.	① Protection measures and management measures are not considered; ② The results may be overestimated; ③ The risk levels cannot be differentiated in detail.
	② EPA carcinogenic risk assessment model	IUR = the inhalation unit risk; *d = the exposure dose that equals the chemical concentration in the air; t_E = the exposure duration; t_L = the life expectancy	$IR = IUR \times d \times \frac{t_E}{t_L}$ (IR≥10^{-4}, unacceptable risk; IR<10^{-4}, acceptable risk)		
Semi-quantitative models	① Exposure ratio method	*F = the frequency of exposure per week; *M = the magnitude of exposure; *W = the average working hours per week; *D = the average duration of each exposure; OEL = occupational exposure limit HR = hazard rating; ER = exposure rating	① $E = F \times D \times M/W$ ② $ER = \frac{E}{OEL}$ ③ $Risk = \sqrt{HR \times ER}$	① The exposure concentration is considered.	Protection measures and management measures are not considered.
	② Singapore exposure index method			Protection measures and management measures are considered.	① The classification of the exposure index is relatively crude. ② The exposure concentration is not considered.
	③ Chinese exposure index method	*EI = the exposure index; n = the number of exposure factors; HR = hazard rating; ER = exposure rating	① $ER[EI_1 \times EI_2 \times \cdots EI_n]^{1/n}$ ② $Risk = \sqrt{HR \times ER}$	Protection measures and management measures are considered.	① The classification of the exposure index is relatively crude. ② The exposure concentration is not considered.
	④ Synthesis index method			Protection measures and management measures are considered.	The exposure index classification is relatively crude.

*indicates that the data is obtained by on-site investigation.

TABLE 7 Information on studies in China related to n-hexane occupational poisoning.

References	Work group	Number of cases	Working hours	Ventilation	Personal protective equipment	Occupational health management
Zhou et al. (22)	Cleaning groups	58/58 (100%)	/	Most without local exhaust ventilation	/	/
Hu et al. (23)	Cleaning groups	13/13 (100%)	11–12 h/d, more than 6 days per week	poor general ventilation, no local exhaust ventilation	Some wear gloves and masks	Lack of management
Mao et al. (24)	Cleaning groups	24/24 (100%)	8 h/d	central air conditioning, no local exhaust ventilation	No personal protective equipment	Lack of management
Xuan et al. (25)	Cleaning groups	23/23 (100%)	8–10 h/d	No ventilation	Finger sleeves	/
Li et al. (26)	Printing groups	5/39 (12.8%)	/	/	/	/
	Cleaning groups	32/39 (82.1%)	/	/	/	/
Zhang et al. (27)	Cleaning groups	49/62 (79%)	10 h/d, more than 6 days per week	No ventilation or no use	No personal protective equipment	Perform poorly
	Packing groups	13/62 (21%)	10 h/d, more than 6 days per week	No ventilation or no use	No personal protective equipment	Perform poorly

crude and vague assessment. The results of the semi-quantitative risk assessment model showed that the risk levels were 2 to 4 for the exposure, printing and cleaning groups and 3 to 4 for the packaging group. In the exposure ratio method, exposure concentration was the only factor taken into account for the risk levels, without considering the effects of protective measures. The Chinese exposure index method is used only in the absence of air monitoring data and is similar to the Singapore exposure index method, which focuses on exposure factors other than exposure concentrations. The Singapore exposure index method considers vapor pressure or particle size, hazard control measures, weekly chemical usage, and weekly working hours, while the Chinese exposure index method considers more specific exposure factors, including first aid facilities, personal protective equipment, emergency rescue measures, occupational health management, daily usage of chemicals, and daily working hours. The composite index method has an additional exposure concentration of another exposure factor based on the Chinese exposure index method. As shown in Table 3, in the cleaning groups, the evaluation results of the Singapore exposure index method for certain groups were lower than those of the Chinese exposure index method and the synthesis index method. No change in the results of other groups. In this study, some work groups of each SEGs was considered in a high-risk state because of high exposure concentration or low level of automation or poor occupational health management. In general, the risk of the cleaning groups were the highest. Compared to other two methods, the Chinese exposure index method and the synthesis index method were considered to be more practical, except that their relatively rough index classification. In order to improve the reproducibility of the risk assessment methods used in this study and promote the application of the risk assessment methods, the overview of the application of risk assessment methods was listed in Table 6. In the follow-up study, the risk level of NH poisoning in each post will be more accurately evaluated in combination with the population health data.

In a survey in 2016, NH was detected in the production raw and auxiliary materials of 46 of the 61 companies using organic solvents in Shenzhen. These 46 companies were mainly distributed in the electronic industry and the printing industry, while the work groups exposed to NH were mainly cleaning groups, printing groups and exposure groups, etc. They used chemicals containing n-Hexane in the production process, such as wiping water, detergent, etc. (21). The industry distribution and position distribution were consistent with the investigation of this study. This survey results showed that the qualification rate of cleaning groups was 77.7%, the printing groups was 80.5%, and the packing groups was 86.6%. Therefore, the cleaning group had the most failure points and workers were more prone to occupational poisoning without proper protection. Since 2000, cases of NH occupational poisoning have been reported in some regions of China. As shown in Table 7, work groups, case number, working hours, ventilation facilities, personal protective equipment and occupational health management of the reports have been listed (22–27). It was found that the manufacturers where NH poisoning occurred had some common features, such as most cases were cleaning, packaging and printing workers, with the highest incidence among cleaning workers. This is consistent with the risk assessment results of Chinese exposure index method and synthesis index method. The results of both methods indicated that the cleaning group had a relatively high level of risk, so they were theoretically the most likely to have the highest number of poisoning events. These cleaning workers worked in an enclosed space without proper ventilation or sufficient personal protective equipment, and used hexane-based detergents for cleaning or wiping for more than 8 h per day. In terms of management, most companies do not have an established occupational health management system in place, nor are they hiring full-time management personnel with occupational health-related knowledge. To sum up, these cases shared some common feathers, such as long working duration, poor ventilation in workplace, and ineffective protection, etc. It suggested that the above factors that closely related to the risk of NH poisoning could be the common problems in most manufacturers using NH and can be used as critical control points to propose risk management measures to reduce the risk level.

Combined with the results of this study and related research, the proposed risk management measures are mainly aimed at companies and workers. For manufacturers, the most effective measure is to replace NH with low or non-toxic chemicals, such as medical alcohol, isopropanol, n-heptane. If NH cannot be replaced according to the production process, effective control measures should be taken. Such as improving mechanization, automation, confinement and remote operation of the process, reducing the chance of direct contact of manual work, adjusting working hours to reduce workers' contact time, avoiding the use of NH in air-conditioned workshops as much as possible and setting up effective local exhaust facilities to reduce NH concentration in the workplace. In addition, enterprises should strictly implement occupational health management, regularly monitor NH concentration in the workplace, conduct occupational health checkups for employees at least once a year, and provide workers with effective personal protective equipment, such as respirators and protective gloves. It has been proved that the NH concentration in the workplace air can be greatly reduced after using NH-free chemicals and installing efficient local ventilation facilities (28). On the other hand, workers need to raise their awareness of self-protection. For instance, they should stand in the upwind of the airflow as closed to the exhaust hood as possible without affecting operations. In addition, workers should properly wear personal protective equipment and seek medical treatments if physical abnormalities appear.

Conclusions

The OHRA model in the Chinese standard GBZ/T 298-2017 can be used to assess the occupational health risks of NH, while the Chinese exposure index method and the synthesis index method may be more practical. Some work groups that use NH in the air-conditioned enclosed workshops in China are still in a high risk, especially printing groups and cleaning groups. It is critical to take risk management measures to reduce the risks.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Author contributions

SS, CW, and ML contributed to the data acquisition, analysis, interpretation, drafted, and critically reviewed the manuscript for intellectual content. HX, JZ, and TWcontributed to the data analysis. SS and JZ conceived and designed the study. SS is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors reviewed and approved the final version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The prediction of occupational health risks of benzene in the printing industry through multiple occupational health risk assessment models

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Background: Benzene poisoning is a common occupational poisoning event in the printing industries. Up to now there is still a lack of research data on risk assessment of benzene operations in enclosed workshops. It is crucial to assess the risk level of these positions and put forward effective measures and suggestions.

Methods: The information of selected companies and air samples were collected through on-site investigation, data collation and sample testing were carried out according to the requirements of Chinese standards. The Control of Substances Hazardous to Health (COSHH) Essential, the EPA non-carcinogenic risk assessment model, the Singapore exposure index method and the Chinese semi-quantitative risk assessment models were used to assess the risks of benzene.

Results: The exposed groups all worked more than 8 h per day, and the cleaning, pasting, and packaging groups used general ventilation rather than local ventilation. 28.6% of the printing group and 16.7% of the pasting group had benzene concentrations that exceeded the permissible concentration-time weighted average (PC-TWA) in China. Over 60.0% of the work groups were evaluated at high risk and over 20% of the work groups were evaluated at high cancer risk by the risk assessment models.

Conclusion: The Chinese exposure index method and the synthesis index method may have a stronger practicability. The printing and pasting groups may have a higher risk for benzene exposure. It is necessary to increase protective measures and strengthen occupational hygiene management to reduce risks.

KEYWORDS

occupational health, risk assessment, benzene, printing industry, occupational hygiene management

Background

Benzene is a colorless, sweet and transparent liquid at room temperature. Benzene is considered as a volatile organic compound (VOC) because of its boiling point of 80.1°C and saturated vapor pressure of 12.66 kPa at 25°C (1). Benzene is widely used as fuel and solvent, while it can also be used to synthesize chemical substances. As an important basic raw material of petrochemical industry, benzene is widely used in various industries. At present, the ink used in the packaging and printing industry usually uses benzene as an organic solvent (2).

The primary exposure route of benzene is inhalation. The main health hazard of occupational exposure to benzene is acute poisoning. Data showed that occupational diseases in the printing industry were mostly sporadic with various types, such as benzene poisoning, n-hexane poisoning, toluene poisoning, methanol poisoning, etc. Benzene poisoning is the most common one (3). It was reported that a glue brush worker in a wine box printing plant died of aplastic anemia after working in a high benzene concentration environment for 4 months. In a printing equipment factory, pure benzene was used as a rubber solvent to produce printing rubber cloth. From 1989 to 1994, 33 people were exposed to pure benzene. The prevalence rate of benzene poisoning was 15.2 and 33.3% of the 33 observed objects were benzene poisoning (4). In a private printing plant, a worker who had been working in printing and laminating and had been exposed to adhesives and thinners containing benzene was diagnosed with severe aplastic anemia after 2 years when he developed headaches, bleeding gums, and petechiae on the skin and mucous membranes (5). Several occupational health risk assessment (OHRA) models have been developed to assess health risks from occupational hazards and provide control measures. OHRA not only estimates the likelihood and extent of hazard occurrence through qualitative or quantitative assessments, but also takes appropriate measures to minimize occupational risks (6). Currently, the U.S. Environmental Protection Agency (EPA), Singaporean, Australian, Romanian, International Council of Mines and Metals (ICMM) and UK Basic Model for The Control of Hazardous Substances to Health (COSHH) are considered to be the six most common OHRA models, with the Singapore model having good overall compatibility (7). In 2017, China issued the Occupational health standard "Guidelines for Occupational Health Risk Assessment of Chemicals in the Workplace" (GBZ/T 298-2017) (8), which introduced the basic definition, content and specifications for the use of OHRA. The principles of qualitative risk assessment model are the same as that of COSHH Essential model (9, 10). The semi-quantitative risk assessment models in China include three risk assessment methods: exposure ratio method, exposure index method and synthesis index method. The qualitative and quantitative models in the standard are based on the same principles as the COSHH basic model and the EPA model, respectively. The exposure ratio method, the exposure index method and the synthesis index method were included in the semi-quantitative models. The exposure ratio method and the Singapore model had the same principle, while the exposure index method and synthesis index method are further developed based on the Singapore model (11).

Considering the health and toxic effects of benzene, some industries are gradually adopting other raw materials as substitutes for benzene. However, as benzene is also an excellent chemical solvent, itis still used by many enterprises in China, especially in the printing industry in Shenzhen, China, where cases of benzene exposure poisoning or death remains (12). In this study, multiple OHRA models (COSHH, EPA, Singapore and semi-quantitative risk assessment models) were used to assess the occupational health risks of benzene in China's printing industry. In view of this phenomenon, this study puts forward risk management strategies to reduce the risk of benzene exposure.

Materials and methods

Description of the similar exposure groups

Thirty enterprises in the printing industry in Shenzhen, Guangdong Province, China were selected as the research objects. Among these enterprises, benzene is one of the most widely used chemicals. Eight enterprises used benzene as an organic solvent. SEGs were divided into printing groups, cleaning groups, paste groups and packaging groups according to different production processes. In the selected enterprises, the numbers of the four groups are 7, 3, 6, and 3, respectively. The working time, benzene usage, benzene exposure time, process automation, first aid facilities, ventilation, emergency rescue measures, personal protective equipment, occupational health management and benzene concentration of workers in each group were investigated.

Site survey and on-site testing

Through on-site testing, information on the number of employees, working hours, daily usage of benzene, exposure time, engineering protective measures, personal protective equipment were collected. The collection of air samples and the testing of laboratory benzene samples were performed according to the methods described in Chinese Standards "Specifications of air sampling for hazardous substances monitoring in the workplace (GBZ159-2004)" (13) and "Workplace air aromatic hydrocarbon compounds determination Method" (GBZ/T 160.42-2007) (14). The 8 h time-weighted average concentration (C-TWA) and short-term exposure concentration (C-STEL) were tested. According to the Chinese standard requirements “Occupational Exposure Limits for Hazardous Agents in the workplace Part 1: Chemical hazardous agents (GBZ 2.1-2019)” (15), the permissible concentration-time weighted average (PC-TWA) of benzene is 6 mg/m^3, and the permissible concentration-short-term exposure limit (PC-STEL) should be less than twice the PC-TWA.

Occupational health risk assessment models

The China's Occupational health Risk Assessment Guide for Workplace Chemicals (GBZ/T298-2017), COSHH Essential model, EPA model (including non-carcinogenic model and carcinogenic model), Singapore model and domestic semi-quantitative risk assessment model were used to assess the occupational health risk of Benzene. The rationale of these models had been described in detail in the literature and was briefly described as follows.

The COSHH essential model

This model provided a risk assessment by both exposure levels and health hazards of chemicals. Health hazards were determined by the range of occupational exposure limits (OELs) or by assigning the assessed substance to a hazard band using a Risk-phrase. The exposure level was determined by the physical property and the use of substance.

The EPA models

These models include non-carcinogenic and carcinogenic risk assessment models. The non-carcinogenic risk is calculated by Equation (1):

$$HQ = \frac{EC}{RfC}. \tag{1}$$

Where EC represents the exposure concentration for the acute exposure period, RfC represents the reference concentration for inhalation toxicity (mg/m3), and HQ represents the hazard quotient, which is the value of the non-carcinogenic risk. EC equals to the chemical concentration in the air of the workplace (mg/m3). When the value of HQ is ≥1, it indicates that the toxic and harmful chemicals have a relatively high non-carcinogenic risk (unacceptable risk). Conversely, if the value is lower than 1, it indicates that the toxic and harmful chemicals have a relatively low non-carcinogenic risk (acceptable risk).

Cancer risk is calculated by Equation (2):

$$IR = IUR \times d \times \frac{t_E}{t_L} \tag{2}$$

In the above formula, IUR represents the inhaled unit risk (m3/μg), estimated lifetime cancer risk upper limit from continuous exposure to 1 μg/m3 airborne chemical, D represents the exposure dose to airborne chemical concentration (μg/m3), tL represents life expectancy (a), and tE represents the exposure time (A). tE can be calculated by the following formula: tE = (number of hours per workday x number of workdays per year x duration) / 24 h per day / 365 days per year. When the value of IR is $>10^{-4}$, toxic and hazardous chemicals have a relatively high cancer risk (unacceptable risk). Conversely, when the value is lower than 10^{-4}, the toxic and hazardous chemical has a relatively low cancer risk (acceptable risk).

The Singapore exposure index method

The risk level can be calculated by the equation: $sk = \sqrt{HR \times ER}$, where HR represents the hazard rating, and the ER represents the exposure rating).

In this formula, the HR value can be determined by the carcinogenicity classification determined by the American Conference of Governmental Industrial Hygienists (ACGIH) and the International Agency for Research on Cancer (IARC), or by the median lethal dose (LD50) and median lethal concentration (LC50) of the chemical in the Material Safety Data Sheet (MSDS). The ER was calculated using equation: $[EI_1 \times EI_2 \times \cdots EI_n]^{1/n}$, where EI represents the exposure index, and n represents the number of exposure factors, such as hazard control measures, weekly usage of the chemicals, particle size, vapor pressure, and duration of work per week.

The semi-quantitative risk assessment model in China

The exposure ratio method, exposure index method and synthesis index method were included in this method. The calculation method of risk level was the same way as the Singapore exposure index method.

In the exposure ratio method, the ER was determined by the ratio of the exposure level (E) and OEL, and the E was calculated using the equation: $E = F \times D \times M/W$ (F = the frequency of exposure per week, M = the magnitude of exposure, W = the average working hours per week, and D = the average duration of each exposure). The EI of the Chinese exposure index method takes into account more factors, such as occupational health management, emergency rescue measures, first aid facilities, PPE, daily usage of chemicals and daily working hours. The ratio

TABLE 1 Survey results of SEGs exposed to benzene.

SEG		Printing group	Cleaning group	Pasting group	Packaging group
Number of group		7	3	6	3
Number of workers per group		4–30	5–6	5–84	6–44
Duration of work (months)		200 (160–240)	184 (160–200)	196 (160–240)	197 (160–240)
Daily usage (kg/L)		104.7 (6–2181)	68.0 (10–118.2)	523.1 (7–3052.5)	14.3 (0.5–30.3)
Weekly usage (kg/L)		596.8 (24–870)	331.9 (50–491)	2628.9 (35–15262.5)	85.4 (2.5–181.8)
Hours of work per day		8.7 (8–10)	8.7 (8–10)	8.7 (8–10)	8.7 (8–10)
Days of work per week		5.3 (5–6)	5.3 (5–6)	5.7 (5–6)	5.7 (5–6)
C-TWA (mg/m^3)		4.67 (<0.02–24.08)	<0.02	3.47 (<0.02–20.73)	<0.02
C-STEL (mg/m^3)		<0.07			<0.07
E/OEL		0.78 (0.003–4.01)	0.003	0.58 (0.003–3.45)	0.003
Result					
	C-TWA disqualified	28.6% (2/7)	0 (0/3)	16.7% (1/6)	0 (0/3)
	C-STEL disqualified	0			
Automation level					
	Full automation	57.2% (4/7)	0 (0/3)	16.7% (1/6)	33.3% (1/3)
	Semiautomation	0 (0/20)	66.7% (2/3)	33.3% (2/6)	0 (0/3)
	Manual operation	42.8% (3/7)	33.3% (1/3)	50.0% (3/6)	66.7% (2/3)
Ventilation					
	General ventilation	57.2% (4/7)	100% (3/3)	83.3% (5/6)	33.3% (2/6)
	Local exhaust ventilation	57.2% (4/7)	0% (0/3)	16.7% (1/6)	0 (0/3)
First-aid facility equipped		42.8% (3/7)	33.3% (1/3)	33.3% (2/6)	100% (3/3)
Personal protective equipment					
	Equipped	85.7% (6/7)	100% (3/3)	83.3% (5/6)	100% (3/3)
	Used or worn	85.7% (6/7)	66.7% (2/3)	66.7% (4/6)	100% (3/3)
Emergency rescue measures complete		42.8% (3/7)	33.3% (1/3)	33.3% (2/6)	100% (3/3)
Occupational health management					
	Performs well	42.8% (3/7)	66.7% (2/3)	50.0% (3/6)	100% (3/3)
	Performs poorly	57.2% (4/7)	33.3% (1/3)	50.0% (3/6)	0 (0/3)
	Lack of management	0 (0/20)	0 (0/3)	0 (0/6)	0 (0/3)

C-STEL, short-term exposure concentration; C-TWA, 8-h time weighted average concentration; E/OEL, the ratio of exposure concentration to the occupational exposure limit; the results here represent the larger ratios of C-TWA/PC-TWA and C-STEL/PC-STEL; PC-TWA, the permissible concentration-time weighted average; PC-STEL, the permissible concentration-short term exposure limit; SEG, the similar exposure group.

of exposure level to OEL (E/OEL) was added to the EI in the synthesis index method.

Statistical analysis

Statistical analysis was performed by SPSS 22.0 software (IBM, Armonk, NY, USA). There were statistical significance of differences between the groups, which was determined by one-way analysis of variance (ANOVA) and the Tukey *post-hoc* test. Cohen's Kappa was used to assess the consistency of the two occupational health risk assessment models ($k < 0.40$, indicating lack of consistency, $0.75 > k \geq 0.40$, indicating average consistency, $k \geq 0.75$, indicating good consistency).

Results

On-site survey and test results

The usage of benzene, exposure time of benzene, emergency rescue measures, first aid facilities, process automation, control facilities, occupational health management, benzene concentration of SEG and other information were listed in Table 1. According to the on-site investigation results, the cleaning group and the printing group had relatively high degree of automation, while more than half of the processes in the pasting group and the packaging group were manually operated. The printing groups of many enterprises were equipped with partial ventilation facilities, while the cleaning group, the pasting group and the packaging group were usually equipped with

TABLE 2 Evaluation results of the COSHH essential model and the EPA models of benzene.

SEG	Number of group	COSHH essential model			EPA non-carcinogenic risk assessment model		EPA carcinogenic risk assessment model		
		HR	ER	Risk level	HQ	Risk level	IR	Unacceptable risk ratio	Acceptable risk ratio
Printing group	7	E	3	4 (Very high risk)	31.66 (0.17–220.64)	Unacceptable risk (42.9%)	1.45×10^{-3} (2.9×10^{-6}-0.01)	42.9% (3/7)	57.1% (4/7)
Cleaning group	3	E	3	4 (Very high risk)	0.19–0.66	Acceptable risk (100.0%)	2.14×10^{-5} (2.9×10^{-6}-4×10^{-5})	0	100% (3/3)
Pasting group	6	E	3	4 (Very high risk)	2.88 (0.02–17.04)	Unacceptable risk (33.3%)	1.67×10^{-3} (2.9×10^{-6}-0.01)	33.3% (2/6)	66.7% (4/6)
Packaging group	3	E	3	4 (Very high risk)	0.23	Acceptable risk (100.0%)	6.55×10^{-6} (2.9×10^{-6}-1×10^{-5})	0	100% (3/3)
Total	19	E	3	4 (Very high risk)	12.68 (0.02–220.64)	Unacceptable risk (26.3%)	1.07×10^{-3} (2.9×10^{-6}-0.01)	26.3% (5/19)	83.7% (14/19)

COSHH, UK Control of Substances Hazardous to Health; EPA, U.S. Environmental Protection Agency. ER, exposure rating; HR, hazard rating. HQ, the hazard quotient; IR, the excess personal risk of carcinogenic inhalation; SEG, the similar exposure group.

integrated ventilation facilities. Most of companies provided the personal protective equipment for their workers, but a few workers did not wear them at work. Only a few companies were equipped with first-aid facilities, and most of them had poor or lacking occupational health management. The cleaning group and the sticking group had poor emergency rescue measures, and the utilization rate of personal protective equipment was low as well. The benzene concentration in cleaning group and packaging group was significantly lower than the other two groups. The average C-TWA of benzene in printing groups was 4.67 mg/m3, ranging from 0.02 to 24.08 mg/m3. The C-TWA of benzene in cleaning groups were all below 0.02 mg/m3. The average C-TWA of benzene in pasting groups was 3.47 mg/m3, ranging from 0.02 to 20.73 mg/m3. The C-TWA of benzene in packaging groups were all below 0.02 mg/m3. Both the average values of C-STEL and C-TWA in the printing groups were higher than those in the pasting groups. The results of this study showed that C-TWA of 28.6% of the printing group, 16.7% of the paste group and 33.3% of the packaging group exceeded the PC-TWA in the Chinese standard.

Risk assessment results

As illustrated in Table 2, the risk level of benzene was R45, which indicated a risk of carcinogenic effect on the human body. Therefore, in the COSHH model, hazard level could be classified as grade E. The COSHH Essential model showed that all the working groups exposed to benzene had high risk. The EPA's non-carcinogenic risk assessment model showed that HQs of both the printing groups and the paste groups were >1, indicating that these groups had high non-carcinogenic risk. At the same time, the cancer risk of the printing groups and the pasting groups were 0.004 and 0.003, respectively. Some of the two groups were assessed to be at high carcinogenic risk, accounting for 42.9 and 33.3%, respectively.

According to the IARC, benzene can be classified as a class 1 substance, also known as a confirmed carcinogen in humans. The HR of benzene can be divided into five levels in the semi-quantitative risk assessment model. As shown in the exposure index method results, the risk levels of each working groups ranged from 2 to 5. 28.6% of the printing groups, 16.7% of the pasting groups and 33.3% of the packaging groups were at very high risk. The Singapore exposure index method showed that the risk levels of the work groups were distributed from grade 4 to 5. The Singapore exposure index method showed that the risk levels of the work groups were distributed between 4 and 5, with 84.2% of the work groups at very high risk, including 71.4% of the printing group, 100% of the cleaning group, 100% of the pasting group, and 66.7% of the packaging group. The China exposure index method showed that the risk levels of the working groups ranged from 3 to 5, and 73.7% of the work groups were at high risk, which were 75.8% of the printing groups, 100% of the cleaning groups, 66.7% of the pasting groups, and 33.3% of the packaging groups. Only one of the pasting groups was at very high risk. 21.1% of the work groups were at medium risk, including 14.3% of the printing groups, 16.7% of the paste groups and 66.7% of the packaging groups. The synthesis index method showed that the risk levels of the work groups were distributed from 2 to 4, among with 75.8% of the printing groups, 66.7% of the cleaning groups, 66.7% of the paste groups bring at high risk, and the

TABLE 3 Evaluation results of semi-quantitative risk assessment models of benzene.

SEG	Number of group	*R*	exposure ratio method	Singapore exposure index method	Chinese exposure index method	Synthesis index method
Printing group	7	2	71.4% (5/7)	0	0	0
		3	0	0	14.3% (1/7)	14.3% (1/7)
		4	0	28.6% (2/7)	75.8% (6/7)	75.8% (6/7)
		5	28.6% (2/7)	71.4% (5/7)	0	0
Cleaning group	3	2	100.0% (3/3)	0	0	0
		3	0	0	0	33.3% (1/3)
		4	0	0	100% (3/3)	66.7% (2/3)
		5	0	100% (3/3)	0	0
Pasting group	6	2	83.3% (5/6)	0	0	0
		3	0	0	16.7% (1/6)	33.3% (2/6)
		4	0	0	66.7% (4/6)	66.7% (4/6)
		5	16.7% (1/6)	100% (6/6)	16.7% (1/6)	0
Packaging group	3	2	66.7% (2/3)	0	0	33.3% (1/3)
		3	0	0	66.7% (2/3)	66.7% (2/3)
		4	33.3% (1/3)	33.3% (1/3)	33.3% (1/3)	0
		5	0	66.7% (2/3)	0	0
Total	19	2	78.9% (15/19)	0	0	5.3% (1/19)
		3	0	0	21.1% (4/19)	31.6% (6/19)
		4	5.3% (1/19)	15.8% (3/19)	73.7% (14/19)	63.2% (12/19)
		5	15.8% (3/19)	84.2% (16/19)	5.3% (1/19)	0

R, risk level; SEG, the similar exposure group.

TABLE 4 Cohen's Kappa results of semiquantitative risk assessment models of benzene.

Cohen's Kappa (A vs. B)	Value	Approx. Sig.
Exposure ratio method vs. Singapore exposure index method	0.019	0.656
Exposure ratio method vs. Chinese exposure index method	0.027	0.597
Exposure ratio method vs. Synthesis index method	−0.013	0.845
Singapore exposure index method vs. Chinese exposure index method	−0.066	0.243
Singapore exposure index method vs. Synthesis index method	−0.052	0.243
Chinese exposure index method vs. Synthesis index method	0.438	0.018

risk grade of the packaging groups being at medium or low (Table 3).

According to the available literature (16), the WBC counts of workers exposed to low concentrations of benzene did not change significantly over time, except when benzene concentrations were relatively high. In this study, the cleaning and packaging groups were exposed to low concentrations of benzene, while the printing and pasting groups were exposed to relatively high concentrations of benzene, and thus had a higher occupational health risk.

The consistency of bidirectional ordinal classification data was evaluated by the Cohen's Kappa generally. As shown in Table 4, there was a lack of consistency between the exposure ratio method and all three methods. Furthermore, there was a lack of consistency between the Singapore Exposure Index method and the Chinese Exposure Index method, as well as between the Singapore Exposure Index method and the Synthesis Index method. In addition, there was general consistency between the Chinese exposure index method and the Synthesis index method.

Discussion

The COSHH Essential model, (EPA model) and semi-quantitative risk assessment model (Singapore model and China semi-quantitative risk assessment model) were used to assess occupational health risk of benzene in this study. Each occupational health risk assessment model has its own advantages and disadvantages (6, 7, 17). The COSHH Essential model is mainly used for small and medium-sized enterprises. This method is relatively simple and easy to operate, but sometimes it would overestimate the risk level and make a possible deviation. The strengths and weaknesses of the EPA model are equally apparent. As a quantitative assessment model, this model can fully assess the non-carcinogenic and carcinogenic risks of chemicals, and its reference concentration (Rfc) and inhalation unit risk (IUR) are determined based on epidemiological and toxicological data. However, the EPA model also has some shortcomings. For instance, the model can not assess the chemicals lack of Rfc and IUR values. In addition, for different risk levels, the model is also difficult to distinguish between different risk levels, and the results can only be expressed as "high" and "low." Semi-quantitative risk assessment models are based on semi-quantitative calculations, using both quantitative and qualitative methods. The Exposure Ratio Method focuses on the exposure level of chemical substances, and the exposure index method is used when there is a lack of air monitoring data. The Singapore Exposure Index Method is evaluated by steam pressure or particle size, chemical dosage, working hours and hazard control measure, while the Chinese exposure index method has a higher exposure index than the Singapore exposure index method, including personal protective equipment, first aid facilities, emergency rescue facilities, occupational health management, etc. The composite index method considers not only the exposure level, but also all exposure indicators. The disadvantage of the semi-quantitative risk assessment model is that the classification of the exposure indices is relatively rough.

In all enterprises involved in this study, C-TWA of benzene in printing group and pasting group exceeded the occupational exposure limits, while the C-TWA in the packaging group and the cleaning group is relatively low. This is due to the higher chemical use in the printing and bonding groups, insufficient local ventilation, and relatively poor occupational health management.

The results of the COSHH Essential model showed that all working groups were at very high non-carcinogenic risk, while the EPA non-carcinogenic risk assessment model showed a high non-carcinogenic risk for the printing and paste groups. In the COSHH Essential model, since the HR of benzene was E, the principle of the model states that the risk level is 4 (very high risk) regardless of the exposure level. The RfC in the EPA's model of carcinogenic risk assessment represents the reference concentration at which sustained inhalation would not result in a lifetime health risk. Because of the low RfC of benzene, the risk level remained high even when the detected concentration was below the detection limit. In fact, low concentrations of benzene exposure (<0.5 OEL), high levels of automation, good ventilation, good emergency response, good management, and high use of personal protective equipment in some industries could reduce the risk. In this case, the EPA's non-carcinogenic risk assessment model and the COSHH Essential model generally overestimated the risk level of exposure to benzene in the working group. The results of the semi-quantitative risk assessment model indicated that the working group's risk levels ranged from 2 to 5. In the Exposure Ratio Method, the level of risk was only related to the concentration of exposure, ignoring the effect of protective measures. The Chinese exposure index method and the Singapore exposure index method focus on exposure factors other than exposure concentration. The Chinese Exposure Index Method focused on more exposure factors compared with the Singapore Exposure Index Method, such as personal protective equipment, emergency rescue measures, first aid facilities, occupational health management, etc. Based on the Chinese exposure index method, the synthesis index method added exposure concentration as another exposure factor. The results showed that the evaluation results of Singapore exposure index method were higher than those of China exposure index method and comprehensive index method, while the evaluation results of the other two methods for these four working groups were basically the same. According to the actual situation of each working group, the lower the exposure concentration of benzene, the more effective the hazard control measures, the better the emergency rescue facilities, the more sound the occupational health management, and the lower the risk will be. To sum up, the Chinese exposure index method and synthesis index method were relatively more practical. At the same time, since occupational health management and engineering control measures may affect the concentration of chemicals in the workplace, the exposure factors to be considered by the integrated index method should be carefully chosen in order to avoid bias. Results from the EPA cancer risk Assessment model showed that nearly half of the working groups within the printing and paste groups in the printing industry were assessed as having a high risk of cancer. Cancer risk levels tended to be lower only when benzene doses were lower and work hours were shorter. China is one of the industrial power in the world. In the traditional occupational health assessment, the assessment of occupational health hazards of benzene has always been in line with the national health standards. When the concentration of benzene exposure is lower than the national health standards, it is considered as a safe operation. A study by Lan et al. (18) showed that workers exposed to 1 ppm (3.19 mg/m3) benzene showed homosexuality and impaired hematopoietic stem/progenitor cell self-renewal. In other words, the risk of benzene exposure is still high and can cause health damage to workers even at low dose levels, which is consistent with the assessment results of this study. Huang et al. developed a model for cancer risk assessment of benzene exposure based on a physiological toxicokinetic model and a dose-response relationship model using a benzene exposure cohort population in collaboration with the Chinese Society for Preventive Medicine and the American Institute for

Cancer Research (19, 20). He also found that the predicted cancer risk for workers at exposure concentrations of 50–500 mg/m3 ranged from 1.52×10^{-4} to 1.19×10^{-3}, which was higher than the maximum acceptable risk value and consistent with the actual cancer incidence rate. Therefore, it is recommended that the health administration departments carry out the risk assessment of carcinogenic and non-carcinogenic effects of benzene along with the occupational health risk assessment of benzene to promise a safe working environment for workers.

According to the results of this risk assessment, most of the working groups in the printing industry that are exposed to benzene are at high risk, with higher exposure risks in the printing and paste groups. Due to the high occupational health risk of benzene in the printing industry in China, risk management measures should be carried out. Enterprises should optimize and reform the operating conditions. For high-risk jobs, risks should be reduced according to the priorities of replacement, improved design, isolation, administration and personal protection. Benzene should be replaced by non-toxic toluene and ethanol should be used as organic solvents or extraction agents. The production process should be sealed, automated, programmed, and regularly maintained. The workplace should contain sufficient local ventilation and detoxification equipment. In addition, occupational health training is arranged regularly to raise workers' awareness of self-protection and make them wear gas masks voluntarily. Regular medical checkups should be conducted for workers, and workers should be immediately stopped from the position once they are diagnosed with low white blood cells.

Conclusion

The OHRA model in Chinese standard GBZ/T 298-2017 can be used for occupational health risk assessment of benzene. China exposure index method and composite index method are more realistic than the others. The results of the current study indicated that there are many high-risk of benzene exposure in the printing industry in China, and the risk of benzene exposure may be in the printing group and the pasting group. It is necessary to take measures to reduce the risk of benzene exposure in these work positions.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

BS was responsible for the design of experimental methods, actual research, analysis of experimental data, visualization of experimental results, and writing of the first draft of the paper. SS was responsible for the concept generation, funding acquisition, supervision and guidance, and review and revision of the paper. CW was responsible for the actual research and analysis of experimental data. TW, HX, and ML was responsible for the data collection. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Noise exposure assessment of non-coal mining workers in four provinces of China

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Objective: This study aimed to understand the noise exposure of non-coal mines in China to take appropriate controls to protect workers' health.

Methods: An assessment of non-coal miners' noise exposures was conducted in four provinces in China. Individual noise exposure levels were measured, and the survey on the hearing protector device (HPD) equipment was administered.

Results: 423 noise dosimeter measurements were obtained, including drilling, blasting, ore drawing, transportation, winching, crushing, screening and ball milling, and auxiliary (air pressure, pump, and maintenance). A total of 31.9% of the individual noise levels ($L_{EX,8h}$) exceeded 85 dB(A), and the median dosages of non-coal miners with high noise exposure were: excavation workers-89.1 dB(A), mill operators-88.7 dB(A), and crusher operators-87.0 dB(A). The noise dose of underground mine workers is higher than that of surface mine workers ($P < 0.001$). A total of 53.7% of non-coal mining enterprises are not equipped with HPD for workers, mainly small and micro enterprises.

Conclusions: High levels of hazardous noise exposure are typical in non-coal mines. Noise exposure data can help to develop more feasible noise controls.

KEYWORDS

non-coal mine, individual noise, position, exposure, HPD

Introduction

Noise is one of the most common occupational hazards, and overexposure to noise continues to be a problem throughout the mining industry (1). Occupational hearing loss is a common work-related illness among mining workers: miners work in a high-noise environment for a long time, and their hearing gradually decreases (2–4). It takes several hours or even longer to recover their hearing after leaving the environment. If they continue to work in such an environment without noise controls, it will cause permanent hearing threshold displacement, resulting in irreversible hearing loss and even noise-induced deafness. In general, noise levels above 85 dB(A) are considered hazardous, depending on the time and frequency of noise exposure and hearing protector device (HPD) use.

In recent years, the degree of mining mechanization has increased, and many large, efficient, and high-power pieces of equipment have been widely used. While improving production efficiency, the noise hazard problem is becoming more serious. In a platinum mine in South Africa, more than 80% of miners were exposed to noise exposure levels that were higher than 85 dB(A), with 64% of the miners having higher noise exposure than 91 dB(A) (5). Sixty-nine percent of workers in sand and gravel mines were exposed to noise above the exposure limits recommended by NIOSH (6). A survey of hard-rock miners in the western United States found that 96% of operators had daily noise doses of more than 90 dB(A) (7). Measured 102 dB(A) from underground mining in the mining industry in Zimbabwe (8). Another study of Tanzanian miners also suggested that high noise exposures were common among miners (9). In China, a study of three metal mine enterprises found that the average individual noise is above 89.7 dB(A), especially the noise of drilling workers above 102.5 dB(A) (10). According to another study on six metal mines, 56.3% of the area noise exceeds 85 dB(A) (11). Among the eight non-coal mining enterprises in Dalian (five limestones and silica mining, three granite mining), 55.56% of the area noise exceeds 85 dB(A) (12). However, currently reported mining noise levels are primarily the result of one or more mines, with some studies only reporting the noise doses from areas or equipment, lacking assessments of workers' noise exposure. Extensive data on miner noise levels in China have rarely been reported. To address this problem, the National Institute for Occupational Health and Poison Control conducted a series of noise surveillance and evaluation studies for the non-coal mining industry. This research effort was conducted at 82 non-coal mines in four provinces to determine miners' noise exposure levels. Four hundred twenty-three noise exposure measurements were obtained from mining workers.

Materials and methods

Study setting

This research is analytical in the form of an observational study. Due to China's uneven geographical distribution of mineral resources, this study adopted the typical sampling method and selected 82 non-coal mines in four provinces. Non-coal mines refer to mines other than coal mines, which mainly include metal and non-metal mines. This exposure study was conducted among workers in non-coal mines to evaluate their noise exposure, and a noise dosimeter was used to measure workers' noise exposure during their work day. The study started in January 2019 and ended in December 2020.

TABLE 1 Summary of job descriptions by job title.

Job title	Job description
Excavation worker	They are excavating roadways, including drilling and blasting.
Miner	Mining the ore from the face and transporting it to the pit (referring to underground mining) or steps (referring to surface mining)
Winch operator	Operate the winch to lift heavy objects
Belt operator	Operate the belt conveyor and ensure the regular operation of the ore transport belt
Crusher operator	Operate the crusher to break large chunks of ore into smaller pieces
Screening operator	Operate the screening machine to separate the mixed ore of different sizes into various particle size classes
Mill operator	Operate the mill to pulverize the ore
Pump operator	Operation and maintenance of various pump equipment
Air compressor operator	Operation and maintenance of air compressors and air supply
Transporter	Operate forklifts, transport vehicles
Control worker	Monitor and oversee work activities
Maintenance worker	Maintenance and repair of mining equipment

Description of the production process

Mining is divided into surface mining and underground mining. The part close to the surface and buried shallowly adopts surface mining, and the deep part adopts underground mining. The production process is divided into six sections: excavation (drilling and blasting), ore drawing, transportation, winching, beneficiation (crushing, screening, and ball milling), and auxiliary (air pressure, pump, and maintenance). According to the production process, the noise mainly comes from the aerodynamic noise of pneumatic rock drilling tools, the mechanical noise generated by vibration, friction, and collision of various equipment during operation, and the electromagnetic noise caused by electrical equipment. The noise-related equipment includes air compressors, various pumps, fans, winches, blasting equipment, crushing equipment, rock drilling equipment, transportation equipment, rock loaders, and machine repair equipment. The workers were categorized according to job titles and descriptions (Table 1).

Individual noise measurement

To ensure the validity and authenticity of the measurement, we selected workers who had been in their current jobs for more than 1 year as participants and determined before the measurement that workers could work an entire shift. The shift-long individual noise exposure was measured for each participant using a Casella dBadge2 individual noise dosimeter. The dosimeter microphone was placed at the midpoint of the participants' shoulders and worn throughout the work shift. The dosimeters were equipped with a single ½-inch microphone, the dynamic range of the dosimeters was 55.0–140.3 dB(A), and the exchange rate was 3 dB. Before the measurement, each dosimeter was calibrated using the Casella 120/2 Acoustic Calibrator. Each dosimeter was used to detect a complete work shift. Individual noise exposure measurements were performed for all operational jobs, with 1–3 participants were selected to detect three shifts for the jobs. The measurement recorded was the normalization of equivalent continuous A-weighted sound pressure level to a normal 8 h working day ($L_{EX,8h}$) or a nominal 40 h working week ($L_{EX,40h}$). The noise level exposed to 5 days per week was equivalent to $L_{EX,8h}$, and the noise level exposed to non-5 days per week was equivalent to $L_{EX,40h}$. The $L_{Ex,8h}$ and $L_{EX,40h}$ were calculated by the formula in ISO 1999:2013:

$$L_{EX,\,8\,h} = L_{Aeq,\quad T_e} + 10\lg\left(\frac{T_e}{T_0}\right)\ dB$$

where T_e is the effective duration of the working day in hours; T_0 is the reference duration ($T_0 = 8$ h); and $L_{Aeq,Te}$ is the L_{Aeq} for T_e.

$$L_{EX,\,40\,h} = 10\lg\left(\frac{1}{5}\sum_{i=1}^{n}10^{0.1(L_{EX,\,8\,h})\,i}\right)\ dB$$

where n is the actual number of working days per week; $L_{EX,8h}$ is the noise exposure level normalized to a nominal 8 h working day.

According to GBZ2.2-2007 (13), individual noise exposure should not exceed 85 dB(A). This level is defined as the permissible exposure level (PEL). These measurements include information about the mine region, scale, type (surface or underground), and mining content (metal or non-metal), as well as the job title or task description for each measurement. Moreover, we collected information on employers equipping HPD for their workers.

Risk assessment of occupational noise-induced hearing loss

ISO 1999:2013(E) (14) is an international standard for risk assessment of occupational noise-induced hearing loss (NIHL), which can be applied to the calculation of the risk of sustaining hearing loss due to regular occupational noise exposure. In statistical terms, it presents the relationship between noise exposures and the "noise-induced permanent threshold shift" (NIPTS) in people of various ages.

The hearing threshold level associated with age and noise (HTLAN), H', can be calculated by the formula in ISO 1999:2013:

$$H' = H + N - \frac{H \times N}{120}$$

where H is the hearing threshold level associated with age (HTLA), expressed in decibels; N is the actual or potential noise-induced permanent threshold shift (NIPTS), expressed in decibels.

ISO 1999:2013 permits two databases (databases A and B) to be used for the hearing threshold level associated with age (HTLA). Database A was derived from otologically normal persons. In this study, database A was selected to predict HTLA changes in 10, 50, and 90% of workers.

All mine workers in the study were male. We assumed the workers started working at the age of 20 and worked on a job for 40 years.

According to the Diagnosis of Occupational Noise Deafness (GBZ 49-2014) (15), the definitions, frequencies, and fences of high-frequency hearing loss and noise-induced deafness were determined. High-frequency hearing loss was defined as an average hearing threshold of bilateral high-frequency (3,000, 4,000, 6,000 Hz) ≥ 40 dB. The frequencies of 3,000, 4,000, and 6,000 Hz (1/3 of each) were selected, and 40 dB was set as the fence. Noise-induced deafness was defined as the optimal whisper frequency, and the weighted value of 4,000 Hz in high-frequency hearing loss ≥26 dB. The frequencies of 500, 1,000, 2,000, and 4,000 Hz (ratio 3:3:3:1) were selected, and 26 dB was set as the fence.

The ISO1999 formula was used to calculate the HTLAN of 10, 50, and 90% of the workers and NIPTS of 10, 50, and 90% of the workers. Based on the noise exposure level of the corresponding job, the changes in the hearing threshold level of workers of each position after 40 years of work were predicted. The risk of high-frequency hearing loss and noise-induced deafness were calculated for workers in different jobs at the same age (60 years old) and exposure years (40 years of working). The risk of NIHL was represented by the percentage of people whose NIPTS, HTLAN, and HTLA exceeded the selected fence.

Statistics

The data of the noise dosimeter were checked for validity, and invalid data with battery failure or incorrect settings were eliminated. Statistical analysis was performed using SPSS (version 22.0, SPSS Inc., Chicago, IL, USA). The median (M), interquartile range (**P_{25}, P_{75}**), and percentage of measurements with levels above PEL were calculated to describe the distribution of the noise exposure level, and the chi-square test or Fisher's exact test was applied to analyze the difference in individual noise exposure levels in non-coal mines among mineral type, mining mode, and scale. The HPD equipment was also obtained from the survey of mining enterprises to analyze the differences in mineral type, mining mode, and scale. A significant difference was considered when $P < 0.05$.

Ethical approval

Clearance was issued by the National Institute for Occupational Health and Poison Control, the Chinese Center for Disease Control and Prevention (NIOHP, China CDC). This study did not cause any physical or psychological harm or disturb the operators during the operation. Informed consent was obtained from all individual participants involved in the study. Information on HPD was obtained from communication with company occupational health managers and confirmed during this investigation.

Results

Table 2 shows the results of the non-coal mine workers' noise data. Noise dosimeter measurements ($L_{EX,8h}/L_{EX,40h}$) were recorded for 423 workers in non-coal mines. The median individual noise exposure was 83.4 dB(A). The worker dose measurements indicated that 31.9% (135/423) of all measurements were above the PEL of 85 dB(A).

This table shows the distribution of noise exposure among non-coal miners. This illustrates that the noise dose range within different jobs varies considerably. The individual noise exposure levels of the pump operators, air compressor operators, control workers, and maintenance workers involved in the test were lower than 80 dB(A). Mines, winch operators, belt operators, screening operators, and transporters were exposed to noise between 80 and 85 dB(A). Excavation workers, crusher operators, and mill operators were exposed to high doses of noise, with 89.1 dB(A) for excavation workers, 88.7 dB(A) for mill operators, and 87.0 dB(A) for crusher operators.

Mining mode (underground or surface) had a significant effect on the noise exposure of workers ($P < 0.001$). The noise exposure was significantly higher in underground mines than in surface mines.

According to ISO 1999:2013, there was a risk of NIHL for workers exposed to 80 dB(A) sound. This NIHL risk was assessed in Table 3 for the workers of this study.

Enterprises must provide hearing protection for noise-exposed workers, especially for employees exposed to >85 dB(A). Based on Table 4, only 46.3% (38/82) of mining enterprises had equipped HPD for their workers. More than half of mining employers had never been equipped with HPD for their workers (53.7%). The proportion of non-metallic mines (74.5%), surface mining (69.4%), and small or micro-mining enterprises (59.5%) not equipped with HPD is relatively high.

Discussion

This study found high levels of hazardous noise exposure in the sampled non-coal mines from four provinces in China. Workers were exposed to a median noise level of 83.4 dB(A), with 31.9% of individual noise measurements exceeding the PEL of 85 dB(A).

In this survey, excavation workers, mill operators, and crusher operators were exposed to high noise levels; 71.6–90.9% exceeded 85 dB(A). Among them, excavation workers were the job with the highest noise exposure in non-coal mines. Armah et al. (17) stated that the maximum average level of cubic operators (drill service holes and production of slots) was 103.9 dB, and Lutz et al. (18) found that the noise exposure for jumbo drill operation was 103.0 ± 0.8 dB(A). In this study, the highest noise level of excavation workers in the underground mine was 103.2 dB, and the results were close to the studies above. These workers are located close to large, noisy equipment for long periods and are chronically affected by noise levels that have the potential to cause NIHL.

According to ISO 1999:2013, it is predicted that excavation workers, mill operators, and crusher operators in this survey had the highest NIHL risk over a 40-year working life, with a 60-year-old male exposed to noise at a level of 87.0 dB(A) for 40 years having a 9.7% risk of high-frequency hearing loss and a 2.7% risk of noise-induced deafness. At a level of 88.7 dB(A), the risk of high-frequency hearing loss was 13.4%, and the risk of noise-induced deafness was 4.1%. At a level of 89.1 dB(A), there was a 14.3% risk of high-frequency hearing loss and a 4.5% risk of noise-induced deafness. Hearing loss requires long-term exposure to hazardous noise levels before a significant decline in hearing levels can be noticed. The prevalence of NIHL increased with higher noise levels and higher duration of exposure (19). In the case of the same gender, age, and working years, the predicted hearing loss depended entirely on the noise exposure intensity of workers, which increased with the increase in individual noise exposure. The prediction results of the ISO 1999:2013 model were consistent with the development law of hearing loss. These jobs (excavation worker, mill operator, and crusher operator) were likely to have a high incidence of occupational hearing loss, which was consistent with the high noise exposure positions identified in other studies (20, 21).

Previous studies have shown that the prevalence of hearing loss among workers in the mining industry in the United States was 27.3% (22). The prevalence rates of high-frequency hearing loss and noise-induced deafness hearing loss among blasting, excavation and mining workers in a mining enterprise in China were 73.52 and 13.11%, respectively (23). Among three non-ferrous metal mines in Gansu Province, 41.84% of workers suffered from hearing loss (24). Zhang et al. (25) investigated 25 outdoor quarries and found that 54.1% of workers suffered from hearing loss. The prevalence of NIHL in the above studies was higher than the predicted result by ISO 1999:2013. Research

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TABLE 2 Distribution of noise exposure among non-coal mining workers in four provinces of China.

Group	*N*	Individual noise exposure level $L_{EX,8h}/L^{*}_{EX,40h}$ [dB(A)] M (P_{25}, P_{75})	The proportion of individual noise exposure levels ≧ 85 dB(A) N (%)	χ^2	*P*
Total	423	83.4 (79.6, 86.4)	135 (31.9)		
Job				—	—
Excavation worker	67	89.1 (84.9, 96.6)	48 (71.6)		
Miner	134	82.7 (81.1, 84.6)	22 (16.4)		
Winch operator	16	80.8 (79.3, 82.4)	1 (6.3)		
Belt operator	23	82.8 (79.7, 86.6)	9 (39.1)		
Crusher operator	51	87.0 (85.0, 89.2)	38 (74.5)		
Screening operator	19	84.1 (83.4, 84.5)	2 (10.5)		
Mill operator	11	88.7 (88.3, 91.0)	10 (90.9)		
Pump operator	8	73.4 (72.2, 76.0)	0 (0)		
Air compressor operator	9	77.8 (77.1, 78.1)	0 (0)		
Transporter	63	80.8 (78.8, 83.0)	4 (6.3)		
Control worker	14	76.1 (72.5, 77.9)	0 (0)		
Maintenance worker	8	76.8 (75.7, 84.7)	1 (12.5)		
Mineral type				3.340	0.068
Non-metal	231	83.5 (80.9, 85.6)	65 (28.1)		
Metal	192	83.0 (78.2, 87.9)	70 (36.5)		
Mining mode				10.964	0.001
Underground	144	84.1 (79.6, 90.6)	61 (42.4)		
surface	279	83.3 (79.6, 85.4)	74 (26.5)		
Scale (16)				6.103	0.107
Large	25	86.2 (76.6, 92.2)	13 (52.0)		
Medium	100	83.0 (80.6, 87.2)	35 (35.0)		
Small	152	81.8 (78.1, 86.5)	44 (28.9)		
Micro	146	83.8 (82.0, 85.7)	43 (29.5)		

*$L_{Ex,8h}$: Normalization of equivalent continuous A-weighted sound pressure level to a nominal 8 h working day. $L_{Ex,40h}$: Normalization of equivalent continuous A-weighted sound pressure level to a nominal 40 h working week.

has shown that the prediction of NIHL by ISO 1999:2013 may be underestimated (26–28). There were many reasons for this underestimation. First, ISO 1999:2013(E) used a single noise-equivalent sound level as an evaluation index, which could not adequately reflect the exposure level of complex noise (27, 29, 30). Second, non-occupational noise exposure was ignored in the ISO 1999:2013 model. Noise-induced hearing loss is not only a part of occupational noise exposure but also important in non-occupational exposure. The use of earphones has been a major concern in studies on non-occupational noise exposure. Listening to music with headphones for a long time and loud volume will lead to hearing loss (31–33). In addition, co-exposure to noise and chemicals resulted in greater hearing loss than noise exposure alone (34, 35). However, since hearing loss is a process of gradual development, the application of ISO 1999:2013 in the risk assessment of high-frequency hearing loss can be used as an early warning method of hearing loss to find the potential risk of hearing loss in the population.

The noise exposure levels of miners, winch operators, belt operators, screening operators, and transporters ranged from 80 to 85 dB. ISO 1999: 2013 predicted that the risk of high-frequency hearing loss in these male workers over a 40-year working life ranged from 1.1 to 4.7%,

TABLE 3 The estimated risk of hearing loss during 40 years of working in workers who are exposed to noise above 80 dB(A) based on ISO 1999:2013.

Group	$L_{EX,8h}$ [dB(A)]	Estimated NIHL risk of high-frequency hearing loss (%)	Estimated NIHL risk of noise-induced deafness (%)
Job (exposed to noise over 80 dBA)			
Excavation worker	89.1	14.3	4.5
Miner	82.7	2.9	0.6
Winch operator	80.8	1.1	0.2
Belt operator	82.8	3.1	0.7
Crusher operator	87.0	9.7	2.7
Screening operator	84.1	4.7	1.1
Mill operator	88.7	13.4	4.1
Transporter	80.8	1.1	0.2
Mineral type			
Non-metal	83.5	3.9	0.9
Metal	83.0	3.3	0.7
Mining mode			
Underground	84.1	4.7	1.1
Surface	83.3	3.7	0.8
Scale			
Large	86.2	8.2	2.2
Medium	83.0	3.3	0.7
Small	81.8	2.0	0.4
Micro	83.8	4.3	1.0

TABLE 4 The equipment of HPD in non-coal mining enterprises in four provinces of China.

Group	Number of mines	HPDs		χ^2/Fisher	*P*-value
		Equip	Un-equip		
Total	82	38 (46.3)	44 (53.7)		
Mineral type				29.306	<0.001
Non-metal	55	14 (25.5)	41 (74.5)		
Metal	27	24 (88.9)	3 (11.1)		
Mining mode				25.186	<0.001
Underground	20	19 (95.0)	1 (5.0)		
Surface	62	19 (30.6)	43 (69.4)		
Scale (16)				10.265*	0.001
Large and medium	8	8 (100)	0		
Small and micro	74	30 (40.5)	44 (59.5)		

*Fisher's exact test.

and the risk of noise-induced deafness ranged from 0.2 to 1.1%. The investigation revealed that the transporters operate in the cab, the winch operators also work in the dedicated operating room, and their environment is relatively closed to reduce noise exposure. A study of construction equipment operators confirmed that operators were exposed to less noise with the cab's proper design and the cab's insulation (36).

The studied pump operators, air compressor operators, and control workers were exposed to individual noise levels below 80 dB(A). The operating mode of these workers is inspection, with ∼2 h of inspection per shift, and they spend more time in the quiet duty or control room.

Workers in underground mines are exposed to more noise than in surface mines ($P < 0.001$). Compared to surface mines, underground mines operate in relatively confined spaces with equipment closer to operators, resulting in higher noise exposure for miners. This result was supported by the Mine Safety and Health Administration (MHSA), which confirmed that underground metal mining has the highest noise exposure of all mine types (37). The data from MSHA indicated that the mean exposure for an 8-h time-weighted average was 81.9 dB(A) in metal mines and 82.1 dB(A) in non-metal mines (37). The results of this study showed that the noise exposure of metal mines was 83.0 dB(A) and that of non-metal mines was 83.5 dB(A), which is slightly higher than the results of MSHA, but there is no significant difference in noise exposure between metal mines and non-metal mines ($P > 0.05$).

Larger mines may have tended to use more powerful mining equipment, but the differences in noise exposure doses for workers in mines of different sizes were not significant ($P > 0.05$).

HPDs such as earplugs and earmuffs are low-cost and straightforward noise mitigation devices. A total of 53.7% of mining enterprises did not equip personal hearing protective devices for workers. Although there is no significant difference in noise exposure between small and micro-sized mining enterprises and large and medium-sized enterprises, the HPD equipment rate of small and micro-sized enterprises is only 40.5%, which is much lower than that of large and medium-sized enterprises.

The rate of HPD equipment in underground mines was significantly higher than that in surface mines ($P < 0.001$), and 95% of underground mining enterprises provided HPD for workers. On the one hand, it shows that the occupational health management of underground mines is better than that of surface mines, and on the other hand, it indirectly shows that the noise hazards of underground mines cannot be ignored.

From the perspective of mineral type, the HPD equipment rate of non-metallic mines is much lower than that of metal mines, only 25.5%. Landen et al. (6) found that hearing protection usage was low among sand and gravel miners, with 48% of workers reporting that they never used hearing protection. Sun and Azman (38) also found that stone, sand, and gravel mines at surface operations exposed a more significant number of miners to excessive risk, and management commitment to hearing loss prevention was low. The non-metallic mines in this survey were surface mines, 98.2% of which are small and micro enterprises. The mining mode and scale of the mine may be the main reasons for the low HPD equipment rate of non-metallic mines. These results suggest that noise control and management in small mines and micro mines should be improved to reduce overexposure before these workers develop occupational hearing loss.

The study did not investigate workers' actual use of HPD, but the reality is not optimistic. Studies have shown (39) that <50% of workers use hearing protectors in a large gold mine in South Africa. The use of HPD can effectively reduce the noise exposure dose of workers, but how to improve the use of HPD has been difficult to solve. Occupational noise-related policies can positively impact hearing protection and increase the use of HPD (40, 41).

Controlling noise exposure is the fundamental method of protecting workers from high noise exposure risk. According to the NIOSH information, the hierarchy of controls was recommended to determine feasible and effective controls to implement, including elimination, substitution, engineering controls, administrative controls, and personal protective equipment (PPE) (42). To protect the hearing health of non-coal workers, improving the production processes and implementing automation could be considered to reduce the intensity of noise generated from equipment. For equipment that generates noise at a high intensity, engineering control measures should be taken, such as muffling or adding sound insulation, reducing the impact and friction of machinery, or controlling the length of stay in these high-noise environments. PPE can provide worker protection when other levels of control combined do not adequately eliminate noise hazards.

The Chinese government attaches great importance to preventing and controlling workers' occupational disease hazards and has formulated regulations and norms related to occupational health. Occupational health-related laws and regulations require employers to provide hearing protection and appropriate training for noise-exposed workers. The focus of the next step in noise protection should be to strengthen the management and supervision of hearing protection in small and micro-sized mining enterprises. In addition to providing workers with appropriate HPD as required by laws and regulations, employers need to monitor the proper use of HPD closely.

The findings in this report are subject to at least two limitations. Subjects were from selected areas, and the summary of the findings may be limited. Nevertheless, we obtained 423 individual dosimeter measurements. To our knowledge, no previous studies conducted in non-coal mines have been able to obtain a similar number of dosimeter measurements. Second, during the surveillance, we did not acquire information on workers' occupational health.

Conclusion

Noise Exposure continues to be a problem in non-coal mines. In this study, non-coal mining workers at different scales, mineral types, and modes were examined by placing a noise dosimeter on the shoulders of mining workers during an entire work shift. More than 31.9% of the non-coal mining workers were exposed to noise higher than 85 dB(A), which can seriously affect human health. The HPD equipment rate of small and micro-sized enterprises is only 40.5%, indicating that small and micro-sized enterprises have an insufficient investment in noise control. It is necessary to focus on strengthening the management and supervision of hearing protection in small and micro-mining enterprises.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the National Institute for Occupational Health and Poison Control, the Chinese Center for Disease Control and Prevention. The patients/participants provided their written informed consent to participate in this study.

Author contributions

XW: investigation, formal analysis, and writing-original draft. NK, YD, and KN: methodology and investigation. KL: investigation and data processing. HB, FH, and YC: formal analysis. MY: conceptualization, funding acquisition, writing—review and editing, and supervision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Characteristics and occupational risk assessment of occupational silica-dust and noise exposure in ferrous metal foundries in Ningbo, China

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Introduction: To investigate the major existing occupational hazards and to assess the occupational health risks for ferrous metal foundries (FMFs) in Ningbo, China.

Methods: Unified questionnaires were formulated to investigate the information on the basic situations, occupational hazards, and occupational health management for 193 FMFs in Ningbo. Furthermore, we used the semi-quantitative risk assessment model, which was developed by the International Council on Mining and Metals (ICMM), to assess occupational health risks for 59 of 193 the FMFs.

Results: The casting process of FMFs in Ningbo was mainly divided into sand casting and investment casting, and silica-dust and noise were the major occupational hazards in both sand casting and investment casting foundries. Silica-dust mainly occurred in industries with such work as sand handling, modeling, falling sand, and sand cleaning, with the median of the permissible concentration-time weighted average (PC-TWA) was 0.80, 1.15, 3.52, 0.83 mg/m^3, respectively. The noise mainly existed in industries with such work as sand handling, core making, falling sand, sand cleaning, cutting and grinding, and smelting with median of PC-TWA was 81.72 dB(A), 82.93 dB(A), 90.75 dB(A), 80.18 dB(A), 90.05 dB(A), 82.70 dB(A), respectively. In addition, the results of the ICMM assessment model indicated that 100 and 98.7% of the jobs exposed to silica-dust and noise in 59 FMFs have an "intolerable risk" level of risks of causing pneumoconiosis and noise deaf, respectively.

Discussion: The hazard risk of silica-dust and noise is serious for FMFs in Ningbo. It is necessary to supervise enterprises to improve operating environmental conditions, accelerate the reduction of silica-dust and noise exposure risks, and promote the healthy and sustainable development of the foundry industry.

KEYWORDS

risk assessment, occupational and environmental exposure, ferrous metal, silica-dust exposure, noise exposure

Introduction

As the largest developing country, China is experiencing one of the worst occupational health problems in the world and faced with more severe threats and challenges induced by occupational hazardous factors than most other countries. Over 200 million workers from at least 20 million enterprises are at risk of occupational diseases in China (1). It is estimated that at least one million subjects suffered from occupational diseases (OD) with nearly 30,000 newly diagnosed cases per year over the past decade, leading to a considerable burden on the society (2). The increase in OD incidence in China, in large part, is ascribed to serious occupational hazards in workplace, such as silica-dust and noise, and inadequate personal protective equipment (3).

Ningbo is an economic center of Zhejiang Province, which is also a coastal city with a population over than 9 million, with a high level of economic development comparing to the general situation of China (GDP per capita in 2021 $2,3846 vs.$1,2462) (4). With the rapid growth of social economy, the foundry industry has developed rapidly and has become a pillar industry in Ningbo (5). However, FMFs are one of the industries with serious dust hazards, and the newly diagnosed cases of pneumoconiosis in Ningbo in recent years were concentrated in this industry (6). Currently, 20% of newly diagnosed occupational hearing loss was observed in this industry, according to the investigation by Zhejiang Provincial Center for Disease Control and Prevention (7). Due to regulatory and legal measures, more and more companies and organizations give attention to employee health and safety, try to control occupational hazards, and seek to improve the level of worker safety (8, 9).

Occupational Health and Safety (OHS), defined as the science of the anticipation, recognition, evaluation and control of hazards arising in or from the workplace that could impair the health and wellbeing of workers, is an important issue for both employees and employers (10–12). As one critical process in OHS practice, occupational health risk assessment (OHRA) is an effective tool to assess the risk of occupational hazards in workplace and take required control measures for providing safety (13, 14). Developed countries and international organizations have developed several OHRA methods, including the models from the United States Environmental Protection Agency (EPA) (15), the United Kingdom's Control of Substances Hazardous to Health Essentials (COSHH Essentials) (16), Australia (17), Romania (18), the International Council on Mining and Metals (ICMM) (19), and Singapore (20). The ICMM model was used to evaluate the occupational health risk in this study mainly attributing to several reasons: first, the model has a broad scope of evaluated substances; second, the model could be applied to various industries, including ferrous metal casting industry; third, the model was based on qualitative or subjective descriptions, and less detailed information was required for use (13).

According to Ningbo Municipal Statistics Bureau, there were ∼267 FMFs with over workers until June 2020 (5). It is necessary to understand the characteristics of occupational hazards in the main positions of the FMFs and evaluate the corresponding occupational hazard risks to provide a scientific basis for formulating policies of occupational disease prevention and control.

The primary purpose of this study was to investigate the exposure characteristics and occupational health risks of silica-dust and noise, and provide a basis for developing reasonable control measures to reduce the health risks for workers. Accordingly, the following two step were conducted successively: (1) occupational hygiene survey and field investigation for normally operating ferrous metal foundries (FMFs); (2) assess occupational health risk by using the model developed by ICMM.

Methods

Description of Ferrous metal casting industry

Ferrous metal casting industry, one of the most important foundry industries in Ningbo, is the process of smelting iron and steel metal into a liquid that meets certain requirements and pouring it into a mold, in order to obtain castings of predetermined shape, size, and properties, after cooling, solidification, and cleaning (21). Currently, commonly used process flow of casting including sand casting, investment casting, pressure casting and centrifugal casting, etc., (21). The process flow of sanding casting and investment casting were selected for this study. The inherent risk (IR) of ferrous metal casting industry was directly obtained from a normative document, Catalog of Classification and Management of Occupational Disease Hazard Risks in Construction Projects, formulated by the National Health Commission of China (22). Based on the document, the occupational hazards are assigned a level of risk according to the advice and consultation of China's top occupational health experts. Accordingly, the IR level of ferrous metal casting industry was classified as "severe" in this study. In addition, the enterprises classification standard was formulated by the National Bureau of Statistics of China (23).

Occupational hygiene survey

Questionnaires were used to investigate the basic information of FMFs, including enterprise size, production process, job setting, and etc. For occupational health management information, engineering protection facilities, personal protective equipment and occupational hygiene management system formulation and implementation, and etc. were investigated. In order to maintain the quality of the survey, we formulated unified questionnaire, compiled survey operation technical manuals, and conducted technical training for investigators. In this study, the field measurements and interviews were performed by experts who had title of associate chief physician or senior engineer.

Identification of occupational hazardous factors

Occupational hazardous factors were determined through field investigation, air sampling, and laboratory tests based on two occupational health standards in China, that is, the "Specifications of air sampling for hazardous substances monitoring in the workplace (GBZ 159)" and "Determination of toxic substances in workplace air (GBZ/T 160 and 300)." The levels of occupational hazards in FMFs were qualified by using the Chinese Occupational Exposure limits for Hazardous Agents in Workplace (GBZ 2.1-2019). Onsite measurement of noise was conducted according to the standard "The physical factor measurement in the workplace (GBZ/T189.8-2007)." The exposure levels of silica-dust and noise at various locations in the sand conditioning, molding and core making, melting, shakeout sand, shot blasting, and cutting and polishing had different degrees of exceed the permissible concentration time weighted average (PC-TWA) permitted by China. The evaluation of silica-dust and noise was based on the PC-TWA. "Qualified" or "Disqualified" was equal to the exposure level of risk factor not exceed the standard of PC-TWA or exceed the standard of PC-TWA, respectively. For silica-dust, the PC-TWA by China was 0.3 mg/m^3 for free SiO_2 content higher than 50% and lower than 80%, according to GBZ 2.1-2019. The permissible level of noise was 85 dB(A), according to GBZ 189.8-2007.

Methodology for the ICMM model

The ICMM model was based on two factors: the inherent harmful consequences and their probability of occurrence, which were evaluated by four procedures step by step: hazard identification, hazard characterization, exposure assessment, and risk characterization. The detailed principles of the ICMM model were reported in previous publication (19). The ICMM model applies a matrix method to evaluate risk levels, including matrix combinations of health hazards and the probability of exposure occurring in a similar exposure group or process, as well as matrix combinations of health hazards and exposure levels with existing control measures.

$$RR = C \times PrE \times PeE \times U$$

In this equation, RR is the risk ratio; C is level of occupational hazard health consequences; PrE is the probability of exposure, based on the ratio of the exposure level (E) and occupational exposure limit (OEL); PeE is the length of exposure; U is uncertainty factor. The result of ICMM model (RR) was also converted into a classification of five risk levels, which could vary from 1 to 5: Level 1, RR <20 represents a tolerable risk; Level 2, RR ranges from 20 to 70, which represents a potential risk; Level 3, RR ranges from 70 to 200, which represents a high risk; Level 4, RR ranges from 200 to 400, which represents a very high risk; Level 5, RR greater or equal to 400 represents an intolerable risk. Risk scoring for risk criteria is showed in Table 1. In this study, quantitative risk assessment was performed by statisticians who had background of medical or public health, and examined by experts subsequently.

Briefly, the process of performing the ICMM model had two phases in the current study. The first phase was identification of risk criteria. According to previous investigations and publications, three risk criteria were considered for this method, which included the probability of exposure to hazardous factors (PrE), the duration of exposure criteria (PeE), and the severity of consequence (C).

The second phase was determining the risk scoring system and risk level. To rate this criterion for PrE, control measures for any potential hazard are required to be assessed directly or indirectly. In direct assessments, the exposure level needs to be measured and compared with the standards. In indirect assessments, documents of recent measurements can be used. If the exposure rate was lower than 50% of occupational exposure limit (OEL), the corresponding score was three points. If the exposure rate was between 50 and 100% of OEL, the corresponding score was 6 points. While if the exposure rate was over the OEL, the corresponding score was 10 points. For the duration of exposure criteria, the exposure duration criterion was set at 4 levels: one a year, short periods several times a month, 2–8 h on average during shift work, and over 8 h of exposure (within overtime and shiftwork), which were equal to scores of 0.5, 2, 6, 10 points, respectively. For severity of consequence, the score of 4 levels was 1, 15, 50, 100 points, which represents exposure at this level does not harm the personnel, health effects are reversible and not a threat to one's life, undesirable health effects that are permanent or temporary but have little effect on one's quality of life and life expectancy, and health effects that are usually permanent and can significantly decrease quality of life or life expectancy, respectively. Finally, the equation "RR = C × PrE × PeE × U" was used to calculate the RR.

TABLE 1 Risk scoring table for risk criteria.

Risk criteria	Description	Score
PrE[a]	Exposure rate lower than 50% of OEL	3
	50–100% of OEL[e]	6
	Above OEL	10
PeE[b]	One a year	0.5
	Short periods several times a month	2
	2–8 h on average during shift work.	6
	Over 8 h of exposure (within overtime and shiftwork)	10
C[c]	Exposure at this level does not harm the personnel	1
	Health effects are reversible and not a threat to one's life	15
	Undesirable health effects that are permanent or temporary but have little effect on one's quality of life and life expectancy	50
	Health effects that are usually permanent and can significantly decrease quality of life or life expectancy	100
RR[d]	Tolerable risk	<20 (Level 1)
	Potential risk	20–70 (Level 2)
	High risk	70–200 (Level 3)
	Very high risk	200–400 (Level 4)
	Intolerable risk	≥400 (Level 5)

[a]PrE, Probability of exposure criteria; [b]PeE, Duration of Exposure Criteria; [c]C, Severity of Consequences Criteria; [d]RR, Result of risk assessment; [e]OEL, occupational exposure limit.

Statistical analysis

Results are presented as median and interquartile range (IQR) for continuous data under biased distribution and categorical data. We performed a logarithmic conversion for the concentration of silica-dust before statistical analysis in this study. Exposure time and exposure concentration are also showed as median (range). The permissible concentration time weighted average (PC-TWA) was used to assess if the exposure level of silica-dust and noise exceed the standard in the current study. The ANOVA and LSD-test were used to analyze the differences between different tasks for silica-dust and noise. EpiData 3.1 was used to compile the database and input the data of occupational hygiene survey. All statistical analyses were calculated by SAS version 9.4 (SAS Institute, Cary, NC, USA).

TABLE 2 Basic information of ferrous casting foundries in Ningbo.

Variables	Enterprise size[a]			Total
	Medium	Small	Micro	
Process type				
Sand casting	8 (7.77%)	67 (65.05%)	28 (14.00%)	103 (53.37%)
Investment casting	4 (4.65%)	82 (91.10%)	4 (4.65%)	90 (46.64%)
Region				
Urban	9 (6.87%)	109 (83.21%)	13 (9.92%)	131 (67.88%)
Rural	5 (8.06%)	43 (69.35%)	14 (22.59%)	62 (32.12%)
Total	14 (7.25%)	152 (78.76%)	27 (13.99%)	193 (100%)

[a]Enterprise size, the enterprises classification standard was formulated by the National Bureau of Statistics of China.

Results

Basic information of FMFs in Ningbo

Finally, a total of 193 FMF were included in this study (Table 2). They comprised 14 (7.25%) medium enterprises, 152 (78.75%) small enterprises, and 27 (14.00%) micro enterprises. For process type, there were 103 (53.37%) sand casting foundries and 90 (46.64%) investment casting foundries in the present study. Besides, most of FMFs in Ningbo (131, 67.88%) were located in urban area.

We observed that silica-dust and noise were the main occupational hazards for the 193 FMFs of Ningbo in the occupational hygiene survey. Sand conditioning, molding and core making, melting, shakeout sand, shot blasting, and cutting and polishing were key locations, which were exposed to the silica-dust and noise.

Characteristic of occupational hazards

Table 3 shows the key locations and exposure level of silica-dust by different process type. The levels of silica-dust from the majority of location were disqualified both for sand casting foundries and investment casting foundries. For noise, we observed that the levels of noise were qualified from sand conditioning, molding and core making, and melting in sand casting foundries and melting in investment casting foundries. For different locations, the exposure level of silica-dust in shakeout sand was higher than other location ($P < 0.05$) in both sand casting foundries and investment casting foundries. Besides, the exposure level of noise in shakeout sand was also higher than other location ($P < 0.05$).

Results of occupational risk assessment

In Table 4, we observed that the RRs for silica-dust in the positions of sand conditioning, molding and core making, melting, shakeout sand, and shot blasting were all greater or equal to 400, which represented that workers were exposed to intolerable health risk of silica-dust in the workplace. The RR for 7.32% of No. cutting and polishing was between 200 and 400, which represented very high risk of silica-dust exposure in the workplace. For noise, the RRs in all positions were also greater or equal to 400, which represented that workers were exposed to an intolerable health risk of noise in the workplace.

Discussion

In this study, most of the ferrous metal foundries in Ningbo were small and micro enterprises, which was in accordance with the distribution of previous studies in other cities. This might be related to the overall distribution of enterprises in China. At present, most of FMFs in China are small enterprises, because small enterprises are the main force of development. Besides, it might also be related to the small investment, low cost and flexible operation required by small foundry enterprises.

Silica-dust is the most common occupational hazard in the foundry industry. Silica-dust is one of the most harmful to human health, and the occupational exposure limit (OEL) is the lowest among all dusts. Silicosis caused by silica dust accounts for the largest proportion of pneumoconiosis and is the most harmful. In this study, the dust excess rate of all FMFs, sand casting foundries, and investment casting foundries in Ningbo was 40.61, 37.97%, and 44.11, respectively. However, we found no statistical significant difference between casting process and dust excess rate, which was similar to the previous study (24). The silica dust concentration rate of the main positions was lower than 40%, which was significantly lower than the Shanghai (25) and Jiangsu Province (26). This might be related to the transformation and upgrading of the foundry industry in Ningbo in 2014 (27). Besides, the concentration of silica-dust in sand casting foundries is higher than that in investment casting foundries, which is partly due to the relatively large castings of sand casting technology enterprises, the large amount of sand used, and the poor effectiveness of dust protection facilities (5). The concentration of silica-dust in the shakeout sand of sand casting is higher than that of the sand conditioning and shot blasting. This may be due to the completeness of protective facilities in the shakeout sand is lower than that in the sand conditioning and shot blasting (28). In addition, artificial hammers are usually used to shake the sand and vibrating sand machines are used to shake the sand in the process of shakeout sand, which lead to a serious dust escape, and finally, it is difficult to be effectively captured by local ventilation and dust removal facilities (29).

Silica in foundry dust not only causes silicosis, Gabriella et al. found in a study of two cases of accelerated silicosis that respirable silica could enter the liver and cause granulomas and liver involvement (30). Vihlborg et al. (31) in Sweden In the Iron Foundry Occupational Silica Exposure Risk Study, moderate to high exposure to respirable silica was associated with an increased risk of sarcoidosis and seropositive rheumatoid arthritis. Andjelkovich et al. (32) found that gastric cancer in foundry workers may be associated with respirable silica exposure. In addition to high silica content, foundry dust also contains a certain amount of carcinogenic cadmium, chromium, nickel, etc. and their compounds, as well as other chemically harmful components such as binders and curing agents (33). Studies have shown that these harmful components Causes respiratory and lung inflammation more closely than respirable silica.

In this study, the overall noise exceeding rate of FMFs in Ningbo was 54.47%, among which the noise exceeding rate of sand casting foundries and investment casting foundries were 45.69 and

TABLE 3 Identification of main occupational hazards in ferrous casting foundries.

Location	Risk factor	Sand casting				Investment casting			
		No. of locations	Exposure levels [mg/m3 or dB (A)][a]	Length of exposure (median, range) [hours/day]	Evaluation by China PC-TWA[b]	No. of locations	Exposure levels [mg/m3 or dB(A)]	Length of exposure (median, range) [hours/day]	Evaluation by China PC-TWA
Sand conditioning	Silca-dust	56	0.48 (0.07–4.33)	8 (4–11)	Disqualified	23	0.35 (0.05–1.79)	6 (2–9)	Disqualified
	Noise	23	81.70 (71.32–98.45)	8 (4–11)	Qualified	14	90.95 (81.70–99.65)	6 (2–9)	Disqualified
Molding and Core Making	Silca-dust	93	1.15 (0.09–4.30)	8 (4–12)	Disqualified	37	0.38 (0.12–2.80)	8 (6.5–11)	Disqualified
	Noise	99	82.90 (74.2–91.6)	8 (4–12)	Qualified	23	82.90 (73.50–90.65)	8 (6.5–11)	Qualified
Melting	Silca-dust	109	0.26 (0–0.90)	8 (4–10)	Qualified	72	0.29 (0.10–1.05)	8 (4–10)	Qualified
	Noise	89	82.70 (74.62–91.38)	8 (4–10)	Qualified	46	85.40 (69.50–91.20)	8 (4–10)	Disqualified
Shakeout sand	Silca-dust	15	1.47 (0.17–5.11)	8 (4–10)	Disqualified	43	0.61 (0.09–2.26)	7.5 (3–11)	Disqualified
	Noise	22	90.75 (78.62–99.78)	8 (4–10)	Disqualified	27	98.60 (85.60–104.35)	7.5 (3–11)	Disqualified
Shot blasting	Silca-dust	39	0.45 (0.03–2.05)	6 (1–12)	Disqualified	34	0.52 (0.09–6.35)	7.5 (3–11)	Disqualified
	Noise	57	88.10 (76.32–101.36)	6 (1–12)	Disqualified	63	89.60 (79.70–99.85)	7.5 (3–11)	Disqualified
Cutting and polishing	Other dust	41	1.50 (0.15–7.40)	7 (4–9)	Disqualified	80	0.43 (0.05–6.35)	7.5 (2–11)	Disqualified
	Noise	60	90.05 (83.62–105.66)	7 (4–9)	Disqualified	75	90.70 (83.40–105.35)	7.5 (2–11)	Disqualified

[a]The exposure level of silica-dust and other dust is expressed by mg/m^3, and the exposure level of noise is expressed by dB (A).
[b]PC-TWA: Permissible concentration-time weighted average.

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TABLE 4 Composition of risk ratios (RRs) of different positions for sand casting foundries and investment casting foundries.

Position	OH[a]	Concequence	Composition of RR (%) for sand casting foundries						Composition of RR fro investment casting foundries					
			No. of locations	≥400	200–399	70–199	20–69	<20	No. of locations	≥400	200–399	70–199	20–69	<20
Sand conditioning	Silica-dust	Silicosis	56	100	/	/	/	/	23	100	/	/	/	/
	Noise	Occupational noise deafness	23	100	/	/	/	/	14	100	/	/	/	/
Molding and core making	Silica-dust	Silicosis	93	100	/	/	/	/	37	100	/	/	/	/
	Noise	Occupational noise deafness	99	100	/	/	/	/	23	100	/	/	/	/
Melting	Silica-dust	Silicosis	109	100	/	/	/	/	72	100	/	/	/	/
	Noise	Occupational noise deafness	89	100	/	/	/	/	46	100	/	/	/	/
Shakeout sand	Silica-dust	Silicosis	15	100	/	/	/	/	43	100	/	/	/	/
	Noise	Occupational noise deafness	22	100	/	/	/	/	27	100	/	/	/	/
Shot blasting	Silica-dust	Silicosis	39	100	/	/	/	/	34	100	/	/	/	/
	Noise	Occupational noise deafness	57	100	/	/	/	/	63	100	/	/	/	/
Cutting and polishing	Other dust	Metals and their compounds dust pulmonary disease	41	92.68	7.32	/	/	/	80	95	5	/	/	/
	Noise	Occupational noise deafness	60	100	/	/	/	/	75	100	/	/	/	/

[a]OH, occupational hazards.

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64.86%, respectively, with the average noise intensity 85.07 and 83.92 dB(A), respectively. The overall noise exceeding rate of sand casting foundries in Ningbo is lower than that in Zhangjiagang City (34), and higher than that of foundry enterprises in Shanghai (25) and Jingjiang City (35). In this study, statistically significant difference was observed between the noise exceeding rate of the sand casting foundries and investment casting foundries, which indicated that FMFs should strengthen noise management, reduce noise pollution, and avoid hearing fatigue or even occupational noise deafness, especially for those adopting the investment casting process. Noise-induced hearing loss is sensory deafness caused by prolonged exposure of the auditory system to a noisy environment (36). Auditory fatigue is an early symptom of noise-induced hearing loss, and hearing can gradually recover after people leave the noisy environment. Prior studies observed that occupational noise exposure is associated with permanent hearing loss (37). The NIH reported that nearly 20 million workers are regularly exposed to noise, of which 50% (10 million) suffer hearing damage of varying severity (38). The WHO estimated that ∼16% of disabling hearing impairment results from occupational noise exposure (39). In addition to the damage to the auditory system, noise can also cause damage to the non-auditory system, such as stress, damage to the cardiovascular system, and decline in cognitive and behavioral abilities, so attention should be paid to the impact of noise (40).

The result of occupational health risk evaluation showed that the health risk of silica-dust was the highest level, that is, an intolerable risk (RR ≥400), which was in accordance with the evaluation results of previous studies by using other OHRA models. In addition, we observed that the health risk of noise was also the highest level, which was inconsistent with the result of Gu et al. (40). This may be mainly due to taking different occupational health consequences. However, some occupational health examination results were not available, such as lung and inner ear examination, which limited our further analysis.

In conclusion, there were intolerable risks for silica-dust and noise for FMFs in Ningbo. Exposure to silica-dust and noise in the workplace remains a major concern in the field of occupational health in developing and developed countries, therefore, mature experience in silica-dust and noise control should be performed as soon as possible. Besides, as an important foundry production base in China, it is necessary to supervise enterprises to improve operating environmental conditions, accelerate the reduction of silica-dust and noise exposure risks, and promote the healthy and sustainable development of the foundry industry.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

DD and AW conceived and coordinated its overall structure. DD, PL, and AW acquired data and performed statistical analyses. DD and PL contributed to the writing and editing of draft. DD worked closely with other authors to align the structure and develop the conclusions. DZ contributed to the overall concept of the draft. DD, PL, XL, GM, DZ, and AW contributed to the editing and revising the draft. All authors interpreted data, revised the manuscript for intellectual content, and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Occupational health risk assessment of workplace solvents and noise in the electronics industry using three comprehensive risk assessment models

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Background: Occupational hazards such as solvents and noise in the electronics industry are serious. Although various occupational health risk assessment models have been applied in the electronics industry, they have only been used to assess the risks of individual job positions. Few existing studies have focused on the total risk level of critical risk factors in enterprises.

Methods: Ten electronics enterprises were selected for this study. Information, air samples and physical factor measurements were collected from the selected enterprises through on-site investigation, and then the data were collated and samples were tested according to the requirements of Chinese standards. The Occupational Health Risk Classification and Assessment Model (referred to as the Classification Model), the Occupational Health Risk Grading and Assessment Model (referred to as the Grading Model), and the Occupational Disease Hazard Evaluation Model were used to assess the risks of the enterprises. The correlations and differences between the three models were analyzed, and the results of the models were validated by the average risk level of all of the hazard factors.

Results: Hazards with concentrations exceeding the Chinese occupational exposure limits (OELs) were methylene chloride, 1,2-dichloroethane, and noise. The exposure time of workers ranged from 1 to 11 h per day and the frequency of exposure ranged from 5 to 6 times per week. The risk ratios (RRs) of the Classification Model, the Grading Model and the Occupational Disease Hazard Evaluation Model were 0.70 ± 0.10, 0.34 ± 0.13, and 0.65 ± 0.21, respectively. The RRs for the three risk assessment models were statistically different ($P < 0.001$), and there were no correlations between them ($P > 0.05$). The average risk level of all of the hazard factors was 0.38 ± 0.18, which did not differ from the RRs of the Grading Model ($P > 0.05$).

Conclusions: The hazards of organic solvents and noise in the electronics industry are not negligible. The Grading Model offers a good reflection of the actual risk level of the electronics industry and has strong practicability.

KEYWORDS
electronics industry, occupational health, risk assessment, comprehensive risk, solvent, noise

Background

The electronics industry is a strategic emerging industry in China, and its production process is characterized by rapid renewal and complex intermediate products. The Chinese electronics industry has a wide range of occupational hazards, a large number of employees, and a high risk of occupational disease. There exists a coexistence of outdated and advanced production processes (1). Wen et al. (2) analyzed the disease spectrum of new occupational diseases in Guangdong Province from 2006 to 2010, and the number of new cases in the electronics industry ranked third among all industries. Tian et al. (3) measured the noise intensity exposure of job positions in electronics enterprises and combined it with the results of workers' health examinations for a comprehensive analysis. It was found that the noise exceedance rate was relatively high, and nearly half of the workers had abnormal pure-tone audiometric results, suggesting that noise may be a significant hazard factor in this industry. Yang et al. (4) explored the exposure to organic solvents and found a variety of organic solvents in the electronics industry, such as *n*-hexane and benzene. In summation, workers in the electronics industry are facing high occupational health risks, particularly exposure to noise and organic solvents, and supervision and management should be strengthened by regulations and employees.

Occupational health risk assessment is considered an essential tool for maintaining the health of workers (5). As a result, many countries and organizations have developed various occupational health risk assessment models, including the Singapore model (6), the US EPA quantitative risk assessment model (7), the ICMM model (8), the Romanian risk assessment model (9), and the COSHH essential model (10). Previous studies (11–14) have explored whether occupational health risk assessment models can be applied in the electronics industry, to provide scientific guidance for enterprises to accurately identify high-risk positions and take appropriate control measures. Xu et al. (15) and Tian et al. (16) used quantitative or qualitative–quantitative methods to explore the consistency, relevance, and other indicators of the assessment results of six models commonly used for risk assessment in the electronics industry and established a more comprehensive framework for model comparison.

However, traditional models evaluate the risk levels of specific job positions, and although the results may be highly accurate, they are not always useful for helping occupational health regulators decide which enterprises require intervention. Therefore, some studies have developed comprehensive risk assessment methods for evaluating the overall occupational health risks of enterprises. A comprehensive risk assessment method was mentioned in the Romanian risk assessment model, where the comprehensive risk level in the workplace was calculated from weighted average of the identified risk factors. Li et al. (17) proposed a new method of occupational health risk assessment based on Set Pair Analysis, which could assess the comprehensive risk of welding workshops. Jahangiri et al. (18) used a comprehensive occupational health risk assessment model to prioritize occupational health hazards in petrochemical companies and to determine resource allocation and required control measures. Ji et al. (19) in New Zealand revised the conventional risk assessment approach to a comprehensive risk assessment method that considered both safety accidents and chronic health issues, providing a way to incorporate long-term health outcomes into occupational health risk accessment. The purpose of this study was to explore the application of three Chinese comprehensive risk assessment models to the electronics industry in China based on the hazard characteristics of the electronics industry, organic solvents and noise, and to quantitatively compare the difference and correlation of their assessment results to provide new ideas for implementing efficient occupational health supervision.

Materials and methods

Description of study subjects

To obtain a large sample size and fully reflect the characteristics of the production process in the electronics industry, 10 electronics enterprises in Shenzhen, Guangdong Province, China, were selected for the study, with a labor quota distribution of 350–1,000 employees and a complex range of major products, including electronic sports watch-related accessories, relays, computers, printers, LCD monitors, printing consumables, hard disk drive components, connectors, printed circuit boards, inductors, conductive silicone, and inverters.

Site survey and on-site testing

In this study, a uniform questionnaire was used to investigate the basic information, production process, production system of each position, daily exposure time, weekly exposure days, and occupational health management of each enterprise. Air sampling for chemical poisons was performed according to the Chinese sampling standard described in "*The sampling specification for hazardous substances monitoring in workplace air* (GBZ 159-2004)" (20). Laboratory testing of these chemicals was based on "*The determination of toxic substances in the workplace* (GBZ/T 160-2004)" (21) series of standards. The 8-h time-weighted average concentration (C-TWA) of chemical toxicants were tested and compared with the permissible concentration-time weighted average (PC-TWA) in the Chinese standard "*Occupational exposure limits for hazardous agents in the workplace Part 1: Chemical hazardous agents* (GBZ 2.1-2019)" (22). Field measurements of noise were conducted according to the standard "*The physical factor measurement in the workplace* (GBZ/T 189.8-2007)" (23). If the work shift was 5 days per week, the noise exposure level was defined as the equivalent continuous A-weighted sound pressure level normalized to a nominal 8 h working day, $L_{EX,8h}$. If the work shift was not 5 days per week, the equivalent continuous A-weighted sound pressure level normalized to a nominal 40 h working week, $L_{EX,W}$ was used to reflect the noise exposure level.

Risk assessment models

In this study, three models were used to assess the comprehensive risks of 10 electronics enterprises, including two newly developed comprehensive risk assessment models—the Occupational Health Risk Classification and Assessment Model (referred to as the Classification Model) and the Occupational Health Risk Grading and Assessment Model (referred to as the Grading Model)—and the Occupational Disease Hazard Evaluation Model used in China. The risk assessments of the three models were completed by professional occupational health institutions or relevant departments of the enterprises.

(1) The Classification Model. This model was developed by the National Administration of Disease Prevention and Control, PRC, and the National Health Commission, PRC. According to the requirements of the Chinese guideline, "*Guidelines for Occupational Health Risk Classification and Grading Assessment of Employers.*" the comprehensive risks of the 10 selected enterprises were devided into levels A, B, and C from high to low risk. The detailed principles are shown in Table 1.

(2) The Grading Model. This model was developed by Chinese scholars with reference to various occupational health risk assessment models such as the Singapore model, the ICMM model, and the Romanian model, and adjusted based on the management situation of enterprises. The Grading Model was applied in this study as follows. First, the risk level of each occupational disease hazard was determined by the hazard rating (HR) and exposure rating (ER). HRs and ERs of chemical hazard factors could be identified according to the Singapore model. The calculation of ER depended on the ratio of the weekly exposure E to the occupational exposure limit (OEL). E was calculated using the equation: $E = \frac{F \times D \times M}{W}$, where F is the frequency of exposure per week, M is the magnitude of exposure, W is the average working hours per week, D is the average duration of each exposure. Depending on the severity of the health effects of the hazards (in the order of minor health effects, reversible health effects, permanent irreversible health effects, significant and severe health effects, and death), the HRs of physical factors were classified into five classes according to the method described in the ICMM model. As shown in Table 2, the ER of noise was graded according to the A-weighted equivalent sound pressure level (L_{Aeq}). R_i was interpreted as the risk level of different hazards in the position. Due to the complexity of the types of hazards present in the workplace, R_i had multiple values. And R_i was calculated by the equation: $R_i = \sqrt{HR \times ER}$. In addition, according to the Romanian risk assessment model, the comprehensive risk level R_O was calculated by a weighted average of R_i for each position through the equation $R_o = \frac{\sum_{i=1}^{n} R_i \times r_i}{\sum_{i=1}^{n} r_i}$. Finally, the 12 major items—such as the management measures for occupational disease prevention and control, declaration of occupational disease hazards, "three simultaneous" of occupational disease protection facilities in construction projects, and occupational health conditions in the workplace—were checked and assigned scores, using the self-inspection form for the implementation of occupational disease prevention and control responsibilities of the enterprises in the appendix of the Chinese guideline "*Occupational Health Risk Classification and Assessment Guide for Employers*." The ratio of the actual score to the total score was the standardized score. The standardized score divided the Occupational Health Management Index (MI) into four levels: A (90–100 points), B (80–89 points), C (70–79 points), and D (<70 points). Referring to the matrix method of the COSHH essential model, the matrix shown in Table 3 was used to determine the adjusted comprehensive risk R_O' of the enterprises.

(3) The Occupational Disease Hazard Evaluation Model (24). This model was established by combining the Occupational Hazards Risk Assessment Index Method (25) with the occupational health management level of an enterprise. According to this model, the comprehensive risk level of the enterprise depends on the two key indicators, the occupational hazard risk index grade and management quality. Therefore, in this study, the occupational hazard risk index was calculated using the formula: risk index $= 2^{\text{health effect level}} \times 2^{\text{exposure ratio}} \times$ operating condition level and then divided into five levels according to the risk index, no hazard (risk index ≤ 6), mild hazard ($6 <$ risk index ≤ 11), moderate hazard ($11 <$ risk index ≤ 23), high hazard ($23 <$ risk index ≤ 80), and extreme hazard (risk index > 80). By calculating the weights to grade the occupational health management of enterprises, the management quality was divided into five categories: fail, pass, average, good, and excellent, using 0.6, 0.7, 0.8, and 0.9 as the boundary. The risk index grade and the management quality grade were used to construct a matrix to determine the comprehensive risk level, as shown in Table 4.

Comparison between different assessment models

Due to the inconsistent presentation of risk assessment results obtained from different models, the risk levels of the three models were appropriately converted in this study to facilitate comparison. First, categories A, B, and C in the results of the Classification Model were converted to levels 3, 2, and 1. Next, levels A, B, C, and D in the results of the Occupational Disease Hazard Evaluation Model were converted to levels 1, 2, 3, and 4. Then, the risk level of each model was standardized using the risk ratio (RR) definerd by Zhang et al. (26). RR was the ratio between the risk level of a given risk factor obtained from each model and the total risk level of the model, and it was obtained from the formula, $RR =$ Actual risk level/Total risk level. As an example, if a particular model's risk level was divided into five levels and level 3 was determined by utilizing the model to evaluate a risk factor, the RR would be equal to 0.6 (3/5).

TABLE 1 The detailed principle of the classification model.

Category	Principle
A	Enterprises belong to specific industries such as mining, manufacturing, electricity, heat, gas and water production and supply, etc. Industry classification refers to the National Economic Classification and Codes (Chinese standard: GB/T 4754-2017).
	1. The presence of high-risk chemicals such as hydrogen cyanide, n-hexane, aniline in the workplace, the concentration of which reaches or exceeds 50% OEL.
	2. The presence of benzene, 1,2-dichloroethane, trichloroethylene, etc. in the workplace in concentrations of 10% OEL or more.
	3. The workplace has chemical substances or productive dust (free silica ≥10%) in excess of the OEL.
	4. Workplace with nuclear facilities, irradiation processing equipment, radiation therapy equipment, industrial flaw detection machines, oilfield logging equipment.
	5. Newly diagnosed occupational diseases within the last 2 years.
	6. Enterprises included in the scope of key management by the health administration.
	7. Enterprises that meet one of the above conditions are included in Category A.
B	The presence of highly hazardous chemicals in the workplace, such as hydrogen cyanide, n-hexane, aniline, etc. in concentrations below 50% OEL.
	1. The presence of benzene, 1,2-dichloroethane, trichloroethylene, etc. in the workplace in concentrations below 10% OEL.
	2. The presence of chemical substances or productive dust (free silica ≥ 10%) in the workplace.
	3. The presence of radioactive occupational disease hazards in the workplace.
	4. Enterprises that meet one of the above conditions are included in Category B.
C	Occupational hazards exist in the workplace, but the enterprise is not classified as Category A or Category B.

TABLE 2 The rank of noise exposure.

Definition (dB(A))	Exposure rank (ER)
$L_{Aeq} < 75$	1
$75 \le L_{Aeq} < 80$	2
$80 \le L_{Aeq} < 85$	3
$85 \ge L_{Aeq} < 90$	4
$L_{Aeq} \ge 90$	5

Accuracy validation of model results

In this study, an attempt was made to validate the results of three comprehensive risk assessment models using the average risk level of all of the hazard factors for 10 enterprises. Organic solvents were assessed using the Singapore semi-quantitative model, and noise was assessed using an ICMM matrix model. The selection of the above models was based on relevant studies (27) and discussions with experts.

Statistical analysis

SPSS 23.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. Spearman rank correlation analysis was used to compare the correlations of RRs among the three models. Wilcoxon signed rank sum test was performed on R_O (the Grading Model) and the risk indices (the Occupational Disease Hazard Evaluation Model). Meanwhile, Wilcoxon signed rank sum test was performed on the standardized occupational health management levels between the Grading Model and the Occupational Disease Hazard Evaluation Model. One-way analysis of variance (ANOVA) was used to analyze the RRs in the three models and the mean RR levels of all of the risk factors. The LSD comparison method was used when the variances were equal, and the Dunnett T3 comparison method was used when there was heterogeneity in the variances.

Results

On-site occupational survey

Table 5 describes the basic information of the 10 enterprises. The number of exposed workers ranged from 308 to 1,929. Three enterprises had single-shift work, five had two-shift work, and the rest had both shift patterns. Workers in these 10 enterprises were exposed to occupational hazards from 1 to 11 h per day, and the frequency of exposure was 5–6 times per week.

The exposure levels of organic solvents and noise in the 10 enterprises are shown in Table 6. Hazards with concentrations exceeding OEL were methylene chloride, 1,2-dichloroethane, and noise. The one hazard at a concentration above 50% OEL but below OEL was isopropyl alcohol. Hazards with concentrations above 10% OEL but below 50% OEL were methanol, tetrahydrofuran, methanol, isopropanol, ethanolamine, n-hexane, methanol, formaldehyde, xylene, and toluene. The concentrations of other hazards were <10% OEL.

As shown in Table 7, six enterprises were found to have hazard factors exceeding the OELs. Among these enterprises, one chemical factor, methylene chloride, exceeded the OEL, with an 8 h time-weighted average concentration (C-TWA) of 331.84 mg/m^3. The noise exposure intensity of different job positions ranged from 80.8 to 91.9 dB(A). In addition, only two enterprises were found to be fully equipped with health engineering protection and personal protective equipment, accounting for 20% of the total, which indicated that the levels of occupational health management of the enterprises were deficient.

Risk assessment results

The risk assessment results of the three risk assessment models are listed in Table 8. The Classification Model classified the 10 enterprises into level 2 (category B) and level 3 (category A); one enterprise belonged to category A and the remaining nine belonged to category B. The Grading Model classified the 10 electronic enterprises into level 1, level 2, and level 3; five enterprises were classified as level 1, four were classified as level 2, and one was

TABLE 3 Comprehensive risk matrix for the grading model.

The comprehensive risk level R_O	The occupational health management index (MI)			
	Grade D	Grade C	Grade B	Grade A
1	2	1	1	1
2	2	2	1	1
3	3	3	2	2
4	4	4	3	3
5	4	4	4	4

TABLE 4 The comprehensive risk matrix for the occupational disease hazard evaluation model.

Management quality (MQ)	Occupational hazard risk index grade				
	No hazards	Mild hazards	Moderate hazard	Highly hazard	Extreme hazard
Excellent	A	A	B	C	C
Good	A	B	B	C	D
General	B	B	C	D	D
Passing	B	B	C	D	D
Failure	B	C	D	D	D

classified as level 3. The Occupational Disease Hazard Evaluation Model classified the 10 electronic enterprises into level 1, level 2, level 3, and level 4; one enterprise was in level 1, three enterprises were in level 2, five enterprises were in level 3, and one enterprise was in level 4.

Correlation analysis of the three models

The results of Spearman correlation analysis of the three model presented in Table 9, indicated that there were no correlations between the risk assessment results of all three models, and the difference was not statistically significant (correlation coefficients 0.192, −0.314, and −0.109, respectively; $P > 0.05$).

Quantitative differences in the risk ratios between the different models

As shown in Figure 1, the RR for the Classification Model was 0.70 ± 0.10, the RR for the Grading Model was 0.34 ± 0.13, and the RR for the Occupational Disease Hazard Evaluation Model was 0.65 ± 0.21. The differences between the RRs obtained from the three models were statistically significant ($F = 17.598$, $P < 0.001$). Compared with the Grading Model, the RRs of the Classification Model and the Occupational Disease Hazard Evaluation Model were significantly higher. The difference was statistically significant ($P < 0.001$). However, the difference between the RRs of the Classification Model and the Occupational Disease Hazard Evaluation Model was not statistically significant ($P = 0.466$). The magnitudes of the RRs of the three models were in the following order: the Classification Model > the Occupational Disease Hazard Evaluation Model > the Grading Model.

The Grading Model and the Occupational Disease Hazard Evaluation Model are similar in principle, both of which combine the inherent risk level and occupational health management levels of enterprises for comprehensive risk assessment. Since the variance analysis showed a statistically significant difference in the risk levels obtained by the two models, the next step of this study was to explore the reasons for the differences between them. The unadjusted risk indicators and the occupational health management indexes of the models were considered. As shown in Table 10, the analysis of R_Os (for the Grading Model) or the risk indices (for the Occupational Disease Hazard Evaluation Model) of the occupational health management level revealed that the risk indices of the Occupational Disease Hazard Evaluation Model were significantly higher than the R_Os of the Grading Model, and the difference was statistically significant ($P = 0.034$). The evaluation results of the two risk assessment models on the occupational health management levels of 10 electronic enterprises are shown in Table 11. The differences between the two risk models were not statistically significant ($P = 0.856$). Therefore, the difference between the assessment results of the two models may be due to the inconsistency in the calculation of the inherent risk level of the enterprise.

Accuracy validation of model results

In this study, the average risk level of all of the risk factors present in all positions was used for accuracy verification, and the results of the three models were evaluated for the total risk of the enterprise. Figure 1 shows that the average risk level of all of the risk factors was 0.38 ± 0.18. Comparing the RRs of the three models with the average risk level of all of the risk factors, the results showed that the Classification Model and the Occupational

TABLE 5 Basic information of 10 electronics enterprises.

Enterprise	Number of exposed workers	Shift system	Work hour per day	Work day per week	Automation level
A	200	Single shift, two shifts	8	5	Semi-automation
B	1,929	Two shifts	11	5	Semi-automation
C	550	Two shifts	10	6	Semi-automation
D	615	Two shifts	10	6	Semi-automation
E	678	Two shifts	10.5	6	Semi-automation
F	498	Single shift, two shifts	10	6	Semi-automation
G	1,100	Two shifts	10.5	5	Semi-automation
H	400	Single shift	8	5	Semi-automation
I	308	Single shift	8	5	Semi-automation
J	500	Single shift	8	6	Semi-automation

TABLE 6 The result of hazard exposure level in 10 enterprises.

Enterprise	Hazards exposure			
	<10%OEL	10%OEL-50%OEL	>50%OEL	>OEL
A	Benzene, ethylbenzene, hexane, methanol, ethanol, acetone, dichloromethane	–	–	–
B	Benzene, methylbenzene, xylene, ethylbenzene, methanol, butanone, ethyl acetate, butyl acetate, N,N-dimethylacetamide	–	Isopropanol	Noise
C	Isopropanol, methylbenzene, methanol, ethanol	–	–	–
D	Acetone, butanone, methyl benzene	Methanol, tetrahydrofuran	–	Dichloromethane, 1,2-dichloroethane, noise
E	Ethanol	Methanol, isopropanol, ethanolamine	–	–
F	Methylbenzene, cyanide, hydrogen cyanide, sulfuric acid, hydrochloric acid	–	–	Noise
G	Ethanol, methyl benzene, xylene, methyl acetate, ethyl acetate	Hexane, methanol, formaldehyde	–	Noise
H	Benzene, methylbenzene, ethylbenzene, hexane, cyclohexane, methanol, isopropanol, butanol, trichloroethylene	Xylene	–	Noise
I	Benzene, xylene, hexane, cyclohexanone, methanol, ethyl acetate, butyl acetate, isoflurone	Methyl benzene	–	–
J	Benzene, xylene, ethyl benzene, hexane, cyclohexane, methanol, acetone, butanone, dichloromethane, ethyl acetate, butyl acetate, isoflurone, trichloroethylene, tetrachloroethylene	Methyl benzene	–	Noise

Disease Hazard Evaluation Model did not agree with the average risk level of all of the risk factors, and the difference was statistically significant ($P < 0.001$). On the contrary, the results of the Grading Model did not differ in any way from the average risk level of all of the risk factors ($P = 0.505$), which indicated that the results of the Grading Model more accurately reflected the actual risk of the enterprise.

Discussion

With the rapid development of the economy, the electronics industry is employing more and more workers, and the occupational health problems of these workers are becoming increasingly prominent (28). Previous studies on the electronics industry have shown that the occupational disease hazards in the electronics industry are mainly organic solvents and noise, and some new occupational disease hazards such as hexane also need to be assessed due to the continuous updating of process technology (29).

Liver damage evidenced by the elevation of alanine aminotransferase and oxidative stress markers has been observed in patients exposed to organic solvents. In addition, chronic or high exposure to organic solvents may be associated with reduced female fertility (30) and hearing organ damage in workers (31). Noise can have direct and cumulative adverse effects that impair health and degrade residential, social, working, and learning environments with corresponding natural (economic) and intangible (welfare) losses (32). Regarding the direct effects, exposure to intense sound

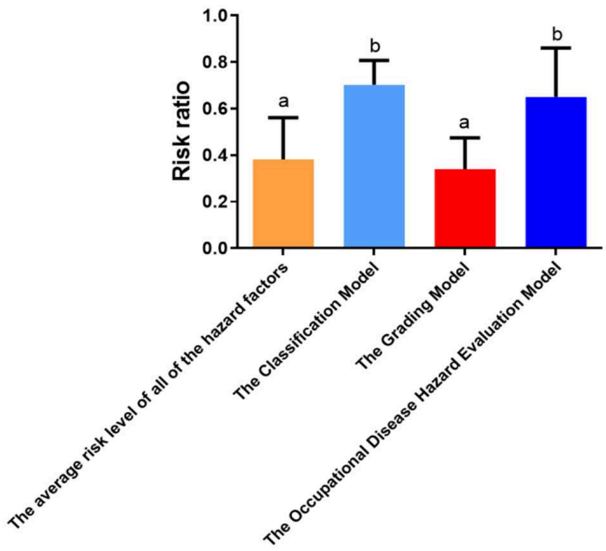

FIGURE 1
Quantitative differences in the risk ratios between the models. Compare with each other, if the symbols (like "a") are same, $P > 0.05$.

TABLE 7 On-site occupational health survey of 10 electronics enterprises.

Item	*N*	Number of enterprise passed	Passing rate
Occupational hazards	10	4	40.00%
Engineering protections	10	2	20.00%
Personal protective equipment	10	2	20.00%
Emergency rescue facilities	10	2	20.00%
Occupational health management	10	2	20.00%

TABLE 8 Results of three occupational risk assessment models.

Enterprise	The classification model		The grading model		The occupational disease hazard evaluation model	
	The result of risk assessment	RR	The result of risk assessment	RR	The result of risk assessment	RR
A	2	0.67	2	0.40	4	1.00
B	2	0.67	1	0.20	3	0.75
C	2	0.67	2	0.40	2	0.50
D	3	1.00	2	0.40	2	0.50
E	2	0.67	1	0.20	1	0.25
F	2	0.67	3	0.60	2	0.50
G	2	0.67	2	0.40	3	0.75
H	2	0.67	2	0.40	3	0.75
I	2	0.67	1	0.20	3	0.75
J	2	0.67	1	0.20	3	0.75

TABLE 9 Correlation analysis of RRs for three models.

Variants	The classification model	The grading model	The occupational disease hazard evaluation model
The classification model[a]	1.000		
The grading model[a]	0.192	1.000	
The occupational disease hazard evaluation model[a]	−0.314	−0.109	1.000

[a]Compare with each other, if the symbols (like "a") are same, $P > 0.05$.

TABLE 10 Comparison of R_os (the grading model) and risk indices (the occupational disease hazards evaluation model).

Model	R_os or risk indices of different enterprises										*Z*-value	*P*-value
	A	B	C	D	E	F	G	H	I	J		
The grading model	0.4	0.4	0.4	0.6	0.4	0.4	0.6	0.4	0.4	0.4	−2.121	0.034
The occupational disease hazard evaluation model	0.8	0.6	0.4	0.6	0.4	0.4	0.6	0.6	0.6	0.6		

R_os and Risk Indices are normalized similarly to the risk ratios for comparison purposes.

TABLE 11 Two risk assessment models to evaluate the level of occupational health management standardization in 10 electronic enterprises.

Model	Enterprises										*Z*-value	*P*-value
	A	B	C	D	E	F	G	H	I	J		
The grading model	1.00	0.50	0.75	0.50	0.25	0.50	0.50	1.00	0.50	0.50	−0.181	0.856
The occupational disease hazard evaluation model	1.00	0.60	0.60	0.40	0.20	0.40	0.60	0.80	0.80	0.80		

or noise may result in a purely temporary threshold shift or cause a residual permanent threshold shifts and alterations in the growth functions of auditory nerve output (33). Regarding the cumulative adverse effects, large epidemiological studies on community noise have reported its association with breast cancer, stroke, type 2 diabetes, and obesity (34). Simultaneous exposure to noise and a mixture of organic solvents may have a secondary effect on the risk of hypertension (35) and additional damage to the auditory organs (36). In this study, the on-site survey of 10 Shenzhen-based electronic companies found that their main occupational hazards were organic solvents and noise. Six companies exceeded the noise standard with an exceedance rate of 60%, indicating that the hazard of noise in the electronics industry was severe and needed to be given high priority, consistent with previous studies (3). Meanwhile, the on-site survey showed that the numbers of workers in the selected enterprises ranged from 300 to 1,900 or more, with workers working up to 11 h, suggesting that the electronics industry was dominated by labor-intensive enterprises, resulting in a high potential risk of occupation-related diseases.

Engineering protections are the primary occupational disease prevention and control measures that can fundamentally control and eliminate the possible occupational hazards in the workplace. Their functions are to prevent workers from being exposed to occupational disease hazards as much as possible or to control the levels of harmful factors in the workplace within the permissible ranges of occupational health standards (37). Besides, personal protective equipment is an important type of protection for workers, and the correct selection and wearing of personal protective equipment is a prerequisite for ensuring the health and safety of workers (38). The on-site survey showed that only 2 out of 10 enterprises complied with the regulations of Chinese occupational health in terms of engineering protection and personal protective equipment, with a compliance rate of only 20%, which was inconsistent with the findings of previous studies on the electronics industry (39). The above results indicate that the electronics industry has poor control of hazard factors. Enterprises should be equipped with self-contained engineering protection facilities and personal protective equipment. Meanwhile, government occupational health supervision departments should strengthen their health supervision.

The application of risk assessment in the field of occupational health is relatively mature, and traditional occupational health risk assessment models—such as the Singapore model, the US EPA quantitative risk assessment model, the ICMM model, the Romanian risk assessment model, and the COSHH essential model—are more accurate in identifying risks of job positions and valuable for helping enterprises quickly implement effective control measures. However, the number of electronics enterprises in China is large, and it does not seem feasible for the supervisory department to urge enterprises to rectify the situation based on job risks. Therefore, it is more effective for regulators to improve efficiency by implementing risk assessment based on the comprehensive risk level of individual enterprises and adjusting the supervision of enterprises with different risk levels accordingly.

The correlation analysis of the three risk assessment models showed that there was no correlation between these three models ($P > 0.05$). Comparing the RRs of the three models, it was found that the Classification Model and the Occupational Disease Hazard Evaluation Model had significantly higher RRs than the Grading Model ($P < 0.001$), which depended on the principle of the model itself. The three comprehensive risk assessment models used in this study have their own advantages and disadvantages due to their different modeling principles. The Classification Model is a qualitative model that classifies the comprehensive risk of an enterprise by the industry classification as well as the types and levels of hazards faced by the enterprises. Its advantage is that it can quickly determine the comprehensive risk of an enterprises, and it is easy for non-specialists to use. Moreover, the Classification Model is sensitive to the identification of severely hazardous occupational hazards (e.g., 1,2-dichloroethane and benzene) and other highly pathogenic or toxic substances, so a higher risk rating may be derived if the above chemical hazards are present in the workplace. This suggests that the results of the Classification Model can work well in preventing workers from developing occupational diseases. However, the assessment results obtained from the Classification Model are crude and do not integrate the actual exposure data of the positions. Both the Grading

Model and the Occupational Disease Hazard Evaluation Model are quantitative models that combine the levels of risk of occupational hazards with the occupational management level of the enterprise. The Grading Model combines the principles of various traditional occupational health risk assessment models. Its greatest advantage is that the specific exposure level of the position is fully considered before quantitative calculation, and then the occupational health management level of the enterprise is weighted, so the result may better reflect the actual risk level of the enterprise. However, it is worth noting that its complicated assessment formula could limit its use and promotion. The Occupational Disease Hazard Evaluation Model considers the health effects, likelihood (exposure time and intensity), and severity (health effects) of hazards, as well as the number of people exposed and protective measures, and the enterprise's occupational health management. The model avoids a complicated calculation process, reduces the subjectivity of the assessment to a certain extent, and reflects the current situation of the enterprise as comprehensively as possible. The Grading Model and the Occupational Disease Hazard Evaluation Model are similar, but yield very different risk assessment results ($P < 0.05$). The risk level R_O (the Grading Model) and risk index (the Occupational Disease Hazard Evaluation Model) of the two models before the adjustment of the occupational health management level were analyzed, and it was found that assessment result of the Occupational Disease Hazard Evaluation Model was higher than the Grading Model ($P < 0.05$), but there was no difference in the occupational health management level derived from the two risk assessment models ($P > 0.05$). This suggests that the reason for the large difference in the assessment results of the two models may be due to the difference in R_O or risk index. In addition, the large difference in risk assessment results between the Grading Model and the Occupational Disease Hazard Evaluation Model could also be due to the difference in the adjustment matrices of occupational health management level. From the matrices of the two models, it can be seen that the Grading Model is more conservative than the Occupational Disease Hazard Evaluation Model, which is reflected by the fact that the Grading Model is less influenced by the occupational health management status of the enterprise when the R_O or risk index is at a low to medium level, and, thus, obtains a lower risk level.

It was found that workers in the in-service group in the electronics industry had significantly higher rates of abnormal blood pressure than those in the pre-employment group (40). Meanwhile, a study analyzed the occupational health results of a street in the electronics industry and found that the current health status of workers in the electronics industry was not optimistic, with a 50% abnormal detection rate (28). In Jiangsu Province, 166 cases of occupational poisoning (including 157 cases of chronic occupational poisoning) occurred in the electronics industry, accounting for 17.2% of occupational poisoning cases in the province (41). Data on the distribution of occupational diseases in the Baoan district of Shenzhen from 2000 to 2011 showed that the composition ratio of the electronics industry (36.8%) was much higher than that of other industries (42). In this study, the average risk level of all of the hazard factors of all positions was analyzed, and the results showed that the average RR was 0.38 ± 0.18, indicating that the risks of the 10 electronics enterprises was at a medium level, which was basically consistent with the results of the above studies. The RRs of the three models were compared with the average risk level of all of the hazard factors of the positions, and there was no difference between the RRs of the Grading Model and the average risk level ($P > 0.05$), which indicated that the Grading Model better reflected the actual risk levels of the electronics enterprises, and the assessment results of the total risk of the enterprises were more scientific and accurate. The other two models may have overestimated the overall risk level of enterprises due to different principles.

Conclusions

The hazards of organic solvents and noise in the electronics industry deserve great attention, and the occupational health management of enterprises also needs to be improved. The Classification Model and the Occupational Disease Hazard Evaluation Model may overestimate the risk level of electronics enterprises, whereas the results of the Grading Model are more in line with the actual risk of enterprises.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the participants was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

SS, CW, TW, and XL contributed to the data acquisition. SS, QH, XZ, and JZ contributed to data analysis, interpretation, and drafted. SS and QH conceived and designed the study. SS critically reviewed the manuscript for intellectual content and is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data, and the accuracy of the data analysis. All authors reviewed and approved the final version of the manuscript and contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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