



## Review

# Health risk assessment from inhalation exposure to indoor formaldehyde: A systematic review and meta-analysis

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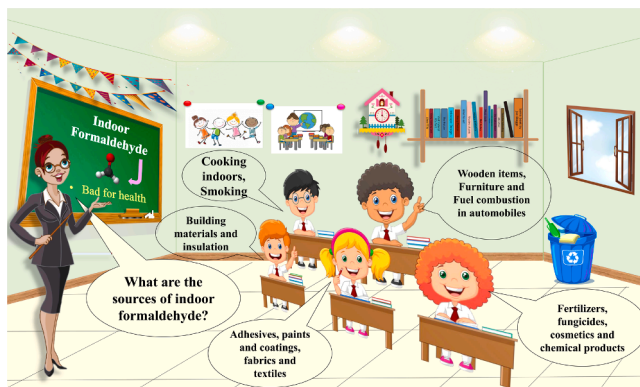
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## HIGHLIGHTS

- Formaldehyde (FA) is one of the most abundant pollutants in indoor air.
- FA concentrations in various indoor environments ranged from 0.01 to 1620  $\mu\text{g}/\text{m}^3$ .
- Formaldehyde levels were higher in kindergartens than in other educational centers.
- In over 90% of the studies, the risk of carcinogenesis was higher than  $1.00 \times 10^{-6}$ .

## GRAPHICAL ABSTRACT



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## ABSTRACT

This systematic review and meta-analysis investigated studies on formaldehyde (FA) inhalation exposure in indoor environments and related carcinogenic (CR) and non-carcinogenic (HQ) risk. Studies were obtained from Scopus, PubMed, Web of Science, Medline, and Embase databases without time limitation until November 21, 2023. Studies not meeting the criteria of Population, Exposure, Comparator, and Outcomes (PECO) were excluded. The 45 articles included belonged to the 5 types of sites: dwelling environments, educational centers, kindergartens, vehicle cabins, and other indoor environments. A meta-analysis determined the average effect size (ES) between indoor FA concentrations, CR, and HQ values in each type of indoor environment. FA concentrations ranged from 0.01 to 1620  $\mu\text{g}/\text{m}^3$ . The highest FA concentrations were stated in water pipe cafés and the lowest in residential environments. In more than 90% of the studies uncertain ( $1.00 \times 10^{-6} < \text{CR} < 1.00 \times 10^{-4}$ ) and actionable carcinogenic risk ( $\text{CR} > 1.00 \times 10^{-4}$ ) due to FA inhalation exposure was reported and non-

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carcinogenic risk was stated acceptable. The meta-analysis revealed the highest CR values due to inhalation of indoor FA in high-income countries. As 90% of the time is spent indoors, it is crucial to adopt effective strategies to reduce FA concentrations, especially in kindergartens and schools, with regular monitoring of indoor air quality.

## 1. Introduction

Formaldehyde (FA,  $\text{CH}_2\text{O}$ ) is a colorless, highly reactive, flammable gas with a pungent and irritating odor, which is used as a precursor to more complex compounds due to its properties and reactivity [1]. This compound is generated naturally in the processes of decomposition and combustion of plant residues. In addition, as one of the natural components of blood, FA plays an essential role in human metabolism for the biosynthesis of purines, thymidines, and some amino acids [2,3].

FA, widely used in building materials and insulation [4,5], furniture and wooden products [6,7], household products such as glue, paints and coatings, fabrics and textiles [8], fertilizers, fungicides, cosmetics, and chemical products [9,10], is one of the most abundant carbonyl compounds released frequently in indoor and outdoor spaces [11]. In addition, smoking [12], indoor cooking [13–15], and fuel combustion in automobiles [16] are also considered as other anthropogenic sources of FA emissions. For this reason, there is a high probability of human exposure to FA as individuals interact with different FA-containing industrial and domestic products in various indoor and outdoor environments. A better understanding of the human exposure mechanism to FA under varying environmental conditions is an important element of the human health risk management [1,11,12].

The main route of human exposure to FA is inhalation, which causes the accumulation and absorption of this gaseous compound in the upper respiratory tract [17]. Almost every human body tissue can quickly decompose FA absorbed into less toxic products such as formic acid and carbon dioxide [18]. Although FA is a natural metabolic product, exposure to elevated ambient levels of FA can increase the risk of acute and chronic toxicity in humans [19,20]. The Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) revealed that exposure to FA at concentrations between 0.1 and 1 ppm causes common side effects such as irritation of the nose, throat, and eyes along with increased tearing. The detection of FA by human senses occurs at FA concentrations (FA conc.) between 0.1 and 0.5 ppm. With increasing FA concentration, the health effects intensify where at first eyes ( $0.5 < \text{FA conc} < 1.0$  ppm) and nose and throat ( $1.0 \text{ ppm} < \text{FA conc}$ ) are stimulated [21]. In addition, chronic exposure to high levels of FA causes numerous health complications, such as menstrual disorders and pregnancy problems [22,23], asthma [24], adverse effects on the central nervous system such as headaches, irritability, sleep disorders, depression, mood changes [25], and also causes various types of cancer [26–28]. For this reason, environmental exposure to FA and related carcinogenicity was a major focus of many research [1,24].

The International Agency for Research on Cancer (IARC), after extensive international human studies, classified FA as a group 1 carcinogen (carcinogenic to humans) [29]. Furthermore, in the European Union (EU) inhalation exposure to FA was classified as carcinogenic category B1 and mutagenic category 2 [30]. Due to the fact that FA is the most abundant air pollutant in indoor environments [31] and since people spend more than 90% of their time indoors, chronic exposure to this pollutant is expected to have adverse health effects [32]. In relation, the World Health Organization (WHO) limited 30 min FA exposure to  $0.1 \text{ mg/m}^3$  (80 ppb or  $100 \mu\text{g/m}^3$ ) in indoor spaces [33]. Also, the Federal Department of Health of Canada (FDH) determined that the permissible concentration of FA in indoor air is  $123 \mu\text{g/m}^3$  (1 h exposure) and  $50 \mu\text{g/m}^3$  (8 h exposure) [34].

Among the most efficient and widely used methods to assess the risk of cancer and toxic effects caused by environmental exposure to pollutants in humans is the human health risk assessment tool (HHRA),

developed by the United States Environmental Protection Agency (USEPA) [35,36]. According to the USEPA methodology, values of the carcinogenic risk ( $\text{CR} \geq 1.00 \times 10^{-4}$ ) indicate an actionable risk, values of the carcinogenic risk between the range  $1 \times 10^{-6} < \text{CR} < 1 \times 10^{-4}$  indicate an uncertain risk, and CR values  $\leq 1.00 \times 10^{-6}$  indicate an inconsequential risk of additional cancer cases in the investigated population [36]. In addition, in terms of non-carcinogenic risk when the values of Hazard Quotient ( $\text{HQ} > 1$ ) it indicates the potential to result in adverse health effects and if  $\text{HQ} < 1$ , the non-carcinogenic risk is within the acceptable range [36]. These risk ranges developed by the USEPA are commonly used in the literature to describe the severity of toxic effects. The advantage of these risk ranges is that they arise as a result of environmental exposure *versus* exposure period, and thus they are a summary of these causal factors in combination.

In relation to the United Nations (UN) Sustainable Development Goal No. 3: Ensure healthy lives and promote well-being for all at all ages, as people spend most of their time indoors, indoor air FA concentration monitoring and health risk assessment become an important tool to determine the risk of exposure [37] and to develop preventive measures to avoid the adverse health effects in exposed populations. In this systematic review and meta-analysis, the current scientific literature on FA exposure was evaluated. The detailed objectives of this paper were (1) to investigate FA concentrations in various types of indoor spaces from existing research, (2) to assess carcinogenic and non-carcinogenic human health risk in those environments of exposure, and (3) to determine the mean effect size (ES) of FA concentrations, CR and HQ values for each type of indoor environment by country, income level, and year of publication of investigated studies.

## 2. Methods

The current review study was registered with the number CRD42023454315 in the International Prospective Systematic Review Registry (PROSPERO) and was conducted according to the PRISMA protocol.

### 2.1. PECO statement

The PECO (Population, Exposure, Comparator, and Outcome) approach was used in this study to create a structured research question to achieve an efficient search of bibliographic information and also to facilitate access to the best scientific evidence for this systematic review and meta-analysis (Table 1). Using PECO framework helps researchers to identify searchable parts of a research question and focus the search on relevant results [38].

**Table 1**  
PECO (Population, Exposure, Comparator, and Outcome) statement used in the study.

PECO	Evidence
Population	All people exposed to indoor formaldehyde (FA)
Exposure	Inhalation of FA in indoor spaces
Comparator	- Comparison of FA levels with the permissible values recommended by WHO and FDH - Comparison of carcinogenic and non-carcinogenic risk values due to inhalation exposure to FA with the acceptable values by the USEPA
Outcome	Risk of cancer and chronic non-cancerous diseases appearance in the exposed population

## 2.2. Search strategy and selection criteria

To the best of the authors' knowledge, this is the first systematic review and meta-analysis that examines the carcinogenic and non-carcinogenic risk caused by inhalational exposure to FA in indoor environments. Studies to be examined were identified through a systematic search in Scopus, PubMed, Web of Science, Medline, and Embase databases until November 21, 2023 using the following keywords:

“exposure”, “environmental exposure”, “inhalation exposure”, “respiratory exposure”, “hazard”, “risk assessment”, “carcinogenic risk”, “non-carcinogenic risk”, “cancer risk”, “non-cancer risk”, “hazard quotient”, “human health risk”, “formaldehyde”, “formal”, “formalin”, “methanol”, “methylene oxide”, “indoor environment”, “indoor air”.

To further identify any other studies that met the inclusion criteria of the present study, the references of the chosen articles were also searched. This was done simultaneously with the primary search. The process of conducting this study was carried out in 8 stages namely: topic selection, conceptualization and creating the protocol, PECO statement, systematic literature search, study selection (screening and data extraction), evaluation of the risk of bias, resolving contradictions and ambiguities, synthesization and interpretation of the achieved results.

In this review, only original peer-reviewed articles in English were included in this study and animal and laboratory studies, as well as books, review articles, conference papers, and letters to editors were excluded. In addition, studies that evaluated the health risk caused by occupational exposure to FA or used a method other than that introduced by the USEPA to calculate CR and HQ values also did not comply with the study.

Finally, from each included study, information on the authors, year of publication, country, sampling location, sampling duration, number of samples, type of sampling method, type of sampling device, type of detection device, average concentration of FA, carcinogenic and non-carcinogenic risk values was extracted and gathered in relevant tables.

## 2.3. Quality control

The quality of studies eligible for inclusion in the systematic review and meta-analysis was assessed by two researchers (A.H.Kh and M.M) independently, using the Joanna Briggs Institute (JBI) checklist to perform cross-sectional studies [39]. This approach is a standard methodology used previously in several published studies [40,41]. The JBI checklist includes 8 questions from 4 criteria, namely exposure assessment, confounding factors, appropriate statistical analysis, and results. For each question, the 4 answers were possible to be answered: “yes”, “no”, “uncertain”, or “inapplicable”. Depending on which answers covered from  $\geq 50$  to 75% of the questions, the studies were classified into one of the 3 categories. The high-quality level and low risk of bias category (Q1) included studies for which “yes” answers constituted  $\geq 50$ –75% of the answers. The medium quality level and unclear risk of bias category (Q2) collected studies for which the “uncertain” responses made up  $\geq 50$ –75% of the answers. The low quality and high risk of bias category (Q3) contained studies for which “no” constituted  $\geq 50$ –75% of the responses [42]. In the further stages of our research studies from the Q1 and Q2 categories were included.

## 2.4. Carcinogenic and non-carcinogenic risk assessment

Carcinogenic and non-carcinogenic risk assessment was carried out using the United States Environmental Protection Agency (USEPA) methods [36,43], to calculate the health risk values associated with respiratory exposure to FA in various indoor environments. Eq. (1) was used to calculate the inhalation exposure concentration ( $EC_{inh}$ ):

$$EC_{inh} = C \times \frac{ET \times EF \times ED}{AT} \quad (1)$$

Where  $EC_{inh}$  is the inhalation exposure concentration ( $\mu\text{g}/\text{m}^3$ ), C is a concentration of FA in indoor air ( $\mu\text{g}/\text{m}^3$ ), ET is exposure time (hours/day), EF is exposure frequency (days/year), ED is exposure duration (years), and AT is the averaging time (ED in years  $\times$  365 days/year  $\times$  24 h/day in hours for non-carcinogens, 70 years  $\times$  365 days/year  $\times$  24 h/day in hours for carcinogens).

Eq. (2) was used to calculate the CR associated with inhalation exposure to FA:

$$CR = EC_{inh} \times IUR \quad (2)$$

Where CR is carcinogenic risk (unitless), EC is exposure concentration ( $\mu\text{g}/\text{m}^3$ ), and IUR is inhalational unit risk factor equal to  $1.30 \times 10^{-5}$  ( $\mu\text{g}/\text{m}^3$ )<sup>-1</sup> [35].

According to the USEPA policy, a CR of less than  $10^{-6}$  is considered a low or inconsequential risk. Risks that fall between  $10^{-6}$  and  $10^{-4}$  are uncertain, while risks greater than  $10^{-4}$  (1;10,000) are considered actionable risk [36].

Eq. (3) was used to calculate the HQ from inhalation exposure to FA:

$$HQ = \frac{EC_{inh}}{RfC_i} \quad (3)$$

Where Hazard Quotient (HQ) (unitless) represents non-carcinogenic risk,  $EC_{inh}$  is exposure concentration ( $\mu\text{g}/\text{m}^3$ ), and  $RfC_i$  is the inhalational reference concentration equivalent to  $9.83 \mu\text{g}/\text{m}^3$  [36].

When the HQ values exceed 1, it indicates a significant non-carcinogenic risk, whereas an HQ value less than 1 implies an acceptable level of non-carcinogenic risk.

## 2.5. Synthesis and analysis of results

In the present systematic review and meta-analysis, where more than three studies were identical in terms of methodology and reporting of results (mean concentration and standard deviation), the data was quantitatively synthesized by meta-analysis. In quantitative synthesis, for clarity in the meta-analysis, studies in 5 sections including dwelling environments, educational centers, kindergartens, vehicle cabins and other indoor environments were examined according to concentration, carcinogenic risk (CR), non-carcinogenic risk (HQ), and the results were presented in tables and figures. If there was not enough data for meta-analysis, the average concentration of FA, carcinogenic and non-carcinogenic risk caused by exposure to this pollutant was combined in narrative form (Tables 2–6). The narrative synthesis in this study was carried out in two stages, (1) the initial synthesis according to the general grouping of the articles based on the type of indoor environment and (2) the comparison of the results within and between the studies of each group of indoor environments in terms of FA concentration and assessed health risk values.

## 2.6. Meta-analysis

A meta-analysis was carried out to determine the mean effect size (ES) of the studies. The meta-analysis uses a simple formula that calculates the sum of the weighted ESs, divided by the sum of the weightings. In this study, we used indoor FA concentrations, CR, and HQ values for each type of indoor environment, such as educational centers, dwelling environments, kindergartens, vehicle cabins, and other indoor environments. All studies included in the meta-analysis reported FA concentration and at least one value of HQ or CR due to inhalation exposure to the investigated pollutant.

The indoor concentration levels of FA for various environments were reported using the mean and 95% confidence interval (CI) of the effect size. To evaluate the heterogeneity between studies, we used Cochran's

**Table 2**  
The characteristics of studies on FA exposure in dwelling environments [44-49].

First Author	Title	Country	Duration of Sampling	Type of method	Number of Samples	Type of Samplers	Type of Analyzer	Location	Mean Concentration (µg/m <sup>3</sup> )	Carcinogenic Risk (CR)	Hazard Quotient (HQ)
Armando Baez (2003) [74]	Carbonyl levels in indoor and outdoor air in Mexico City and Xalapa, Mexico	Mexico	4 months (120 min)	DNPH/ HPLC method	145	Sep-Pak DNPH-Silica cartridges	HPLC with a GBC LC 1200 UV-VIS detector	Two residential houses	House in Satellite County: 37 House in Tlalnequanta County: 47	$4.9 \times 10^{-7}$ $6.1 \times 10^{-7}$	—
Tsun-Tsun Li (2008) [62]	Human Cancer Risk from the Inhalation of Formaldehyde in Different Indoor Environments in Guiyang City, China	China	11 months (2h)	China National Standard Method GB 12997-91	Indoor monitoring sites=74 (Living room =237 Bedroom=236 Kitchen= 222 Classroom = 105 )	A Portable Formaldehyde Analyzer (InterScan Model 4160)	A Portable Formaldehyde Analyzer (InterScan Model 4160)	Living room  Bedroom  Kitchen	0.06  0.06  0.06	$1.32 \times 10^{-7}$ $1.95 \times 10^{-7}$ $8.68 \times 10^{-7}$	—
Mili Weng (2010) [54]	Levels, sources, and health risks of carbonyls in residential indoor air in Hangzhou, China	China	3 months	US EPA method TO-11A (US EPA 1999)	—	The cartridges of glass tubes filled with silica gel (60-80 mesh) coated by a diluted 2, 4-DNPH acidified solution	HPLC-UV	Living rooms Studies Kitchens Bedrooms Total  Living rooms Studies Kitchens Bedrooms Total	Summer 85.4 114.1 84.8 121.6 97.9  Winter 17.9 18.1 21.6 24.2 20.2	Summer: $1.3 \times 10^{-7}$  Winter: $2.6 \times 10^{-7}$	—
Qingyang Liu (2014) [44]	Source Apportionment of Personal Exposure to Carbonyl Compounds and BTEX at Homes in Beijing, China	China	2 months (60 min)	Derivative technique	255	2,4-dinitrophenylhydrazine (2,4-DNPH).	HPLC	Living room Cooking room	15.8 16.6	$4.4 \times 10^{-7}$	—
Florentina Villanueva (2015) [55]	Levels and sources of volatile organic compounds including carbonyls in indoor air of homes of Puertollano, the most industrialized city in central Iberian Peninsula. Estimation of health risk	Spain	2 months (7-day)	—	176	2,4-dinitrophenylhydrazine coated Florisil®	The theoretical sampling rate calculated	Houses	54.6	$7.8 \times 10^{-7}$ $4.1 \times 10^{-7}$	—
Joaquín Rovira (2016) [58]	Human health risks of formaldehyde indoor levels: An issue of concern	Spain	2 months (8 h)	—	30	An Airchek 2000 sampling pump	HPLC-UV	Bedroom Living room	27.3 22.5	$1.94 \times 10^{-7}$	217
Steven Sai Hang Ho (2016) [56]	Risk Assessment of Indoor Formaldehyde and Other Carbonyls in Campus Environments in Northwestern China	China	24 months (3 h)	US EPA method TO-11A (US EPA, 1999)	56	Sampling pump (Thomas, USA) through the cartridge	HPLC coupled with a photodiode array detector (DAD)	Residential units at a university  Bedroom in Staff Apartment: Newly decorated: 86.6 Occupied for a year: 38.3  Student Dormitory: 0.92	—  —  —	Bedroom in staff apartment being newly decorated: $4.22 \times 10^{-7}$  Decorated bedroom in staff apartment being occupied after 1 year: $1.87 \times 10^{-7}$  Student dormitory: $0.0449 \times 10^{-7}$	—
Xiyao Chen (2017) [51]	Monitoring, Human Health Risk Assessment and Optimized Management for Typical Pollutants in Indoor Air from Random Families of University Staff, Wahan City, China	China	2 years	The method specified in the Technical Specification for Indoor Ambient Air Quality Monitoring (HJ/T 167-2004)	99	Method specified in the Technical Specification for Indoor Ambient Air Quality Monitoring (HJ/T 167-2004)	The PGM-6208 Portable Formaldehyde Analyzer	Bedroom Living Room Kitchen	170 140 180	$68.3 \times 10^{-7}$ $43.66 \times 10^{-7}$ $19.3 \times 10^{-7}$	—
Mostafa Hadei (2018) [13]	Indoor and outdoor concentrations of BTEX and formaldehyde in Tehran, Iran: effects of building characteristics and health risk assessment	Iran	3 months	NIOSH method 2541 (Eller)	270	Sing a cartridge containing silica gel coated (2-hydroxymethyl) piperidine	GC-FID	Houses	18	$1.34 \times 10^{-7}$	—
Kailiang Huang (2018) [53]	Indoor air quality analysis of residential buildings in northeast China based on field measurements and longtime monitoring	China	12 months (20 min)	Chinese national standard GB/T 18204.2-2014	70	The atmospheric sampling pump	Spectrophotometer	Bedroom Living room Kitchen  Airtight Spring Nature Spring Airtight Summer Nature Summer Airtight Autumn Nature Autumn Airtight Winter Nature Winter	0.1 0.08 0.09  0.04 0.038 0.038  0.1 0.01 0.01  0.05 0.03 0.04  0.1 0.09 0.06  0.055 0.05 0.05  0.05 0.05 0.05  0.05 0.045 0.04	$8.47 \times 10^{-7}$	—
Zhai Cheng (2018) [45]	Risk assessment of inhalation exposure to VOCs in dwellings in Chongqing, China	China	4 months (20 min)	Chinese National Indoor Air Quality Standard (GB/T 18883-2002)	21	Air sampling pump	UV-VIS spectrometry	Kitchen Bedroom Living room	14 14 14	$1.8 \times 10^{-6}$ $4 \times 10^{-6}$ $2.5 \times 10^{-6}$	0.04 0.17 0.08

(continued on next page)

Table 2 (continued)

Tian Chang (2019) [52]	Evaluation of Indoor Air Pollution during the Decorating Process and Inhalation Health Risks in Xi'an, China: A Case Study	China	3 years and 8 months	China's GB/T 18883-2002 indoor air quality standard	224	Sampler (QC-2, Beijing Municipal Institute of Labour Protection, China) equipped with a bubble tube	Phenol reagent spectrophotometry (GB/T 18204.2-2014)	Apartment: Bedroom Kitchen Living room Bathroom	Hydropower finished: 0.05 0.05 0.05 0.05 Tile finished: 0.1 0.1 0.1 0.1 Putty finished: 0.05 0.05 0.05 0.05 Wallpaper/painting finished: 0.1 0.15 0.48 0.48 Wooden floor finished: 0.19 0.36 0.49 0.55 Door finished: 0.017 0.33 0.45 0.5 Furniture finished: 0.014 0.3 0.45 0.55 1 month after decoration: 0.012 0.28 0.4 0.5 3 months after decoration: 0.15 0.22 0.35 0.36 6 months after decoration: 0.1 0.15 0.2 0.2 12 months after decoration: 0.05 0.07 0.1 0.1	–	0.05 0.001 0.001 0.0005
Lin Fang (2019) [57]	Toxic volatile organic compounds in 20 homes in Shanghai: Concentrations, inhalation health risks, and the impacts of household air cleaning	China	3 months (90-minute)	DNPH/HPLC method	20 homes	Low-cost pump packages	HPLC with UV absorption	Bedrooms	28.7	$1 \times 10^4$	3
Yu Huang (2019) [88]	Evaluation and characterization of volatile air toxic indoors in a heavy polluted city of northwestern China in wintertime	China	11 months (120 min)	DNPH/HPLC method	81	Sep-Pak DNPH-Silica cartridges	HPLC equipped with a photodiode array detector (DAD)	Dwellings	21.45	$8 \times 10^3$	–
Jun Wang (2020) [15]	Analysis of winter formaldehyde and volatile organic compound pollution characteristics of residential kitchens in severe cold regions of northeast China	China	2 months (20 min)	Chinese standard GB/T 18204.2-2014	33	An atmospheric sampling pump	Phenol reagent spectrophotometry	Residential kitchens	Condition 2 (Initial cooking) 157.14 Condition 3 (Cooking period) 189.28	$5.4 \times 10^6$	–
Célia Alves (2020) [46]	Fine Particulate Matter and Gaseous Compounds in Kitchens and Outdoor Air of Different Dwellings	Portugal	2 months (10 days)	–	68	Radiello diffusive passive tubes in triplicate	HPLC equipped with a PLU-900 pump	Kitchens	7.61	–	0.3
Xianglan Zhang (2021) [47]	Variations of HCHO and BTX, human health risk and indoor renovation characteristics of newly renovated rental apartments in Beijing, China	China	5 months (20 min)	Examination methods for public places—Part 2: chemical pollutants—GB/T 18204.2-2014	143	Glass absorption tube containing 3-methyl-2-benzothiazolone hydrazine (MBTH), which reacts with HCHO to form Piperazine	Spectrophotometer	Rental apartments	0.07	$0.93 \times 10^5 + 3.66 \times 10^1$	0.18–0.29
Jiaseu Song (2022) [84]	Characteristics of Formaldehyde Pollution in Residential Buildings in a Severe Cold Area—A Case in Liaoning, China	China	8 months (20 min)	Spectrophotometric method	29 households	Air sampling pumps	Spectrophotometer	Residential buildings: Bedroom Living Room Kitchen	0.0816 0.0748 0.0721	$3.1 \times 10^4$	–
Lu Li (2023) [59]	Molecular Characteristics, Sources, and Health Risk Assessment of Gaseous Carbonyl Compounds in Residential Indoor and Outdoor Environments in a Megacity of Northwest China	China	March 2016 (heating season) September 2016 (non-heating season)	–	–	Acidified 2,4-dinitrophenylhydrazine (DNPH) impregnated cartridge (Sep-Pak DNPH-silica, Waters Corporation, Milford, MA)	HPLC coupled with a photodiode array detector (DAD)	Dwellings	Heating season 45.56 Non-heating season 26.83	–	Birth to <2 years old 214.2 2 to <6 years old 51.8
Yu-Chuan Yen (2023) [48]	Personal exposure to aldehydes and potential health risks among schoolchildren in the city	Taiwan	March–September 2020 October–December 2019 October 2020	–	221	Passive badge (cartridge adsorbent with 2,4-DNPH-coated Florisil)	HPLC-UV	Dwellings	8.79	$1.89 \times 10^4$	–
Lewei Zeng (2023) [49]	Contributions of Indoor Household Activities to Inhalation Health Risks Induced by Gaseous Air Pollutants in Hong Kong Home	Hong Kong	October–December 2019	–	–	–	Online using a Piston Transfer Reaction-Mass Spectrometer (PTR-Q-MS 500)	Dwellings	41	$2 \times 10^4$	0.42

– Lack of data

CR	HQ
$<1 \times 10^4$ insignificant risk	$<1$ acceptable risk
$1 \times 10^4 - 1 \times 10^5$ uncertain risk	$>1$ potential to result in adverse effects risk
$>1 \times 10^5$ actionable risk	

**Table 3**  
The characteristics of studies on FA exposure in educational centers.

First Author	Title	Country	Duration of Sampling	Type of method	Number of Samples	Type of Samplers	Type of Analyzer	Location	Mean concentration (µg/m <sup>3</sup> )	Carcinogenic Risk (CR)	Hazard Quotient (HQ)
Tian-Tian Li (2008) [62]	Human Cancer Risk from the Inhalation of Formaldehyde in Different Indoor Environments in Guiyang City, China	China	11 months (2 h)	China National Standard Method GB 12997-91	105	A Portable Formaldehyde Analyzer (InterScan Model 4160)	A Portable Formaldehyde Analyzer (InterScan Model 4160)	Classroom	40	1.39 × 10 <sup>-5</sup>	–
Steven Sai Hung Ho (2015) [56]	Evaluation of hazardous airborne carbonyls on a university campus in southern China	China	7 months	US EPA 1999	120	2,4-DNPH cartridges	HPLC	At a university campus in Mainland China: faculty apartments student dormitories safeguard hostels	32.5 22.2 37.8	1.85 × 10 <sup>-4</sup> 1.26 × 10 <sup>-4</sup> 2.15 × 10 <sup>-4</sup>	–
Krystallia K. Kalimeri (2016) [63]	Indoor air quality investigation of the school environment and estimated health risks: Two-season measurements in primary schools in Kozani, Greece	Greece	2 months (5 day)	–	12	Radiello passive samplers	–	Three public primary schools: School 1 (S1) School 2 (S2) School 3 (S3)	Winter: S1: 2 S2: 8 S3: 2 Total: 4 Summer: S1: 10 S2: 20 S3: 10 Total: 14.2	Winter: S1: 1.28 × 10 <sup>-6</sup> S2: 9.74 × 10 <sup>-7</sup> S3: 5.42 × 10 <sup>-7</sup> Summer: S1: 3.12 × 10 <sup>-7</sup> S2: 2.83 × 10 <sup>-7</sup> S3: 4.12 × 10 <sup>-7</sup>	Winter: S1: 7.24 × 10 <sup>-3</sup> S2: 3.44 × 10 <sup>-3</sup> S3: 5.31 × 10 <sup>-3</sup> Summer: S1: 1.75 × 10 <sup>-3</sup> S2: 9.99 × 10 <sup>-4</sup> S3: 2.32 × 10 <sup>-3</sup>
Susilo Pakpahan (2019) [64]	School Indoor Air Quality and Health Risk on the Junior High Schools Students in Depok, Indonesia	Indonesia	1 month (30 min)	–	350	Formal Diameter HiV	–	The Junior High Schools Students in Depok, Indonesia: School A School B School C	24.56 24.56 30.7	6.89 × 10 <sup>-11</sup> 6.92 × 10 <sup>-11</sup> 8.64 × 10 <sup>-11</sup>	1.11 × 10 <sup>-1</sup> 1.49 × 10 <sup>-1</sup> 9.88 × 10 <sup>-2</sup>
Máté Szabados (2021) [65]	Indoor air quality and the associated health risk in primary school buildings in Central Europe – The InAirQ study	Central Europe	6 months (30-40h)	–	64	Passive sampling (Radiello®) diffusive body code 1201 (reusable) + cartridge code 165	LC-UV	Primary school buildings	9.06	5 × 10 <sup>-7</sup>	0.1
Rocio Garcia (2022) [61]	Measurement of Indoor-Outdoor Carbonyls in Three Different Universities Located in the Metropolitan Zone of Mexico Valley during the First Period of Confinements Due to COVID-19	Mexico	9 months (8 h)	US EPA method TO-11A	246	Sep-Pack DNPH-Silica cartridges	HPLC UV-VIS	In three different universities in Mexico City: University-1 University-2 University-3	Spring: 2.53 Summer: 5.59 Fall: 4.41	3,2719 × 10 <sup>-6</sup> 8,193 × 10 <sup>-6</sup> 3,62 × 10 <sup>-6</sup>	0.4-95 0.1295 0.567
- Lack of data											

CR

<1 × 10<sup>-6</sup> inconsequential risk

1 × 10<sup>-6</sup> - 1 × 10<sup>-4</sup> uncertain risk

>1 × 10<sup>-4</sup> actionable risk

HQ

<1 acceptable risk

>1 potential to result in adverse effects risk

**Table 4**  
The characteristics of studies on FA exposure in kindergartens.

First Author	Title	Country	Duration of Sampling	Type of method	Number of Samples	Type of Samplers	Type of Analyzer	Location	Mean Concentration (µg/m <sup>3</sup> )	Carcinogenic Risk (CR)	Hazard Quotient (HQ)
Wen-Jing Deng (2016) [66]	Measurement and health risk assessment of PM <sub>2.5</sub> , flame retardants, carbonyls, and black carbon in indoor and outdoor air in kindergartens in Hong Kong	China	3 months (5 to 8 hours)	Based on US EPA method TO-11A	20	Sampling pump through the cartridge	HPLC coupled with a photodiode array detector (DAD)	5 Kindergartens: K1 K2 K3 K4 K5	25 12 15 10 48	1.1 × 10 <sup>-4</sup> 5.3 × 10 <sup>-5</sup> 6.6 × 10 <sup>-5</sup> 4.5 × 10 <sup>-5</sup> 7.1 × 10 <sup>-5</sup>	1.0 0.60 0.77 0.77 1.9
A. Bradman (2017) [67]	Formaldehyde and acetaldehyde exposure and risk characterization in California early childhood education environments	Northern California	13 months	US EPA Method TO-11A	40	A single rotary vane pump	HPLC-UV	In 28 childcare centers and 12 home-based facilities	18.9	–	0-1 year = 0.39 1-2 years = 0.65 2-3 years = 2.6 3-6 years = 3.3
- Lack of data											

CR

<1 × 10<sup>-6</sup> inconsequential risk

1 × 10<sup>-6</sup> - 1 × 10<sup>-4</sup> uncertain risk

>1 × 10<sup>-4</sup> actionable risk

HQ

<1 acceptable risk

>1 potential to result in adverse effects risk

Q-test and I<sup>2</sup>. If the p of heterogeneity, which represents the heterogeneity of the available associations, was higher than 0.1, we applied the fixed effect model. Otherwise, we used the random effect model. We used the Q test and I<sup>2</sup> statistics to examine the significant reduction in heterogeneity of partitioned subgroups (level of income, region, and date). Based on the categories established by the World Bank [50],

countries were classified into two groups: low and middle-income (LMIC), and high-income (HIC) countries. Moreover, the studies were grouped into four regions, including South/North America, Europe, the Middle East, and East/Southeast Asia. The studies based on the date were divided into two categories: 2010 or earlier and after 2010. We conducted data analyses using STATA 14.2.

**Table 5**  
The characteristics of studies on FA exposure in vehicle cabins.

First Author	Title	Country	Duration of Sampling	Type of method	Number of Samples	Type of Samplers	Type of Analyzer	Location	Mean Concentration (µg/m <sup>3</sup> )	Carcinogenic Risk (CR)	Hazard Quotient (HQ)
Mili Weng (2015) [68]	Study on the air pollution in typical transportation microenvironment: Characteristics and health risks	China	20 min	Methods of China (GBT 18204.26-2000)	21	Constant-flow-rate samplers	Phenol reagent spectrophotometry	Buses Taxis	16.2 22.5	2.100 × 10 <sup>-3</sup> 2.925 × 10 <sup>-4</sup>	-
Masahiro Tokumura (2016) [71]	Car indoor air pollution by volatile organic compounds and aldehydes in Japan	Japan	1 month (30 min)	DNPH/ HPLC method	24	Portable pump	HPLC-UV	Unoccupied cars	19.90	-	Typical use: 0.22-0.64 Occupational use: 1.5-4.2
Huaizhou Xu (2017) [69]	Personal exposure and health risk assessment of carbonyls in family cars and public transports - a comparative study in Nanjing, China	China	2h	-	20	DNPH-silica cartridges	UPLC with PDA detector	Cars Metros Buses	75.5 19.7 32.4	Family cars: Age < 6 years old: 2.96 × 10 <sup>5</sup> to 3.62 × 10 <sup>6</sup> 6 ≤ age < 18: 2.24 × 10 <sup>5</sup> to 3.74 × 10 <sup>6</sup> 18 ≤ age < 60: 4.92 × 10 <sup>5</sup> to 6.01 × 10 <sup>6</sup> Age ≥ 60: 1.80 × 10 <sup>5</sup> to 2.20 × 10 <sup>6</sup> Public transport: Age < 6 years old: 9.25 × 10 <sup>5</sup> to 1.51 × 10 <sup>6</sup> 6 ≤ age < 18: 7.00 × 10 <sup>5</sup> to 1.15 × 10 <sup>6</sup> 18 ≤ age < 60: 1.54 × 10 <sup>5</sup> to 2.51 × 10 <sup>6</sup> Age ≥ 60: 5.61 × 10 <sup>5</sup> to 9.18 × 10 <sup>5</sup>	-
Ho-Hyun Kim (2019) [72]	Concentrations of particulate matter, carbon dioxide, VOCs and risk assessment inside Korean taxis and ships	Korean	4 months (50 min)	DNPH/ HPLC method	22	Personal air sampler	HPLC alliance	Corporate and private taxis in the Korean capital Seoul	Winter: Taxis: 23.85 Ships: 55.26 Summer: Taxis: 23.69 Ships: 66.58	Taxis: 7.00 × 10 <sup>6</sup> Ships: 1.20 × 10 <sup>6</sup>	-
Ho-Hyun Kim (2020) [73]	Characteristics of exposure and health risk air pollutants in public buses in Korea	Korea	6 months	DNPH/ HPLC method	40	Personal air sampler	HPLC coupled with a photodiode array detector (DAD)	City buses Express city buses Shuttle buses Community buses	Summer: 43.73 48.49 90.01 51.91 Winter: 38.52 43.01 50.53 21.55	3 × 10 <sup>5</sup> 1.25 × 10 <sup>5</sup> 4.2 × 10 <sup>5</sup> 5 × 10 <sup>5</sup> Total= 8.05 × 10 <sup>5</sup>	-
Haimei Wang (2023) [83]	Observation, prediction, and risk assessment of volatile organic compounds in a vehicle cabin environment	China	1 month	-	43	2,4-dinitrophenylhydrazine (DNPH)	GC-Mass or HPLC	Taxi	82.7	5.5 × 10 <sup>6</sup>	-

- Lack of data

CR	HQ
<1 × 10 <sup>6</sup> inconsequential risk	<1 acceptable risk
1 × 10 <sup>6</sup> - 1 × 10 <sup>7</sup> uncertain risk	≥1 potential to result in adverse effects risk
≥1 × 10 <sup>7</sup> actionable risk	

### 3. Results

#### 3.1. The process of selecting articles

The detailed process of selecting studies is presented in Fig. 1. In total 1642 papers were obtained through systematic search in Scopus (N = 602), PubMed (N = 137), Web of Science (N = 585), Medline (N = 150), and Embase (N = 168) databases. After removing 427 duplicates, 1215 studies were screened according to their title and abstract. After the step of review, 1148 studies that did not meet the inclusion criteria were excluded at this stage, and the remaining 67 full texts were evaluated more specifically based on the inclusion/exclusion criteria and quality control. Further 24 articles were excluded from the review for the following reasons: 3 studies were review, 5 studies did not evaluate the health risk caused by exposure to indoor FA, 8 studies dealt with occupational exposure, 2 studies did not mention the concentration of FA in the indoor environment, 1 study used a method other than the USEPA method to assess health risk, 3 studies had a high-risk of bias, and access to the full text of 2 articles was not available (Fig. 1). In addition, 2 studies were also obtained by checking the reference list of selected articles. Finally, 45 studies with a low risk of bias (Q1 and Q2) were determined eligible for this review.

Distribution analysis of the place of origin of the studies included in this systematic review revealed that following countries investigated the human health risk of inhalation FA exposure: China (24 studies), Iran (3), South Korea (3), Japan, Mexico, Spain (2 in each country), Brazil, United states (California), Central Europe, Greece, Hong Kong, Indonesia, Portugal, Turkey, and Taiwan (1 in each country).

Based on the type all the articles included in this review were

classified into one of the 5 types of indoor environments, namely dwelling environment (Table 2), educational centers (Table 3), kindergartens (Table 4), vehicle cabins (Table 5), and other environments (Table 6).

#### 3.2. Characteristics of studies on FA exposure in dwelling environments

Of the 45 included in this study, 21 articles were identified to investigate FA concentrations in indoor dwelling environments, more specifically in the bedroom, living room, bathroom, and kitchen (Table 2). China was revealed as the country with the highest number of the studies on FA exposure in this indoor environment, with approximately 66% of the articles included in this study coming from this country. Other countries or regions with high research activity in this field were Spain, Mexico, Iran, Taiwan, and Hong Kong. The methods of indoor air sampling reported in the studies carried out in dwelling environments were active and passive. According to the investigations, the most common analyzer used to measure the concentration of FA in indoor air samples was High-Pressure Liquid Chromatography (HPLC). Other methods used in these studies to determine FA concentrations were PGM-6208 Portable Formaldehyde Analyzer, Gas Chromatography-Flame Ionization Detection (GC-FID), spectrophotometry, and Proton Transfer Reaction-Mass Spectrometry (PTR-MS) were used.

The results obtained from the included studies revealed the highest FA concentrations in residential kitchens in China, with concentrations from 157.14 µg/m<sup>3</sup> in the initial cooking to 189.28 µg/m<sup>3</sup> during the cooking process [15]. In addition, Chen et al. (2017) reported high levels of FA in the bedroom, living room, and kitchen [51]. The lowest FA



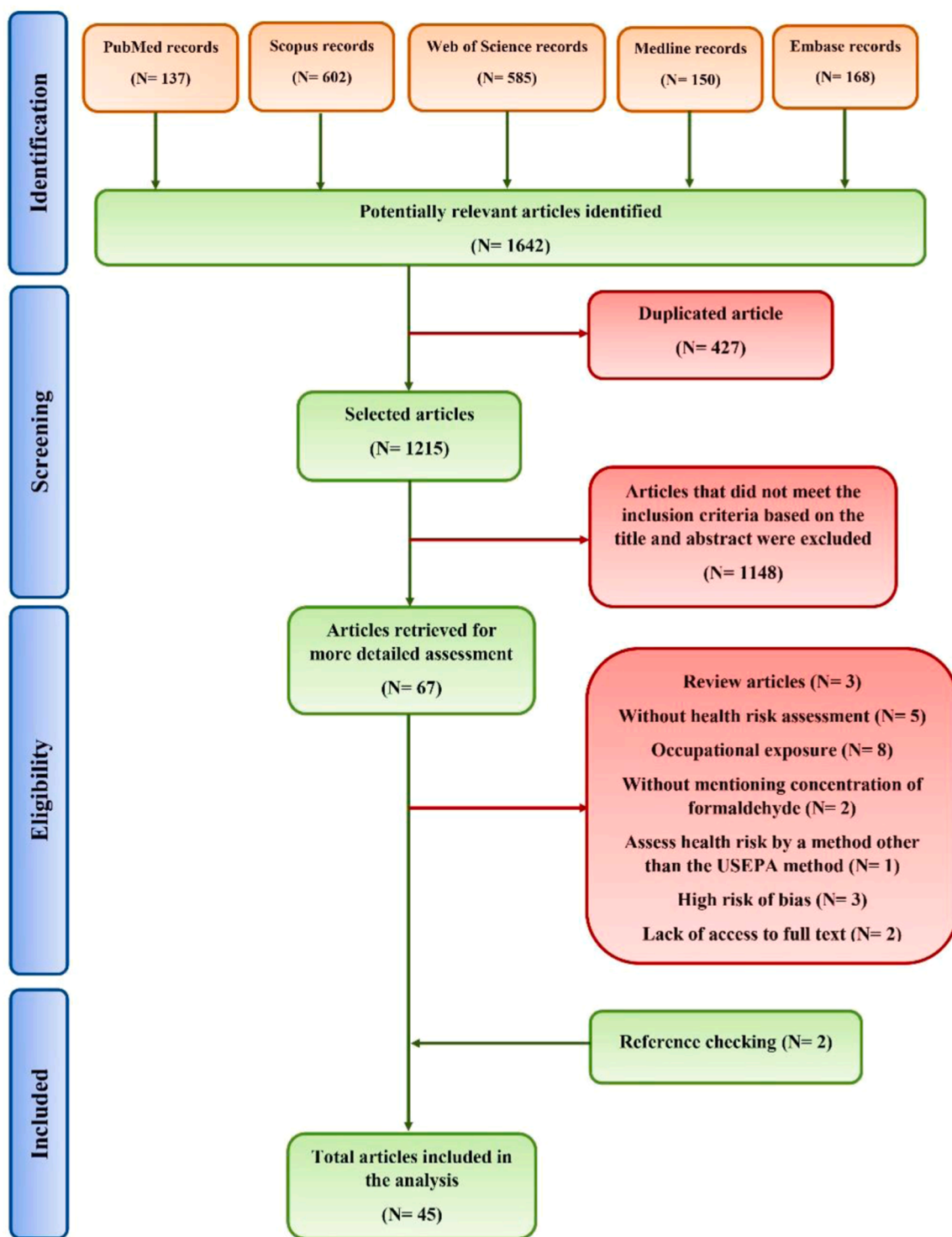


Fig. 1. PRISMA flow diagram of the literature search in this study.

carcinogenic risk values were at the acceptable level ( $CR < 1 \times 10^{-6}$ ). In addition, non-carcinogenic risk values were reported in 8 studies, of which HQ values exceeded the acceptable risk were reported by Fang et al. (2019) [57] with  $HQ = 2.7$ , Rovira et al. (2016) [58] with  $HQ = 3$ , and Lu Li et al. (2023) [59] with  $HQ = 214.2$  for < 2 years old children and  $HQ = 51.8$  for 2–6 years old children.

A comparison of the mean concentration of FA in dwelling environments according to different countries showed that China had the highest level of pollutant with  $61.49 \mu\text{g}/\text{m}^3$  (Fig. 2). This concentration

was higher than the values recommended by FDH for 8-hour respiratory exposure ( $50 \mu\text{g}/\text{m}^3$ ). Next, with the decreasing order of FA concentration, the following were reported: Mexico ( $42 \mu\text{g}/\text{m}^3$ ), Hong Kong ( $41 \mu\text{g}/\text{m}^3$ ), Spain ( $39.75 \mu\text{g}/\text{m}^3$ ), Iran ( $18 \mu\text{g}/\text{m}^3$ ), Taiwan ( $8.8 \mu\text{g}/\text{m}^3$ ), and Portugal ( $7.61 \mu\text{g}/\text{m}^3$ ).

In addition, the assessment of the average carcinogenic and non-carcinogenic risk caused by inhalation exposure to indoor FA in different countries indicated that the highest CR and HQ were observed in Mexico ( $CR = 3.29 \times 10^{-6}$ ) and Spain ( $HQ = 2.7$ ), respectively. These

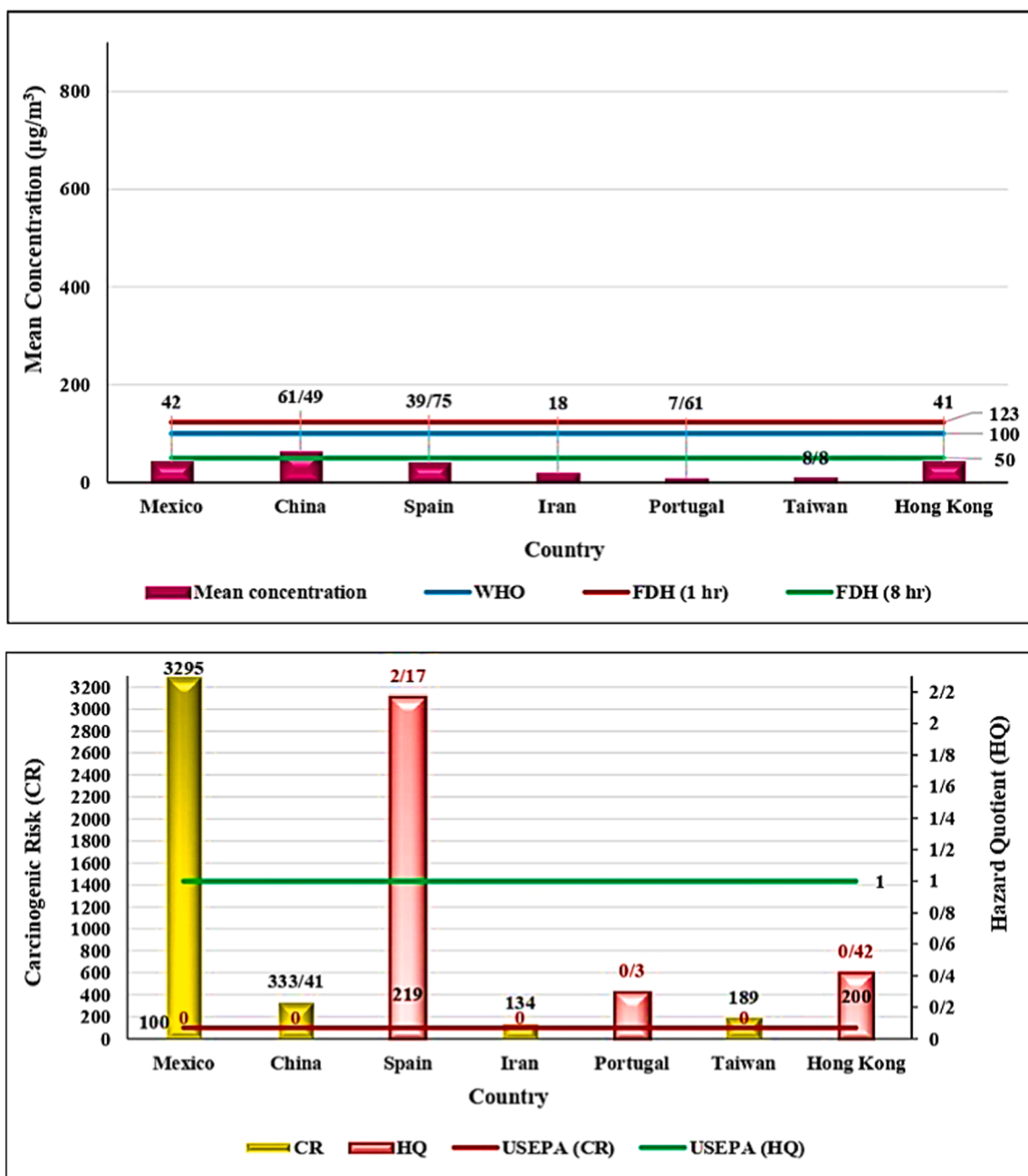


Fig. 2. Comparison of mean FA concentration, carcinogenic risk (CR), and non-carcinogenic risk (HQ) values due to respiratory exposure in dwelling environments; (CR is shown on a scale of  $\times 10^{-6}$ ; WHO – World Health Organization, FDA – Federal Department of Health of Canada USEPA – US Environmental Protection Agency).

values were above the limit recommended by the USEPA ( $CR < 1.00 \times 10^{-4}$  and  $HQ < 1.00$ ).

### 3.3. Characteristics of studies on FA exposure in educational centers

In the group of educational centers, 6 studies from this systematic review were included (Table 3). Regarding the country, these studies were carried out in China, Greece, Indonesia, Central Europe, and Mexico. In 2 studies FA concentrations were investigated in indoor spaces of universities [60,61], and in 4 studies in schools [62–65]. Active and passive methods were used for air sampling and FA concentrations in indoor air samples were analyzed using Portable Formaldehyde Analyzer, High Performance Liquid Chromatography (HPLC), and Liquid Chromatography with UV detection (LC-UV).

The lowest FA concentrations were reported in the study of García

et al. (2022) [61] with a content range from 2.53 to 4.41  $\mu\text{g}/\text{m}^3$  and the highest concentrations were reported by Li et al. (2008) [62] equal to 40  $\mu\text{g}/\text{m}^3$ . In these studies, FA concentrations were determined to not exceed the permissible value of FDH and the recommended values of WHO. In terms of carcinogenic risk, the calculated CR values were  $> 1 \times 10^{-6}$  indicating an uncertain/actionable risk carcinogenic risk of human exposure to FA in these spaces, except for the study of Kalimeri et al. (2016) in Greece [63] and Pakpahan et al. (2019) in Indonesia [64], were CR values indicated  $< 1 \times 10^{-6}$ . This was stated although the non-carcinogenic risk was  $< 1$  in all studies reporting HQ values.

The comparison of the mean levels of FA measured in educational centers of different countries and the carcinogenic and non-carcinogenic risk caused by inhalational exposure to it is shown in Fig. 3. Based on this figure, the highest average concentration ( $43.125 \mu\text{g}/\text{m}^3$ ) and the highest average CR ( $9.44 \times 10^{-5}$ ) were evaluated in China. In addition,

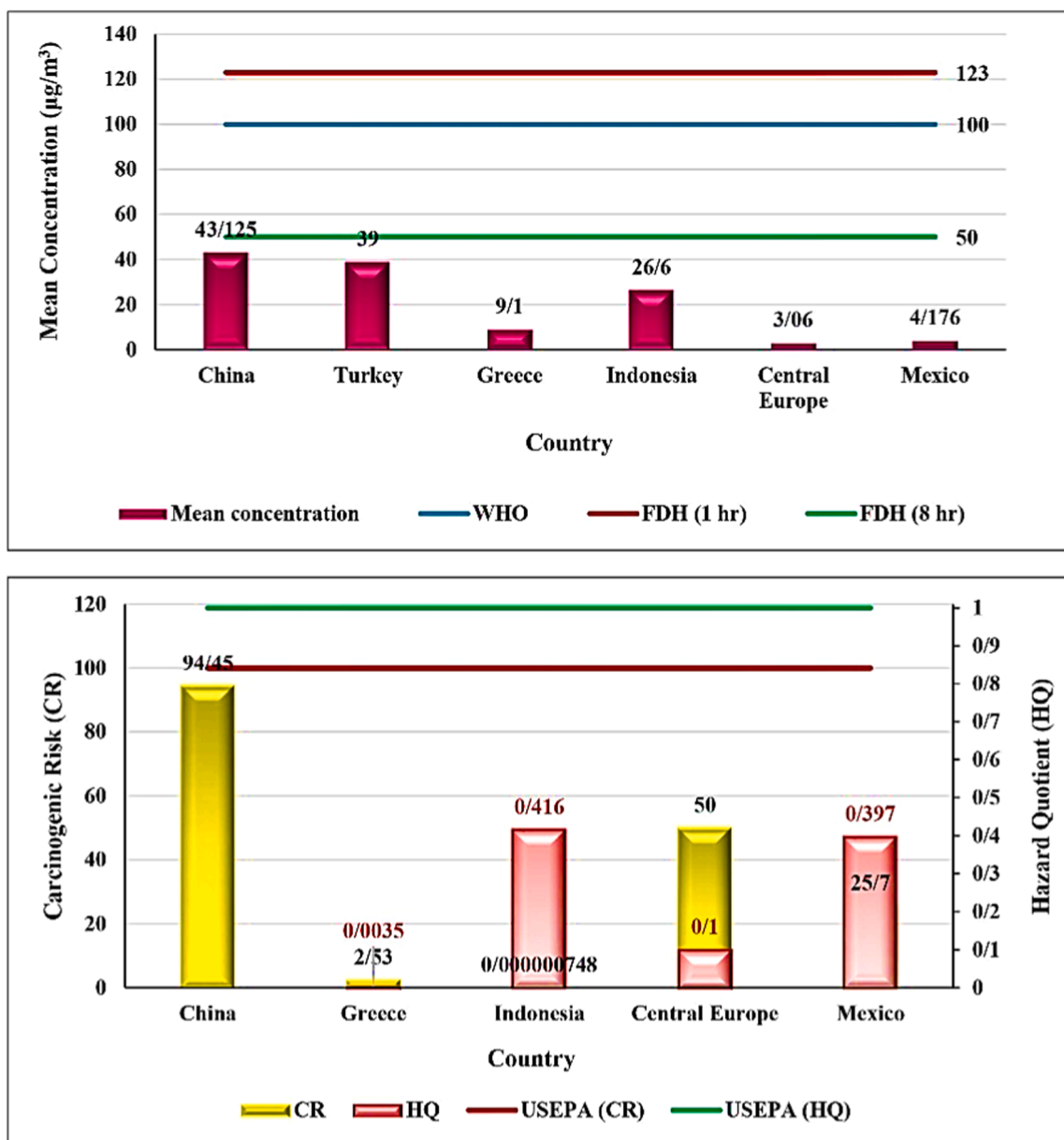


Fig. 3. Comparison of mean FA concentration, carcinogenic risk (CR), and non-carcinogenic risk (HQ) values due to respiratory exposure in educational centers; (CR is shown on a scale of  $\times 10^{-6}$ ; WHO – World Health Organization, FDA – Federal Department of Health of Canada USEPA – US Environmental Protection Agency).

the highest and lowest average non-carcinogenic risks were observed in Indonesia (HQ= 0.416) and Greece (HQ= 0.0035), respectively, and all these values are lower than the recommended limit.

### 3.4. Characteristics of studies on FA exposure in kindergartens

The concentration of FA in kindergartens and related carcinogenic and non-carcinogenic inhalational risk was investigated in 2 studies, in the following countries: China [66] and the northern states of California in the United States [67] (Table 4). In these studies, an active method of air sampling was used and FA concentrations were measured using High Performance Liquid Chromatography (HPLC).

The obtained results showed that the FA concentrations in investigated kindergartens ranged from  $10 \mu\text{g}/\text{m}^3$  to  $48 \mu\text{g}/\text{m}^3$  which was reported by Deng et al. (2016) [66]. Only in one case of the kindergarten in Turkey the determined FA concentration was above the permissible value of FDH ( $50 \mu\text{g}/\text{m}^3$  for 8-hour exposure). Carcinogenic risk values (CR) due to chronic exposure to FA were  $> 1 \times 10^{-6}$  (actionable risk) in

all the investigated spaces. Also, non-carcinogenic risk values (HQ) were at the acceptable level (HQ<1) in 4 out of 5 kindergartens studied by Deng et al. (2016) [66] and for children under 2 years old in the study of Bradman et al. (2017) [67].

Examining the mean concentrations, the CR and HQ values reported in the studies included in the kindergarten section showed that the levels of FA in China and the USA (Northern California) were 22 and  $18.9 \mu\text{g}/\text{m}^3$ , respectively, which was much lower than the limit recommended by WHO and FDH (Fig. 4). Generally, the HQ values calculated in both countries were beyond the limit recommended by the USEPA (HQ < 1.00), which indicates a potential non-carcinogenic risk in the case of chronic exposure. Also, CR was reported only in China ( $9.68 \times 10^{-5}$ ), which indicates the possible carcinogenic risk ( $1.00 \times 10^{-6} < \text{CR} < 1.00 \times 10^{-4}$ ).

### 3.5. Characteristics of studies on FA exposure in vehicle cabins

In 6 studies from the included to the review research, FA

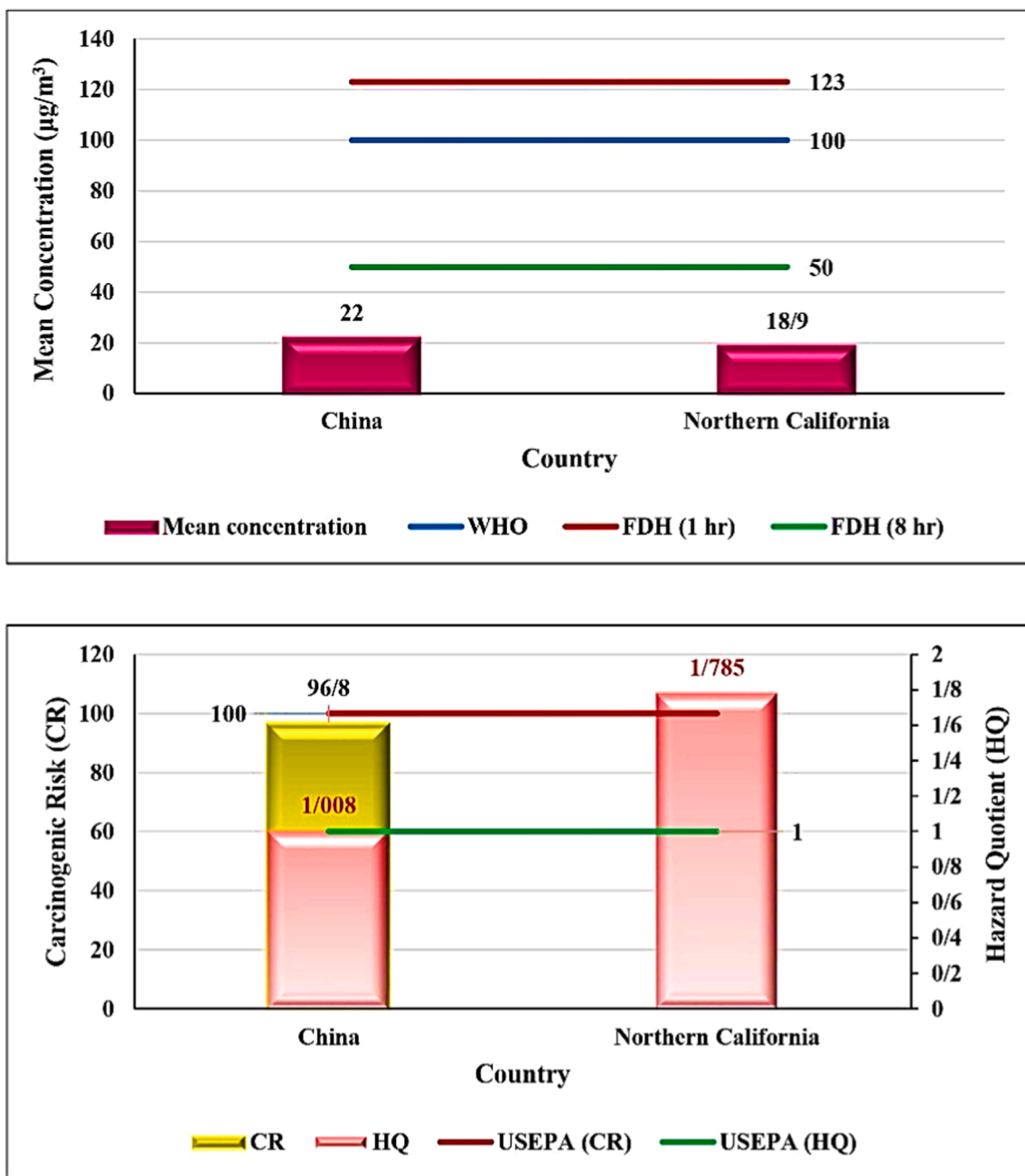


Fig. 4. Comparison of mean FA concentration, carcinogenic risk (CR), and non-carcinogenic risk (HQ) values due to respiratory exposure in kindergartens; (CR is shown on a scale of  $\times 10^{-6}$ ; WHO – World Health Organization, FDA – Federal Department of Health of Canada USEPA – US Environmental Protection Agency).

concentrations were determined in the vehicle cabins such as taxis, buses, subways, cars, and ships (Table 5). In these studies, all air samples were collected using active methods, and FA concentrations were measured using Phenol Reagent Spectrophotometry, High Performance Liquid Chromatography (HPLC), and Ultra-Performance Liquid Chromatography (UPLC) with a Photo-Diode Array (PDA) detector. The research on this type of indoor environment was performed in three countries: China [68–70], Japan [71], and South Korea [72,73].

The obtained results revealed that the lowest FA concentrations in vehicle cabins were observed in buses ( $16.2 \mu\text{g}/\text{m}^3$ ) [68] and the highest in shuttle buses ( $90.01 \mu\text{g}/\text{m}^3$ ) [73]. According to the research, in more than half of the studies FA concentrations exceeded the FDH permissible level of 8-hour exposure ( $50 \mu\text{g}/\text{m}^3$ ). However, considering an exposure time of 1 h or less, the FA concentrations did not exceed the WHO recommended value of  $100 \mu\text{g}/\text{m}^3$  for 30-minute exposure, as well as the

FDH permissible level of  $123 \mu\text{g}/\text{m}^3$ .

Despite that the lowest FA concentrations inside the vehicle cabins were within the permissible range, the calculated carcinogenic risk values indicated actionable risk in these studies. According to the non-carcinogenic risk values calculated in the study of Tokumura et al. (2016), it was revealed that during typical usage of the vehicles, HQ values were  $< 1$  indicating acceptable risk, however during an occupational usage of the HQ values were  $> 1$  indicating non acceptable risk [71].

According to Fig. 5, the highest average levels of FA in vehicle cabins were observed in China ( $48.19 \mu\text{g}/\text{m}^3$ ) and South Korea ( $46.65 \mu\text{g}/\text{m}^3$ ), respectively, which is lower than the limit recommended by WHO ( $100 \mu\text{g}/\text{m}^3$  for 30 min exposure) and FDH ( $123 \mu\text{g}/\text{m}^3$  for 1-hr exposure and  $50 \mu\text{g}/\text{m}^3$  for 8-hr exposure). Although the average concentration of FA in China was higher than in Korea and Japan, it had the

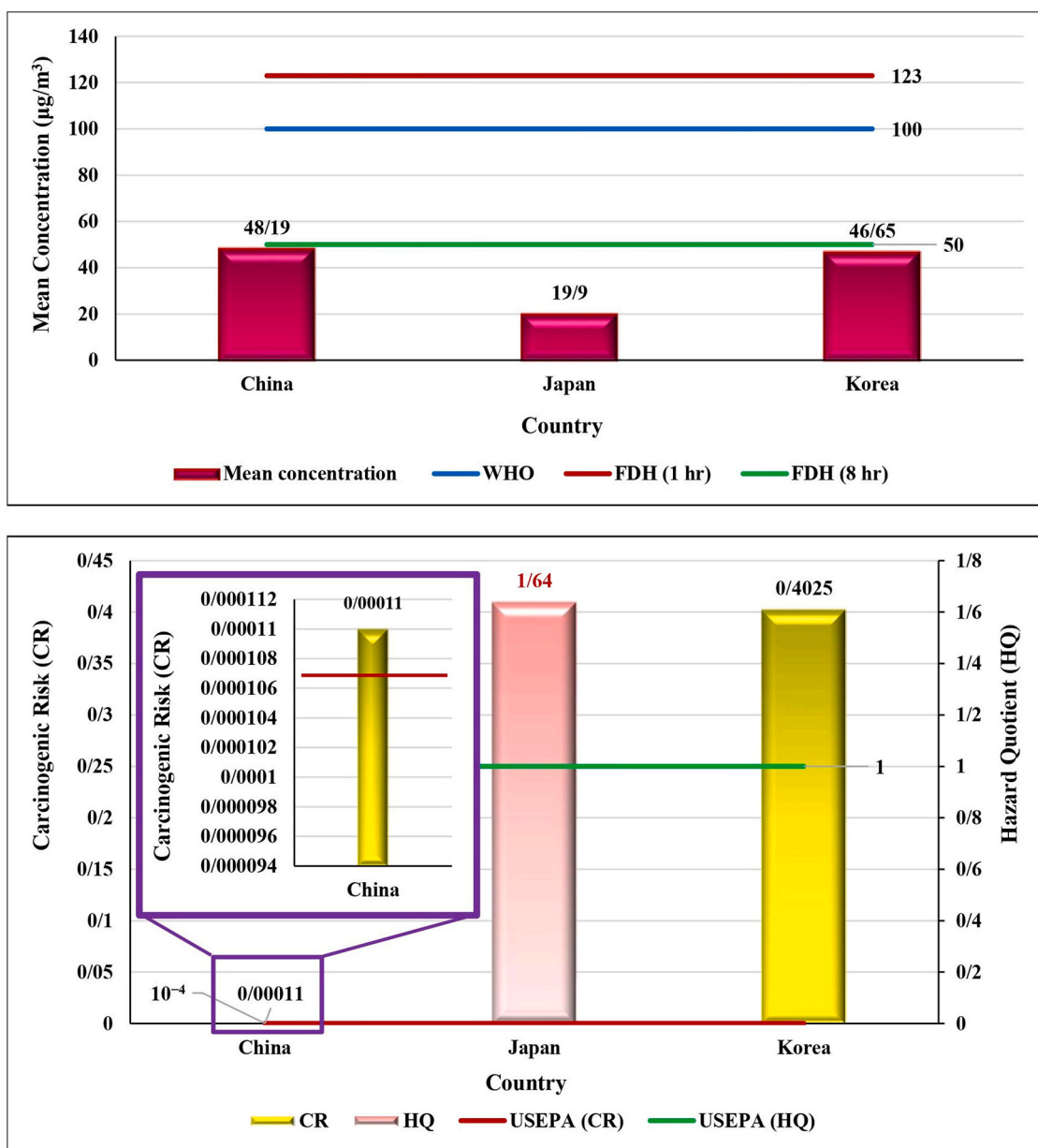


Fig. 5. Comparison of mean FA concentration, carcinogenic risk (CR), and non-carcinogenic risk (HQ) values due to respiratory exposure in vehicle cabins; (CR is shown on a scale of  $\times 10^{-6}$ ; WHO – World Health Organization, FDA – Federal Department of Health of Canada USEPA – US Environmental Protection Agency).

lowest risk of carcinogenesis ( $1.1 \times 10^{-4}$ ). The highest mean CR was also observed in South Korea with 0.4025, which is far above the permissible threshold recommended by the USEPA ( $CR < 1.00 \times 10^{-4}$ ).

### 3.6. Characteristics of studies on FA exposure in other indoor environments

From the articles selected in this systematic review, 12 studies were classified in this group of other indoor spaces. Among these indoor spaces the following environments were included: offices [74], hotels [75], shopping centers [76,77], cinemas [76], health and treatment facilities [78,79], libraries [80,81], vehicle stations [68,76], and water pipe cafés [12,82]. In these articles all indoor air samples were collected by an active method. Concentrations of FA were measured using High Performance Liquid Chromatography (HPLC), Phenol Reagent Spectrophotometry, and Gas Chromatography Mass Spectrometry (GC/MS). The highest number of research in this field was published in China (6 papers). Other countries of origin of the research on FA respiratory

exposure in indoor spaces were: Iran, Mexico, Brazil, South Korea, and Turkey (Table 6).

According to these investigations, the lowest FA concentrations were observed in a hospital in Brazil with levels from 1.98 to 24.8  $\mu\text{g}/\text{m}^3$  [79], while the highest FA concentrations were reported in water pipe cafés [82] with concentrations from 1620 to 1646  $\mu\text{g}/\text{m}^3$ . Concentrations of FA reported in all or part of the indoor air samples reported in the research of Won et al. (2021) [77], Masjedi et al. (2019) [82], Naddafi et al. (2019) [12], and Weng et al. (2009) [76] were above the WHO recommended value of 100  $\mu\text{g}/\text{m}^3$  for 30 min exposure, as well as the FDA permissible value of 123  $\mu\text{g}/\text{m}^3$  for 1 hr exposure.

Carcinogenic risk assessment was reported to be unacceptable as CR values were higher than  $1 \times 10^{-6}$  in the 12 studies, with a range from  $3.778 \times 10^{-6}$  to  $2.2 \times 10^{-3}$ . The highest CR value was reported for the furniture store in the study of Weng et al. (2009) [76] and indicated the potential carcinogenic risk for the exposed population. In addition, non-carcinogenic risk values calculated in water pipe cafés were at the unacceptable level according to the USEPA guidelines; HQ values in

these environments ranged from 2.6 to 25.4, except when water pipes and cigarettes were not used (HQ= 0.3–0.5) [82], and pathology department of primary hospitals in China (HQ= 1.07) [83].

The results of comparing the mean indoor FA concentration are shown in Fig. 6. Based on this, Iran was reported to have the highest levels of this pollutant among other countries and indoor environments with 347.16  $\mu\text{g}/\text{m}^3$ , which is about 3 times higher than the permissible values recommended by WHO (100  $\mu\text{g}/\text{m}^3$  for 30 min exposure) and FDH (123  $\mu\text{g}/\text{m}^3$  for 1-hr exposure and 50  $\mu\text{g}/\text{m}^3$  for 8-hr exposure). After China, South Korea had the highest average concentration reported with 104  $\mu\text{g}/\text{m}^3$ . In addition, the lowest average levels of FA were observed in Turkey and Brazil, respectively.

Also, the countries of Mexico, Iran, China and South Korea had CR  $> 1.00 \times 10^{-4}$ , which indicates the potential risk of carcinogenesis for people exposed during their lifetime. In addition, HQ  $> 1.00$  was reported in China (HQ= 1.3) and Iran (HQ= 4.65).

### 3.7. Results of meta-analysis

Indoor FA concentrations, CR and HQ values due to inhalation exposure to this pollutant were calculated based on different indoor environments (Fig. 7). Because only two studies were included in the section on kindergartens, it did not have the necessary conditions to enter the meta-analysis. In addition, considering that the HQ was only

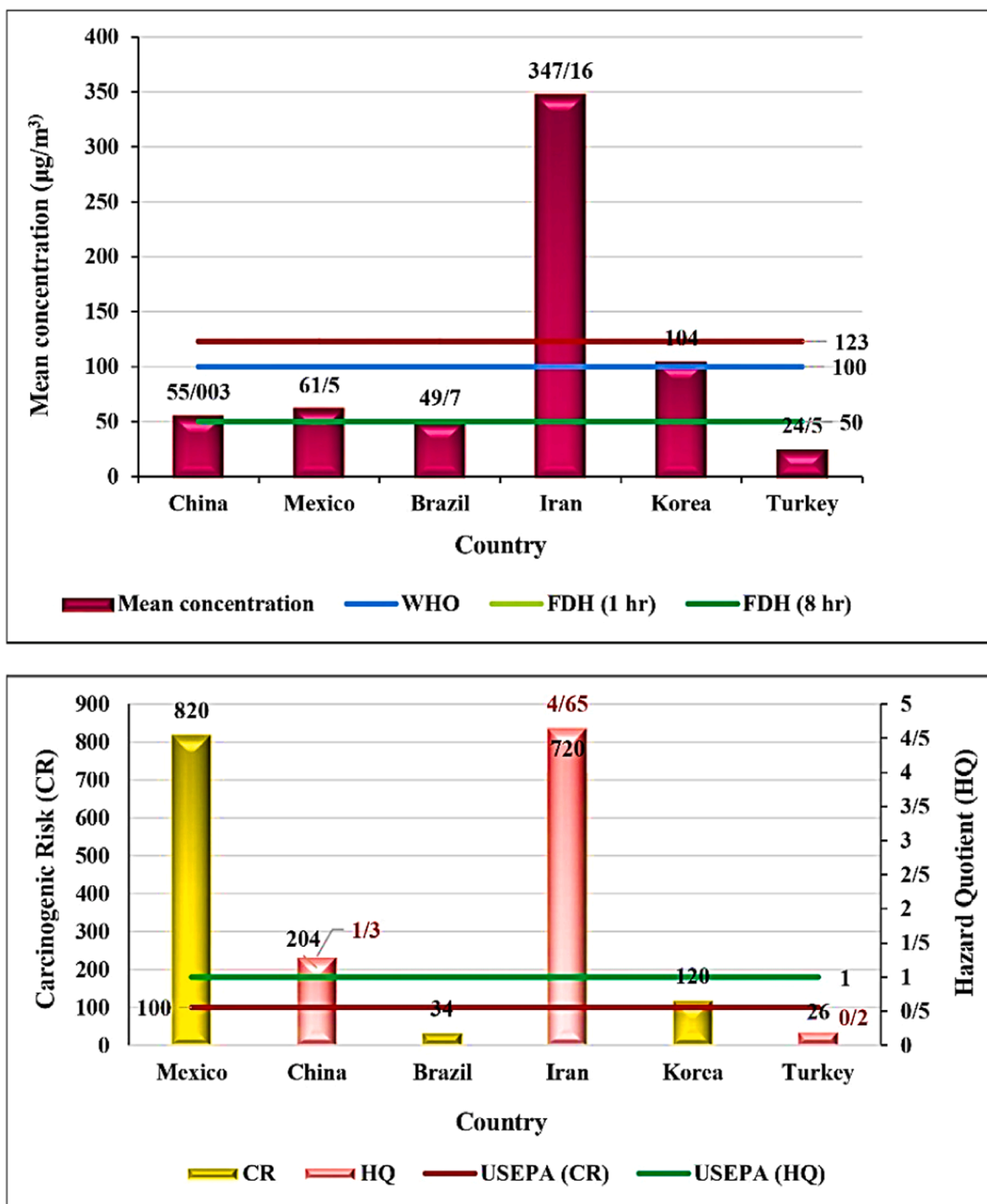


Fig. 6. Comparison of mean FA concentration, carcinogenic risk (CR), and non-carcinogenic risk (HQ) values due to respiratory exposure in other indoor spaces; (CR is shown on a scale of  $\times 10^{-6}$ ; WHO – World Health Organization, FDA – Federal Department of Health of Canada USEPA – US Environmental Protection Agency).

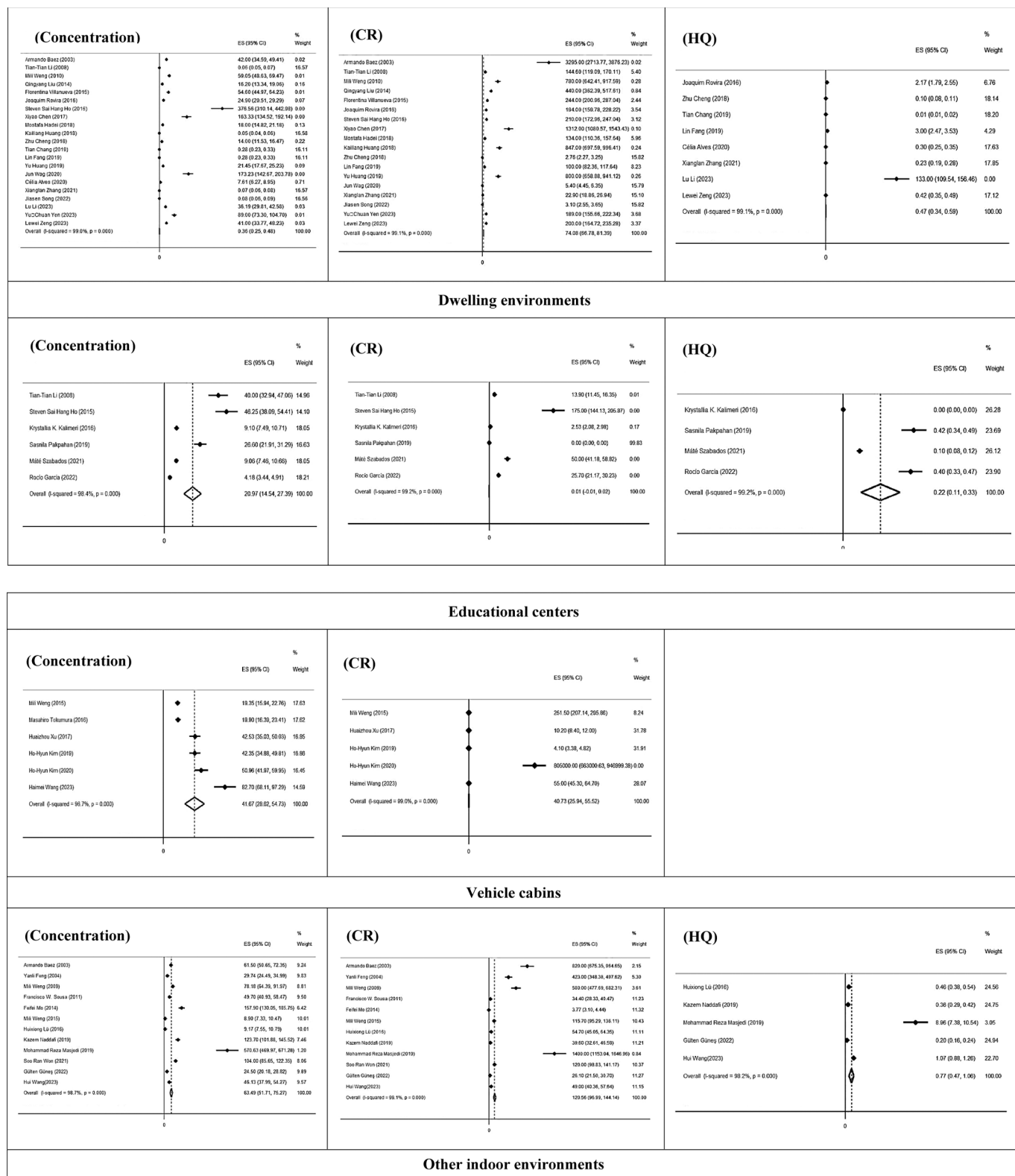


Fig. 7. FA concentrations, carcinogenic (CR) and non-carcinogenic (HQ) risk due to inhalation exposure in different indoor environments (CR is calculated on a scale of  $\times 10^{-6}$ ).

reported in the study of Tokumura et al. (2016), we were unable to calculate the meta-analysis for non-carcinogenic risk in the section related to vehicle cabins.

Based on this meta-analysis, the overall effect size for FA concentration in dwelling environments, educational centers, vehicle cabins

and other indoor environments includes 0.36 (0.25, 0.48), 20.97 (14.54, 27.39), 41.67 (28.62, 54.73) and 63.49 (51.71, 75.27), respectively. Carcinogenic risk due to inhalation exposure to FA was also calculated as follows: educational centers (0.01 (-0.01, 0.02)), vehicle cabins (40.73 (25.94, 55.52)), dwelling (74.08 (66.78, 81.39)) and other

environments (120.56 (96.99, 144.14)).

Also, ES calculated for non-carcinogenic risk included educational centers (0.22 (0.11, 0.33)), dwelling (0.47 (0.34, 0.59)) and other indoor environments (0.77 (0.47, 1.06)), respectively. The comparison of the results obtained in this meta-analysis showed that the calculated ES is higher in other indoor environments, including offices, hotels, shopping, cinemas, healthcare centers, libraries, vehicle stations, and water pipe cafes.

The results of the analysis of subgroups to investigate FA concentrations, CR and HQ values caused by exposure to this pollutant in different indoor environments are shown in Appendix A1-A4. The comparison of indoor FA concentration according to the income of different countries indicates that the highest levels of this pollutant are in educational centers and vehicle cabins in low- and middle-income countries, and dwelling environments and other domestic environments in high-income countries ( $p < 0.001$ ). According to the obtained results, the highest concentration is respectively related to other indoor environments in the Middle East (217.92 [92.75, 343.09]), vehicle cabins in East/Southeast Asia/Oceania (41.67 [28.62, 54.72]), educational centers in East/Southeast Asia/Oceania (37.27 [25.06, 49.49]) and dwelling environments in Europe (28.43 [8.16, 48.70]) ( $p < 0.001$ ). In addition, FA concentrations reported in studies related to in or before 2010 were significantly higher than in studies after 2010 ( $p < 0.001$ ).

Generally, the highest CR values due to inhalation exposure to FA were observed in all indoor environments in high-income countries. This is while LMICs have higher HQ in most indoor environments, except dwellings.

#### 4. Discussion

The present systematic review and meta-analysis retrieved published scientific evidence related to respiratory exposure to FA in indoor environments and evaluated the related carcinogenic and non-carcinogenic risk. To achieve this aim, selected studies were investigated in the following 5 types of indoor spaces according to the research space, namely dwelling environments, educational centers, kindergartens, vehicle cabins, and other indoor environments.

##### 4.1. Dwelling environments

The studies classified in this section included various residential environments, such as kitchen, living room, bedroom, and bathroom. According to the obtained results, the highest FA concentrations were reported in the residential kitchens in China, which were investigated in two modes: initial cooking (mean  $157.14 \mu\text{g}/\text{m}^3$ ) and cooking period (mean  $189.28 \mu\text{g}/\text{m}^3$ ) with the carcinogenic risk value equal to  $\text{CR} = 5.4 \times 10^{-6}$  [15]; which was consistent with the study results of Chen et al. (2017) [51]. In these studies, by examining the concentration of typical pollutants in the houses of the Wuhan University employees in China, it was concluded that the highest FA concentrations were stated in the kitchen ( $180 \mu\text{g}/\text{m}^3$ ), followed by the bedroom ( $170 \mu\text{g}/\text{m}^3$ ), and the living room ( $140 \mu\text{g}/\text{m}^3$ ). Despite the higher FA levels in the kitchen, in this space the lowest carcinogenic risk value ( $\text{CR} = 19.3 \times 10^{-5}$ ) was reported among other spaces sampled [51]. However, Song et al. (2022) [84] in their study reached different results; FA concentrations in residential buildings in cold regions of China were lower in kitchens, compared to bedrooms and living rooms, and as a result the carcinogenic risk was lower in kitchens with CR value equal to  $3.1 \times 10^{-6}$ . In these investigations, the highest FA concentration was determined in the bedroom equal to  $0.0816 \mu\text{g}/\text{m}^3$  [84]. Also, Weng et al. (2010) in their studies obtained similar results [54]: FA concentrations in the bedroom were 1.4 times higher than in the living room and kitchen [54]. To sum up this section, the FA concentrations determined in residential units and the associated carcinogenic risk values were very diverse and ranged from 0.014 to  $157.14 \mu\text{g}/\text{m}^3$  in the case of FA concentrations and from  $3.1 \times 10^{-6}$  -  $1.3 \times 10^{-3}$  for CR values. The reason for this

variability in the results can be attributed to diverse factors such as exposure duration, type of furniture and decoration, type of indoor activity, cooking style, and age of buildings.

The results of the indoor air quality assessment in high-rise residential buildings in Bangkok showed that the age of the buildings has a strong correlation with the concentration of VOCs ( $p$ -value  $< 0.0001$ ), so the levels of this pollutant in old buildings, at the 95% confidence level, are significantly lower than in newly constructed buildings [85]. Also, a recent study proved that VOC emission rates from building materials have an inverse relationship with the age of the buildings [86]. Also, Derbez et al. (2014) in their study concluded that the indoor FA concentration decreases to a stable level 3 years after the construction of a newly constructed building [87].

In addition to the factors mentioned and according to the studies, the main sources of carbonyls release include furniture and building materials (44.5%), household products (17.3%), smoking (14.5%), paints and adhesives (11.9%), and cooking (9.8%) [88]. These observations were consistent with the results obtained from other studies [6,7]. In addition, other human activities that play an effective role in indoor air pollution with FA were reported to be saunas, cleaning, indoor decoration, and equipment functions, such as air purifiers, biomass fuels, biogenic emissions conversion, and cooking can also play an effective role in indoor air pollution with FA [13,89,90]. The results obtained from the investigations on the role of cooking in the indoor air emissions in China showed that cooking processes can generate large quantities of VOCs, Polycyclic Aromatic Hydrocarbons (PAHs), and inhalable particles [91], which were consistent with those reported by Wang et al. (2020) [15]. In these studies, Wang et al. (2020) reported that higher FA concentrations during the cooking period compared to the initial cooking [15]. In addition, the research revealed that the amount of FA emitted can differ depending on the type of cooking method. Accordingly, types of high temperature frying, such as stir-frying, pan-frying, and deep-frying, can emit more FA during the cooking process [92,93].

The results of the analysis of the subgroup of dwelling environments indicated that the concentrations of FA, carcinogenic risk (CR), and non-carcinogenic risk (HQ) values caused by exposure to this pollutant are significantly higher in high-income countries (in this study, European countries), than in low- and middle-income ones ( $p < 0.001$ ). The use of various decorations and furniture, spending the most time indoors, smoking, and cooking fried foods at high temperatures may be the main reasons for these results.

To summarize, in more than 80% of the samples analyzed in the group of dwelling environments FA concentrations were much lower than the WHO recommended limit value of  $0.1 \text{ mg}/\text{m}^3$ , however, it does not necessarily mean that the risk value due to inhalation exposure to FA was acceptable. As shown in Table 2, CR values were  $> 1 \times 10^{-6}$  in the included studies, which indicated the actionable carcinogenic risk. One of the effective factors affecting the risk value was the duration of exposure to FA. This was supported by the Kumar's study (2014) [94], in which the results showed that the risk was higher for female adults due to inhalation exposure to indoor VOCs, than for other household residents, including children [94]. The explanation for this can be related to the fact that housewives spend most of their time in home environments performing activities such as cooking, resulting in the chronic exposure to different levels of FA.

##### 4.2. Educational centers

The studies grouped in educational center environments were divided into two internal groups: universities [60,61] and schools [62–65]. The analysis of FA concentrations in educational facilities showed that the concentrations of this pollutant varied from 2.53 to  $40 \mu\text{g}/\text{m}^3$ , and were lower than the WHO recommended limit value of  $100 \mu\text{g}/\text{m}^3$  and the FDH permissible limit value of  $50 \mu\text{g}/\text{m}^3$  for 8-hour exposure. The results of the study of Pakpahan et al. (2019) [64] showed that the FA concentrations in three schools in Depok, Indonesia were in

the range from 24.56 to 30.7  $\mu\text{g}/\text{m}^3$  and did not exceed the WHO recommended limit value and the FDH permissible limit value. Also, the highest carcinogenic (CR) and non-carcinogenic (HQ) risk values in the study of Pakpahan et al. (2019) [64] were  $8.64 \times 10^{-13}$  and  $1.49 \times 10^{-1}$ , respectively, which revealed the acceptable both carcinogenic and non-carcinogenic risk. Kalimeri et al. (2016) in their studies obtained similar results on the indoor air quality of schools in Greece [63]. Although FA levels in the study of Kalimeri et al. (2016) [63] were much lower than in the study of Pakpahan et al. (2019) [64], the calculated carcinogenic and non-carcinogenic risk values in Greek schools were higher than those of the Indonesian schools [63]. Despite low FA concentrations in the central Europe primary schools (9.06  $\mu\text{g}/\text{m}^3$ ), the carcinogenic risk was higher than acceptable (in the range between  $10^{-4}$ – $10^{-6}$ ) [65]. The non-carcinogenic risk values were  $< 1$ , indicating the acceptable risk of possibility of developing non-carcinogenic diseases due to chronic exposure to FA in these schools [65].

The indoor air quality in educational facilities, especially schools, is crucial due to the long exposure of a large number of children and adolescents. This became a public health concern due to the fact that this age group inhales a larger volume of air in proportion to their body weight than adults. Therefore, exposure to high levels of pollutants can seriously damage children's health [63,95,96] as their systems as central nervous, respiratory, reproductive, digestive, and immunological systems did not yet reach the full maturity yet, making children more vulnerable due to the exposure to chemicals [97,98]. Inadequate classroom air quality can cause several side effects, such as rhinitis, asthma, fatigue, headache, and a drop in student performance [99–101]. This phenomenon can be compounded in the case of old, poorly designed and built, poorly fitted out, and weakly ventilated classrooms.

According to the results obtained from the subgroup analysis, educational centers located in developing countries and LMICs have higher levels of indoor FA and non-carcinogenic risk due to chronic exposure to this pollutant. The age of buildings, inadequate ventilation systems in classrooms, overcrowding, the use of wood and plywood in the furniture construction, proximity to the main roads, pollutant movements from the outside indoors, vapors from laboratories absent in fume hoods, and various art courses are among the most important sources of air pollutants, especially FA, in the educational centers of these countries. [102,103].

Kalimeri et al. (2016) [63] in their study on FA levels in three public primary schools in Kozani, Greece, during the summer and winter seasons concluded that the average concentration of this pollutant was 3.55 times higher in summer than in winter. These results were consistent with the study of García et al. (2022) [61]. Investigations on FA concentrations in the indoor air of three universities in the Mexico City showed the decreasing FA contents as follows: spring (2.53  $\mu\text{g}/\text{m}^3$ )  $<$  fall (4.41  $\mu\text{g}/\text{m}^3$ )  $<$  summer (5.59  $\mu\text{g}/\text{m}^3$ ) [61]. These studies indicated the effective role of temperature in FA release [104]. Based on observations, a 10 °C change in the air temperature causes an increase in FA concentrations from 1.9 to 3.5 times [105]. Wang et al. (2022) in a review study showed the role of various factors in VOC/SVOC emission, such as FA. The results of this review proved that the initial emissible concentration (C0) and the gas-phase SVOC concentration adjacent to the material surface (y0) change depending on environmental conditions, especially temperature. By collecting the results and theories of other researchers, including statistical physics theory [106], they confirmed the existence of a correlation between C0 (VOCs) and temperature.

In summary, from the analysis of the studies included in the environments of educational centers, the most favorable situation was revealed compared to other indoor environments investigated in this review. The range of carcinogenic risk values reported due to FA concentrations in schools and universities ranged from  $8.64 \times 10^{-13}$  to  $2.26 \times 10^{-4}$ . Only the study of Hang Ho et al. (2015) reported higher CR values in three types of longings on the university campus in Mainland

China, namely faculty apartments (CR=  $1.85 \times 10^{-4}$ ), student dormitories (CR=  $1.26 \times 10^{-4}$ ), and safeguard hostels (CR=  $2.15 \times 10^{-4}$ ) [60]. The reason for this situation could be overcrowding, carrying out various laboratory activities, and proximity to the main traffic roads in the city.

#### 4.3. Kindergartens

The examination of studies grouped as indoor environments in kindergartens showed that the lowest FA concentrations were stated at the level of 10  $\mu\text{g}/\text{m}^3$  and the highest at the level of 76  $\mu\text{g}/\text{m}^3$  with the FDH permissible limit for 8 h of FA inhalational exposure equal to 50  $\mu\text{g}/\text{m}^3$  [34], and they were also higher compared to FA concentrations determined in the environments of schools and universities. The explanation of these elevated concentrations in the kindergartens could be related with the special decorations of kindergartens, including various materials inside the buildings to make the environment friendly for children, for example various toys and artistic activities.

The European Union Toy Safety Directive and its amendment (Commission Directive EU 1929/2019) as aims to ensure children's safety introduced certain limit values for some chemicals used in materials for toys productions [107]. This guideline provides test methods and migration limits for FA, permissible contents, and release rate of FA in various types of toys, as well as calls for further FA limitations in the use of FA in children's toys. Based on the directive, the following limit values for FA concentrations were determined for the ingredients of these children's products: textiles, leather, and paper 30 mg/kg, water-based materials 10 mg/kg, polymeric materials 1.5 mg/L (migration limit), and resin-bonded wood 0.1 ml/m<sup>3</sup> (emission limit). Thus, the different types, ages, and combinations of materials used in toys production result in the significant differences in the FA emissions from toys.

Despite the limitations of using FA in toys, FA emissions can come from various sources and therefore increase the carcinogenic and non-carcinogenic risk due to FA. The results of the study of Sofuoglu et al. (2011) [108] on FA exposure in kindergartens in Izmir, Turkey showed that for almost half of the investigated population carcinogenic risk values were  $> 1 \times 10^{-5}$  and they were even higher than risk values for FA exposure in schools of the same city ( $p = 0.018$ ). These results were consistent with the study conducted in Chinese kindergartens [66]. In addition, non-carcinogenic (HQ) values  $> 1$  reported for the age group of children from 2 to 6 years old in Northern California kindergartens also indicated a high non-carcinogenic risk for children [67], which was consistent with the results of the study of Deng et al. (2016) [66]. These results revealed the alarming FA concentrations in kindergartens and the possibility of related serious side effects, including asthma, decreased lung function, inflammation, and airway obstruction in children [100, 109].

#### 4.4. Vehicle cabins

According to the results obtained from the studies grouped in the indoor environments of vehicle cabins, FA concentrations in vehicle cabins of vehicles varied from 16.2 to 90.01  $\mu\text{g}/\text{m}^3$  and carcinogenic risk values were evaluated  $> 1 \times 10^{-6}$  in most of these studies. Kim et al. (2019) [73] in their studies of FA concentrations in taxi and ship cabins in South Korea reported that on average FA concentrations in ship cabins were about 2.5 times higher than in taxi cabins, and this difference in FA concentration increased in the summer season. Despite the higher FA concentrations in ship cabins, the calculated carcinogenic risk values for the taxi cabins (CR= $7.00 \times 10^{-6}$ ) were higher than for ship cabins, which could be explained by the fact that the number of times that taxis are used (exposure frequency) is higher than in the case of ships [73]. These results were consistent with a cross-sectional study conducted in China [68], which results showed that FA concentration in taxi cabins (mean 22.5  $\mu\text{g}/\text{m}^3$ ) were higher than in buses (mean 16.2  $\mu\text{g}/\text{m}^3$ ) and

that related carcinogenic risk was higher in taxis ( $CR=2.925 \times 10^{-4}$ ) than in buses ( $CR=2.106 \times 10^{-4}$ ), posing a long-term health threat to taxi drivers and passengers [68].

The concentration of FA in the vehicle cabins can be affected by a variety of factors, such as vehicle maintenance conditions, fuel consumption, exhaust smoke leakage, ventilation conditions, cabin materials, temperature, and relative humidity of the environment [110–112]. Xiong et al. (2015) [113] in their study revealed that the increasing temperature inside the cabin from 29 °C to 35 °C caused an increase in FA concentrations from the concentration range of 100.6–115.7  $\mu\text{g}/\text{m}^3$  to range of 172.8–251.6  $\mu\text{g}/\text{m}^3$  [113]. The explanation for this phenomenon could be related to the overcrowding of the vehicles, especially in public transportation, inadequate ventilation in the vehicle cabins, and an increase in temperature. Studies have shown that the release of FA in car cabins with leather decorations was 1.42 times higher than in cars with fabric decorations [110]. In addition, the interior materials of the cabin of younger vehicles can also be considered as a potential source of aldehydes, especially FA. A cross-sectional study in China proved that the highest FA levels were observed in bus cabins during the first 0–15 days after leaving the assembly line [114].

The analysis of the results included in this section of the review indicated that the occupational use of cars, compared to typical use, can increase the non-carcinogenic risk caused by inhalation exposure to FA by 1.5–4.2 times, increasing it to the unacceptable level [71]. Also, the carcinogenic risk reported in these studies indicated the unacceptable values in vehicles. Among the most important reasons for the increase in carcinogenic and non-carcinogenic risk in the duration of exposure in vehicle cabins, higher fuel consumption, traffic on crowded streets with high levels of pollutants, and overcrowding in public vehicles were mentioned.

In addition, the consumption of low-quality fossil fuels, the use of low-quality raw materials in cabin furniture, the lack of use of new technologies in vehicle construction of, and inadequate ventilation can also play an effective role in exposure to significant levels of FA. This can increase the risk of carcinogenesis and non-carcinogenesis caused by exposure to this pollutant in the cabin of vehicles in low- and middle-income countries (Appendix A3).

#### 4.5. Other indoor environments

In this section, studies from the 8 types of indoor environments were classified, namely offices [74], hotels [75], shops [76,77], cinemas [76], health and treatment centers [78,79], libraries [80,81], vehicle stations [68,76], and water pipe cafés [12,82]. According to the results obtained from these selected studies, the highest FA concentrations were observed in water pipe cafés [82]. Masjedi et al. (2019) [82] in their studies on FA concentrations under 4 different conditions in water pipe cafés revealed that FA concentrations were the highest (mean 1620  $\mu\text{g}/\text{m}^3$ ) on weekends and when water pipes and cigarettes were used simultaneously indoors, as compared to the conditions when water pipes or cigarettes were used separately. Similarly, under non-smoking conditions, measured FA concentrations were from 46 to 57  $\mu\text{g}/\text{m}^3$  [82]. In addition, Naddafi et al. (2019) reported FA concentrations at the level of 123.7  $\mu\text{g}/\text{m}^3$  in water pipe cafés in the Ardabil metropolis, Iran [12]. Although the concentration was much lower than in the study of Masjedi et al. (2019), it still exceeded the WHO recommended limit value of 100  $\mu\text{g}/\text{m}^3$  for 30 min exposure and the FDH permissible limit value of 123  $\mu\text{g}/\text{m}^3$  for 1-hour exposure. The results of this comparison were consistent with the results of the study of Shihadeh et al. (2012) [115]. Among the main explanations of these variations in the FA concentrations difference in the tobacco type, the environmental conditions of the cafes, such as the type of materials used, the temperature and relative humidity of the environment, the type of ventilation system, the speed of the airflow, the area of the cafe and the number of customers, and the state of the heating system (on/off) are mentioned.

The investigations showed that 45.45% of the included studies

reported unacceptable carcinogenic risk ( $CR > 1 \times 10^{-4}$ ) for offices, hotels, cinemas, and bus stations. For other indoor environments in this section CR values indicated uncertain risk level ( $1.00 \times 10^{-6} < CR < 1.00 \times 10^{-4}$ ). Although the FA concentrations in these environments were much lower than in water pipe cafés, several factors such as people's age, body weight, exposure frequency, and exposure duration were basic parameters in evaluating CR values [36,116]. The analysis of the results of the selected studies in this section showed that in addition to water pipe cafés, all types of shopping also had significant FA concentrations and carcinogenic risk values as compared to other indoor environments. The results of the study by Weng et al. (2009) showed that furniture stores with the mean FA concentrations of 165.4  $\mu\text{g}/\text{m}^3$  and shopping centers with the mean FA concentration of 124.8  $\mu\text{g}/\text{m}^3$  had the highest level of this pollutant compared to railway stations (mean FA concentration 15.7  $\mu\text{g}/\text{m}^3$ ), bus stations (16.57  $\mu\text{g}/\text{m}^3$ ), supermarkets (64.5  $\mu\text{g}/\text{m}^3$ ), and cinemas (82.1  $\mu\text{g}/\text{m}^3$ ) [76]. Due to the high FA level in these shopping malls, the carcinogenic risk (CR) value exceeded  $1 \times 10^{-3}$ , indicating an unacceptable carcinogenic risk [76]. Analysis of the VOC concentrations in underground shopping districts in South Korea showed that the FA concentrations in cafés, clothing stores, electronic products, and nail shops exceeded the WHO recommended limit value of 100  $\mu\text{g}/\text{m}^3$  for 30 min exposure and the FDH permissible limit value of 123  $\mu\text{g}/\text{m}^3$  for 1-hr exposure [77]. As factors increasing the carcinogenic risk due to exposure of the large number of customers in other types of environments during the day, materials used in the buildings, decorations and shelving, sale of a variety of leather types, fabric and wood products, cleaning, and insufficient ventilation are mentioned as effective.

Based on the analyses performed in the subgroup related to other indoor environments, it was found that indoor FA concentrations and CR values due to exposure to this pollutant were higher in high-income countries than in low- and middle-income countries. The reason for this may be the variety of products related to furniture and decoration, crowding, high consumption of products related to cleaning, glue, paint, and the quality of raw materials.

#### 4.6. Environmental controls on air quality conditions

Two main sets of environmental controls were identified that influence air quality conditions in indoor settings, including the release and concentration of pollutants such as FA. These main controls were (1) ambient environmental conditions related to the climate and atmosphere within the enclosed indoor space, and (2) elements of the built and human environments that make up that indoor space. Both components in combination influence air circulation dynamics and resultant air quality, which is then manifested through carcinogenic and non-carcinogenic risk.

The review of the literature highlighted that climatic and atmospheric conditions, such as the role of seasonal changes in temperature and relative humidity, can give rise to increased health risk. It also showed that these conditions can be amplified in situations where air circulation is poor or restricted, and this may arise with poor building design or ventilation systems. In addition, many studies show how climatic and atmospheric conditions within buildings can negatively impact on respiratory and other health indicators. This means that climatic and atmospheric conditions alone are not a simple function of regional ambient climate but can also be influenced by the built environment and by effective environmental management of indoor spaces.

The review also highlighted that air pollution is closely linked to building materials and construction standards, furnishing and cover materials, as well as types of human activities undertaken in these indoor spaces (i.e., cooking, painting). Although there are guidelines today for certain materials and products used in indoor domestic and public spaces today, their fixtures and fittings may have been in place for decades and therefore may not be compliant with today's standards. Research has shown that the formaldehyde release rate from materials

decreases with time. However, it is important to note that when old furniture is used or when it is in old indoor environments where there were no restrictions on the use of formaldehyde during the manufacturing process, it may pose a higher risk value.

The combination of these major environmental controls means that both elements should be considered when seeking to explain and interpret the values of FA or other air pollutants in indoor environments. It should be noted that 'inventories' of the contents of indoor spaces are not made when measurements of air pollutants are taken, and this is a key limitation of almost all studies discussed in this review. Thus, reporting only the levels of certain pollutants, such as FA, is no longer enough if the underlying causes are not also examined.

#### 4.7. Future research directions

The analysis presented in this systematic review and meta-analysis highlights the types of indoor environments investigated in previous studies, their results, and limitations. Based on this analysis, some emerging trends and directions of future research were identified. Much of the research presented focused on active or passive measurements *in situ* rather than on understanding temporal or spatial patterns or linking pollutant values to certain causal factors. Consideration of other sources of air pollutants, such as room furnishings, fabrics and carpets, and paint/wall and floor coverings, are also needed. More effective modeling of air flow and pollutant transport within enclosed spaces should be used to help explain differences in risk values between different rooms in domestic dwellings, or with the distance from pollutant sources such as roads. Consideration of the role of building design and manufacture in pollution emission, particularly in public spaces, should be undertaken, as thus this falls within the remit of public health.

Under climate change, increased temperatures, especially in the summer season, can lead to increased photochemical and particulate air pollution, especially under lower rainfall conditions. These effects of climate change may also be worse in urban areas under the urban heat island effect. Building design can lead to poor indoor air quality where the size of dwellings (houses, apartments) and the rooms within them become smaller over time and where existing buildings are retrofitted for dwelling use. There is increasing research concern with sustainable building design and low-energy and self-regulating (passive) heating/cooling systems within buildings, which can lead to more healthy environmental conditions within indoor environments. However, the relationship of sustainable design to indoor air pollution has not been examined.

Any existing underlying conditions in the human population that may make them more susceptible to the health effects of air pollution should also be considered. This includes the amplifying effects of poor education, healthcare, nutrition, mental health, body mass, and physical activity. This means that CR values may be related to more than just air pollutants alone, and thus air pollution should be considered as part of a portfolio of causal factors influencing public health at both very small (domestic rooms) and very large (global) spatial scales.

## 5. Conclusions

The results of the presented systematic review and meta-analysis revealed that the concentration of FA in most of the indoor environments investigated were lower than the WHO recommended limit and the FDH permissible level. The highest FA concentrations were reported

in water pipes cafes, and the lowest FA concentrations were reported in dwelling environments. In most of the investigated studies, an unacceptable carcinogenic risk values for residents and employees were reported. Therefore, due to the evidence of FA carcinogenicity and adverse health effects caused by the FA exposure to different age groups, especially children, it is very important to monitor indoor air quality. Adopting strict measures to replace FA with technically similar materials but less hazardous, using efficient air conditioning systems, especially in the cold seasons of the year, changing the cooking style, using healthy cooking methods, and cessation of using biomass fuel inside homes are recommended to improve indoor air quality and reduce FA concentrations. Considering the biological conditions of children and their higher vulnerability during exposure to inhaled pollutants, continuous monitoring of air quality in schools and kindergartens should be on the agenda of public health organizations.

## Environmental implication

Indoor formaldehyde exposure increased due to interior decorations and chemical products, and its carcinogenicity and mutagenicity was confirmed by IARC. However, not enough actions have been taken by governments and industry to reduce formaldehyde emissions and improve the environmental performance of their products. This study assesses indoor formaldehyde levels worldwide and associated health risks through a systematic presentation of data available in 5 valid databases. The findings can play a crucial role in developing strategies to control and reduce formaldehyde release in indoor environments, especially schools and kindergartens, before the adverse effects of exposure to this pollutant are encountered.

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## CRediT authorship contribution statement

**Amir Hossein Khoshakhlagh:** Writing – review & editing, Validation, Supervision, Software, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Safiye Ghobakhloo:** Writing – review & editing, Software, Methodology, Formal analysis, Data curation. **Mahdiyeh Mohammadzadeh:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Data curation, Conceptualization, Formal analysis, Investigation, Project administration. **Agnieszka Gruszecka-Kosowska:** Conceptualization, Investigation, Validation, Writing – review & editing. **Hefa Cheng:** Validation, Investigation, Conceptualization, Writing – review & editing. **Jasper Knight:** Writing – review & editing.

## Declaration of Competing Interest

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

## Data Availability

Data will be made available on request.

## Appendix A1. Results of subgroup analysis for the FA variables in dwelling environments section

Variable	Subgroup analysis						
	Subgroup	Category (number of studies)	Pooled value [95% CI]	I <sup>2</sup> (%)	Q statistic (df)	p of heterogeneity	
Concentration	Income level	High income (4)	31.61 [12.74, 50.47]	98.6	3	< 0.001	
		Low and Middle Income (17)	0.24 [0.14, 0.34]	98.9	16	< 0.001	
	Region	Europe (3)	28.43 [8.16, 48.70]	98.6	2	< 0.001	
		East /Southeast Asia/Oceania (16)	0.21 [0.12, 0.31]	98.9	15	< 0.001	
		Middle East (1)	18.00 [14.82, 21.17]	-	0	-	
Study date	Americas (-)	-	-	-	-	-	
	In or before 2010 (3)	33.46 [- 5.26, 72.19]	99.2	2	< 0.001		
Carcinogenic Risk (CR)	Income level	After 2010 (18)	0.48 [0.34, 0.63]	99.0	17	< 0.001	
		High income (3)	210.13 [181.56, 238.70]	43.3	2	0.172	
	Region	Low and Middle Income (15)	54.22 [47.19, 61.24]	99.0	14	< 0.001	
		Europe (2)	217.22 [168.35, 266.10]	68.5	1	0.075	
		East /southeast Asia/Oceania (14)	51.38 [44.51, 58.26]	99.0	13	< 0.001	
		Middle East (1)	134.00 [110.36, 157.63]	-	0	-	
	Study date	Americas (1)	3295.00 [2713.77, 3876.22]	-	0	-	
		In or before 2010 (3)	1300.78 [514.81, 2086.76]	98.9	2	< 0.001	
	Non-carcinogenic Risk (HQ)	Income level	After 2010 (15)	60.65 [53.75, 67.55]	99.0	14	< 0.001
			High income (3)	0.83 [0.47, 1.20]	97.9	2	< 0.001
Region		Low and Middle Income (5)	0.26 [0.13, 0.40]	99.1	4	< 0.001	
		Europe (2)	1.22 [- 0.60, 3.05]	98.9	1	< 0.001	
		East /southeast Asia/Oceania (6)	0.32 [0.19, 0.44]	99.1	5	< 0.001	
		Middle East (-)	-	-	-	-	
Study date		Americas (-)	-	-	-	-	
		In or before 2010 (-)	-	-	-	-	
	After 2010 (8)	0.46 [0.34, 0.59]	99.1	7	< 0.001		

**Appendix 2. Results of subgroup analysis for the FA variables in educational centers section**

Variable	Subgroup analysis						
	Subgroup	Category (number of studies)	Pooled value [95% CI]	I <sup>2</sup> (%)	Q statistic (df)	p of heterogeneity	
Concentration	Income level	High income (2)	9.08 [7.94, 10.21]	0.0	1	0.972	
		Low and Middle Income (4)	29.03 [7.86, 50.20]	98.9	3	< 0.001	
	Region	Europe (2)	9.08 [7.94, 10.21]	0.0	1	0.972	
		East /southeast Asia/Oceania (3)	37.27 [25.06, 49.49]	90.5	2	< 0.001	
		Middle East (-)	-	-	-	-	
Study date	Americas (1)	4.17 [3.43, 4.91]	-	0	-		
	In or before 2010 (1)	40.00 [32.94, 47.05]	-	0	-		
Carcinogenic Risk (CR)	Income level	After 2010 (5)	17.20 [11.19, 23.22]	98.2	4	< 0.001	
		High income (2)	26.05 [- 20.46, 72.57]	99.1	1	< 0.001	
	Region	Low and Middle Income (4)	0.001 [- 0.013, 0.015]	99.2	3	< 0.001	
		Europe (2)	26.05 [- 20.46, 72.57]	99.1	1	< 0.001	
		East /southeast Asia/Oceania (3)	0.000 [- 0.011, 0.012]	99.2	2	< 0.001	
		Middle East (-)	-	-	-	-	
	Study date	Americas (1)	25.70 [21.16, 30.23]	-	0	-	
		In or before 2010 (1)	13.90 [11.44, 16.35]	-	0	-	
	Non-carcinogenic Risk (HQ)	Income level	After 2010 (5)	0.004 [- 0.012, 0.020]	99.2	4	< 0.001
			High income (2)	0.05 [- 0.04, 0.14]	99.1	1	< 0.001
Region		Low and Middle Income (2)	0.40 [0.35, 0.45]	0.0	1	0.714	
		Europe (2)	0.05 [- 0.04, 0.14]	99.1	1	< 0.001	
		East /southeast Asia/Oceania (1)	0.41 [0.34, 0.48]	-	0	-	
		Middle East (-)	-	-	-	-	
Study date		Americas (1)	0.39 [0.32, 0.46]	-	0	-	
		In or before 2010 (-)	-	-	-	-	
	After 2010 (4)	0.22 [0.10, 0.33]	99.2	3	< 0.001		

**Appendix 3. Results of subgroup analysis for the FA variables in vehicle cabin section**

Variable	Subgroup analysis					
	Subgroup	Category (number of studies)	Pooled value [95% CI]	I <sup>2</sup> (%)	Q statistic (df)	p of heterogeneity
Concentration	Income level	High income (3)	37.43 [17.11, 57.75]	96.6	2	< 0.001
		Low and Middle Income (3)	47.31 [18.48, 76.14]	97.8	2	< 0.001

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Variable	Subgroup analysis					
	Subgroup	Category (number of studies)	Pooled value [95% CI]	I <sup>2</sup> (%)	Q statistic (df)	p of heterogeneity
Carcinogenic Risk (CR)	Region	Europe (-)	-	-	-	-
		East /southeast Asia/Oceania (6)	41.67 [28.62, 54.72]	96.7	5	< 0.001
		Middle East (-)	-	-	-	-
		Americas (-)	-	-	-	-
	Study date	In or before 2010 (-)	-	-	-	-
		After 2010 (6)	41.67 [28.62, 54.72]	96.7	5	< 0.001
	Income level	High income (2)	1.8e+ 05 [1.0e+ 05, 2.6e+ 05]	99.2	1	< 0.001
		Low and Middle Income (3)	96.25 [40.28, 152.23]	99.0	2	< 0.001
	Region	Europe (-)	-	-	-	-
		East /southeast Asia/Oceania (5)	40.72 [25.94, 55.51]	99.0	4	< 0.001
		Middle East (-)	-	-	-	-
		Americas (-)	-	-	-	-
	Study date	In or before 2010 (-)	-	-	-	-
		After 2010 (5)	40.72 [25.94, 55.51]	99.0	4	< 0.001

#### Appendix 4. Results of subgroup analysis for the FA variables in other indoor environments section

Variable	Subgroup analysis						
	Subgroup	Category (number of studies)	Pooled value [95% CI]	I <sup>2</sup> (%)	Q statistic (df)	p of heterogeneity	
Concentration	Income level	High income (1)	104.00 [85.65, 122.34]	-	0	-	
		Low and Middle Income (11)	58.84 [47.18, 70.51]	98.6	10	< 0.001	
	Region	Europe (-)	-	-	-	-	
		East /southeast Asia/Oceania (7)	52.43 [40.30, 64.55]	98.6	6	< 0.001	
		Middle East (3)	217.92 [92.75, 343.09]	98.9	2	< 0.001	
		Americas (2)	55.15 [43.62, 66.68]	63.6	1	0.097	
	Study date	In or before 2010 (4)	79.45 [42.53, 16.38]	97.6	3	< 0.001	
		After 2010 (8)	53.96 [41.52, 66.39]	98.6	7	< 0.001	
	Carcinogenic Risk (CR)	Income level	High income (1)	120.00 [98.83, 141.16]	-	0	-
			Low and Middle Income (11)	116.91 [92.90, 140.91]	99.1	10	< 0.001
Region		Europe (-)	-	-	-	-	
		East /southeast Asia/Oceania (7)	151.50 [107.72, 195.27]	99.1	6	< 0.001	
		Middle East (3)	77.77 [31.40, 124.14]	98.4	2	< 0.001	
		Americas (2)	423.74 [- 346.10, 1193.58]	99.1	1	< 0.001	
Study date		In or before 2010 (4)	452.88 [75.29, 830.47]	99.2	3	< 0.001	
		After 2010 (8)	69.80 [49.14, 90.47]	97.5	7	< 0.001	
Non-carcinogenic Risk (HQ)		Income level	High income (-)	-	-	-	-
			Low and Middle Income (5)	0.76 [0.47, 1.06]	98.2	4	< 0.001
	Region	Europe (-)	-	-	-	-	
		East /southeast Asia/Oceania (2)	0.75 [0.16, 1.35]	97.0	1	< 0.001	
		Middle East (3)	0.77 [0.37, 1.18]	98.5	2	< 0.001	
		Americas (-)	-	-	-	-	
	Study date	In or before 2010 (-)	-	-	-	-	
		After 2010 (5)	0.76 [0.47, 1.06]	98.2	4	< 0.001	

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