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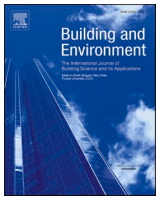

Volatile organic compounds emitted by humans indoors– A review on the measurement, test conditions, and analysis techniques

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ABSTRACT

The impact of indoor air quality on human health is gaining importance as people spend 90% of their time indoors. It has been established that human occupancy is a significant contributor to indoor Volatile Organic Compound (VOC) concentrations and is of significant concern regarding occupant health, and yet human VOC emissions remain largely uncharacterised. In the current study, we review recent research that examines the contributions of humans to the indoor VOC profile in occupied spaces, with a focus on study characteristics. This investigation identified a hierarchy of factors contributing to inter-study variations in human biogenic VOC (HVOC) levels measured indoors. We found that the factors contributing to the variation in reported HVOC emissions are related to the sampling techniques used, the test conditions, occupant related factors sample analysis. Contrasting findings on issues such as the effect of nutrition and smoking are discussed. Conclusions were reached about the recent advancements and nature of results and the need to use larger datasets, and recommendations regarding global guidelines and future testing have been made. We advocate for a unified approach in future studies, promoting more coordinated data collection and reporting and fostering the development of impactful applications.

1. Introduction

Volatile organic compounds (VOCs) are carbon-based chemicals characterized by their relatively high vapor pressure at room temperature, specifically greater than 0.01 kPa at 20 °C [1]. These compounds vaporise at room temperature, quickly changing state and being inhaled. Understanding the dynamics of VOC emissions is crucial for the assessment of indoor air quality (IAQ) and its impact on human health and well-being. IAQ impacts the comfort, health, and wellbeing of occupants [2,3], and poor IAQ has substantial costs due to lost productivity and illness [4]. Numerous VOCs commonly detected in indoor environments have been linked to acute and chronic adverse health effects, including sensory and skin irritation, headaches, breathing difficulties, increased asthma risk, and cancer [5,6] and severe physical and mental health issues [7,8]. Given the wide range of indoor VOC emission sources [9] and the vulnerability of certain populations such as children to toxic pollutants [10], understanding personal exposure and its relationship to health effects has become crucial [11,12]. A build-up of VOCs indoors has been associated with Sick Building Syndrome (SBS), the extent of the effects depends on the compounds, concentrations and length of exposure [13]. Long-term exposure to certain VOCs, even at non-acutely harmful concentrations, may result in mutagenic and carcinogenic effects [12,14,15]. Indoor concentrations of numerous VOCs have been found to be consistently higher (up to ten times) than proximal outdoor concentrations [16]. The prevalence of higher indoor VOC concentrations is primarily due to the presence of various indoor sources [17,18], and the relatively low rates of outdoor air ventilation typically utilized in residential and office spaces [19,20].

Human beings continuously emit hundreds of VOCs both through exhaled breath and skin emissions [21]. It has been established that human occupancy is a significant contributor to indoor VOC emissions, particularly in densely occupied spaces [22–24]. As people spend

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approximately 90% of their time indoors [25], most people are exposed to these emissions constantly. Few studies – particularly given the extensive research on building and material emission — have focused on humans as VOC sources or reactive surfaces [26]. Human biogenic VOCs (HVOCs) reflect both an individual's endogenous metabolic processes and lifestyle – exogenous effects [27–29]. However, the origins of HVOCs and their relationship to health conditions or lifestyle factors remain largely unstudied. Advances in breath analysis since the 1960s have led to more VOCs being identified but their origins have yet to be fully explored [30,31].

Indoors, HVOC emissions interact with thousands of VOCs from other sources [20,32–34]. Moreover, secondary source VOCs, such as those resulting from chemical reactions involving oxidants like ozone and hydroxyl radicals are anticipated to have significant health effects [35,36]. For example, common fragranced consumer products (found on human occupants) emit numerous VOCs which can generate secondary pollutants such as formaldehyde [22] which is carcinogenic at low concentrations and exposures [11].

In 2014, the first central compendium of HVOC emissions of healthy individuals was published online [31]. The compendium — as hence referred to — reported 2746 VOCs emitted from various human sources, including breath, saliva, blood, milk, skin secretions, urine, faeces, and semen. The compendium aimed to provide a database to stimulate further research of the human *volatilome*. This compendium has been used as a reference in this study as it is the most comprehensive dataset of human emissions currently available [31]. Substantial progress has been made since this time, requiring an updated review. Further, methodological approaches differ across studies, causing differences amongst the reported results. The current review thus aims to provide an overview of the current state of knowledge on HVOC emissions in indoor work environments with respect to the discrete VOCs identified. The following categories have been critically reviewed: i) the main study characteristics; ii) the data sampling method and collection; iii) the nature of controls and contributing factors; iv) the core findings. Metadata derived from the reviewed papers was then analytically compared to the 2014 compendium. Our aim in this review is to promote future standardised HVOC testing to characterize HVOC indoors so that safe IAQ can be better defined and maintained globally.

2. Research method

This review has been conducted in line with methodological approaches outlined in the JBI Manual for evidence [37] (Fig. 1). The methodological scaffold has been separated into several steps: i) Scope delimiting; ii) Identification of alternative terminology; iii) Define literature databases, search engines and screening criteria; and iv) Final Screening. Finally, a dataset of VOCs was compiled and compared to the previous compendium of HVOC emissions [31].

2.1. Scope delimiting

The purpose of this literature survey was to investigate the prevalence of HVOC contribution indoors. Hence, the included studies fulfilled several criteria for selection, involving:

- Indoor spaces (>2 m^2 floor area)/or exclusively a breath sample
- Indoor VOCs that were chemically speciated (not TVOCs)
- VOCs were explicitly human emissions (at least 1 occupant in the testing space)
- Involved living persons (not deceased)
- Recent testing results (published since 2010)
- Breath and skin emissions (faecal, blood and other emissions were not considered generally relevant in indoor environments)

2.2. Identification of search terms and logic grid

Once the scope was delimited, a logic grid was established to highlight key search terms. Boolean operators (AND/OR) where used to combine search phrases, and are presented in Table 1.

2.3. Define databases, search and screening criterion

The database search was conducted between August 2022 and May 2023. 185 papers were included in our preliminary assessment of HVOC research. Research papers written in English were found using Elsevier, Science Direct, Wiley and IOP Science databases. To select papers that strictly address indoor HVOC emissions, this review is limited to:

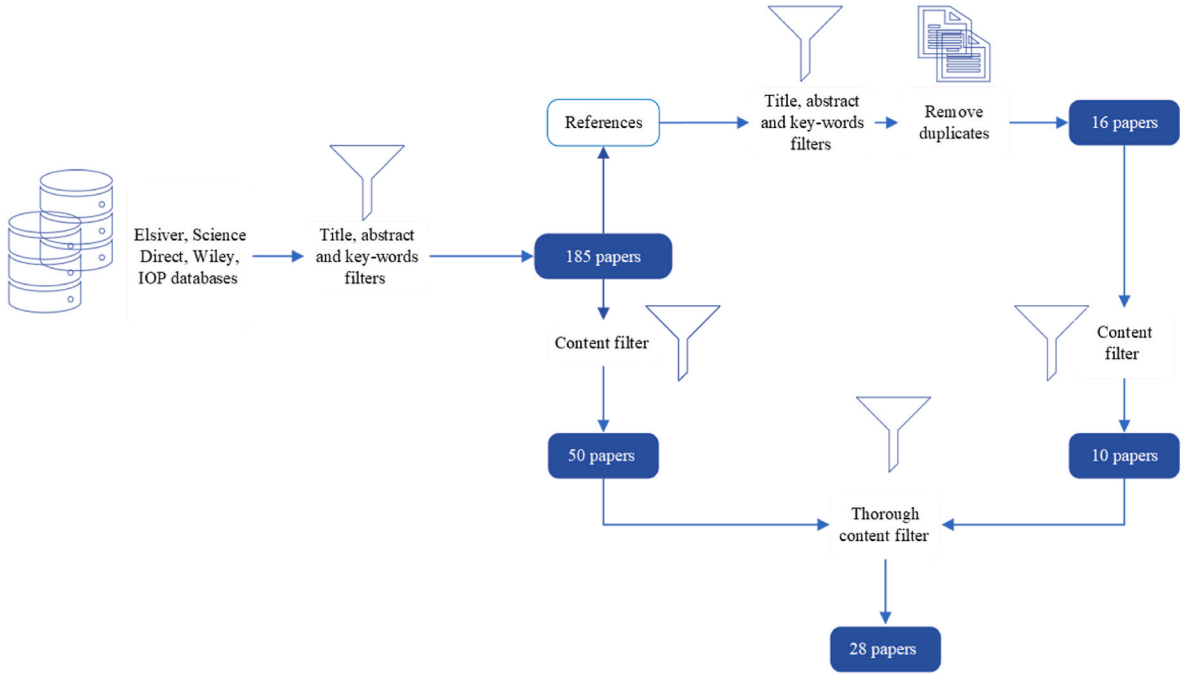

Fig. 1. Flowchart of data collection procedure as per the outline in the JBI Manual for evidence [37].

Table 1
Logic grid of search terms.

Human	VOC emissions	Indoors
"Breath", "exhaled", "occupant", "human", "students", "metabolite", "skin", "human breath", "human body", "headspace" "volatilomic", "clinical study" "pilot study" "metabiome" "volatilome"	"VOC profile", "VOC analysis", "VOC concentration", "VOC emissions", "volatile organic compounds", "emission rates", "emission factor"	"Indoors", "inside",

- Real data sampled (no modelled, theoretical, or derived results)
- Published as a peer-reviewed paper
- Average age of participant over 16 (no children only results)
- No literature reviews (recent data only)
- Original references only (no duplication of findings)
- Nasal/olfactory sampling methods were considered outside the scope of this report
- If experiment included disease or exercise conditions, then only 'healthy human' control data was included in analysis

2.4. Final Screening

The results were thus narrowed to include only papers which had:

- Experimental data from sampling and analysis with specific reference to VOCs found (emission rate, concentration, number of instances or percentage).
- "Untargeted" data is available (untargeted refers to quantifying unknowns within a reasonable mass-to-charge ratio range and not specific or predetermined compounds).

Final screening narrowed the number of papers for review to 28, following a thorough investigation of the inclusion criterion and data available.

2.5. Preparation of metadata and comparison to compendium

For each paper reviewed, the discrete species of VOC identified was compiled in a spreadsheet. The result was a metadata sheet detailing; i) compound; ii) chemical class; iii) CAS number; iv) emission data and units; v) notes and other relevant tags or comments. Papers that referred to different locations, sampling days and conditions that were reported separately were treated as unique entries. Chemical names were used as reported, fragments were included, and unidentifiable (no CAS number) species were not included. Data categorisation into chemical groups was done; i) as given; ii) by general naming suffix rules or (iii) as best researched using the CAS number (using PubChem or ChemSpider). Between 1 and 3 chemical groups were assigned to individual species, where relevant. Misnaming of chemicals in the original papers was not been accounted for. The following chemical groups were included: i) aromatics; ii) ethers; iii) furans; iv) alcohols; v) alkanes; vi) aldehydes; vii) ketones; viii) alkenes; ix) N- containing; x) halides; xi) carboxylic acids; xii) esters; xiii) other.

The final step was to compare the metadata developed the 2014 compendium [31]. Compounds identified as skin and breath emissions were manually counted as reported. Data for individual HVOC species included; i) CAS-number; ii) compound name; iii) chemical group; iv) identification of emission source. No number of instances per species were included in the report, only unique VOCs were listed. No reference to the studies of origin were available in the compendium, so comparisons related to the study or origin could not be made. Thus, the chemical groups listed within the compendium and the current metadata were compared to verify if there was similarity between the presenting chemical groups; indicating that the metadata correlated with HVOC emissions as listed in the compendium.

3. Results

Data included in the current analysis is present in Table 2. For each study included, the sampling procedure, results, and analysis were evaluated based on the main study characteristics — Objective, location, and dataset; the data sampling method and collection; the controls and contributing factors and finally the results.

3.1. Main study characteristics

3.1.1. Objectives

Of the overall investigations, 46% stated that their main objective was capturing human emissions; 32% of the papers reviewed extracted data on healthy control populations; and 21% of the papers focused on specific contributing factors to HVOC emissions. Human emission dedicated studies were mostly rigorously controlled and generally performed in chambers, eliminating as many variables as possible and focusing on endogenous emissions. Those that did not utilise chambers were varied in their approaches and level of detail describing the testing set ups and the different factors incorporated. Several studies were focused on developing diagnostic breath testing capability, and pilot studies with 'healthy controls' which included untargeted VOC sampling were included in this group.

3.1.2. Location

Factors such as temperature, humidity, outdoor air quality, and urban versus rural settings were observed to be variables tested that would likely cause differences in VOC emissions. 46% of the papers reviewed were conducted in Europe, 25% were from North America, with the majority originating in the United States and one study in Canada. Most chamber and residential studies were conducted in the People's Republic of China. These three key geographies have varying levels of outdoor pollution, humidity and temperature ranges and this should be considered when comparing 'standard' HVOC emissions.

17% of the studies were conducted with 1 person at a time in a chamber. Chamber experiments had the most controls and were largely not replicated with the same individual. 53% of the studies were conducted in test facilities, with occupants described as 'participants' with very little information on ambient testing conditions provided. Studies that used healthy controls had the least information about test conditions and all of this type of tests had subjects exhale directly into a bag once for collection. Only 7% of studies were conducted in residences. No reviewed studies were performed in other commonly occupied spaces such as offices, apart from 17% of the studies that were conducted in university related spaces, with 3% of studies conducted in another area (cinema).

3.1.3. Dataset

Occupant information was generally well reported with respect to age, gender, and smoking status. There was a slight bias towards male occupants (Table 2). Some studies provided further detail regarding BMI.

The median number of participants (occupants) in each study was 30, although only 25% of studies tested more than 1 person in a single space at a single time, with most samples conducted on a single occupant at a time (based on the reported information). 64% of the studies specifically studied HVOC emissions whilst at rest. The remaining studies were room studies where there was an assumed mix of occupants at rest and in transit [11]. 57% of studies had less than 50 occupants, with the number of occupants ranging from 1 to 8300. Two studies had substantially more participants that the others, 8300 [38] & 1147 [30]. Almost 10% of the studies reported percentage occupancy over time or per session whilst several did not reference the number of occupants. The approximate number of occupants has been estimated for these

Table 2
Studies of HVOCs indoors and their characteristics.

Ref	Type	Year	Location	Aim	Occupants	Method	Duration	Factors included
[21]	Chamber	2022	Europe	HVOCs emitted under controlled conditions	4	PTR-ToF-MS	24h	Temperature, relative humidity, clothing type, and age, enthalpy rate, length of clothing
[39]	Test facility	2014	Europe	Potential markers of human presence	31	SPME-GC–MS	30 min	Test site (hand and forearm)
[40]	Chamber	2022	China	Emission rates of HVOCs from whole-body skin of healthy people	14	GC-MS and HPLC	56 min	Ozone, temperature, humidity, airtightness, personal care products, bathing routine, diet
[5]	Test facility	2022	North America	Method for headspace collection to analyse human volatilome	20	TD-GC-MS	30 min	Not relevant
[41]	Chamber	2019	China	Whole body HVOC types and emission rates	14	GC-MS	40 min	Not relevant
[42]	Test Facility	2017	China	HVOC emission levels and influencing factors in exhaled breath	117	TD-GC-MS	ND	Age, gender, smoking
[23]	Chamber	2022	China	Whole body skin and breath HVOCs	14	GC-MS	4 min breath; 56 min skin	Not relevant
[43]	Test facility	2020	China	Whole-body skin emissions under controlled conditions	1	GC-MS & HPLC	ND	Not relevant
[44]	Residence	2021	North America	Speciated HVOC emissions from human occupancy	NA	PTR-TOF-MS	10 h	Steady state after once unoccupied, personal care products and application
[45]	Residence (dorms)	2022	China	Indoor odour acts as a surrogate method for IAQ assessment	20–40	TD-GC-MS	10 h	Not relevant
[46]	Chamber	2018	Europe	Monitor HVOCs under conditions that mimic entrapment	11	GC-IMS	1 h skin; 1 h whole body	Dust, temperature and humidity, LODs, fasting
[9]	Residence	2015	North America	Emission sources of VOCs and their contributions to indoor concentrations in residences	26	GC-MS	24 h	Activities
[47]	Test Facility	2010	Europe	Chemical substances in the exhaled breath of ten healthy probands	10	PTR-MS	30 min	Methanol rich food and beverages. Nutrition and smoking. Uncontrolled end-exhaled sampling; sampling bags
[48]	Test Facility	2010	Europe	Identification of HVOCs revealing characteristic rest-to-work transitions	7	PTR-MS & GC-MS	15 min	Breathing rate; breathing volume; cardiac output and blood pressure; activity; rest prior to test; medication; health condition
[49]	Test Facility	2010	Europe	Distinguishing COPD subjects from controls based on VOCs in breath	16	TOF-GC-MS	1 exhaled breath	Interdependencies between inhaled and exhaled air; background noise; raw mass spectra for VOC identification; analysis
[50]	Hospital	2022	Europe	Composition and concentration of clinical-HVOCs	55	TD-GC-qMS	ND	Heterogeneity of patient responses; Exogenous VOCs; Seasonal variations
[51]	Test Facility	2016	Europe	Novel breath sampling device to search for COPD related VOCs	101	TD-GC-MS	5 min	Disease severity; smoking; site location (rural/urban); time since last cigarette; room air; size & ventilation of sampling room; room cleaning procedures; adsorption material; sampling tube
[52]	Test Facility	2014	North America	Differentiate paediatric patients with IBD from healthy controls	55	SIFT-MS	1 exhaled breath	Oral bacteria; ambient air quality; residual air in lungs
[53]	Test Facility	2014	Europe	Metabolites in the exhaled breath of patients affected by coeliac disease under a GF diet	17	PTR-MS	1 exhaled breath	ND
[54]	Test Facility	2017	China	Screen for pneumoconiosis using VOCs	154	GC-MS	1 L exhaled air	Oral bacteria, diet
[54]	Test Facility	2019	Europe	HVOCs in exhaled breath of average-risk individuals with socio-demographic and lifestyle factors, medical conditions and diet analysis	1447	GC-MS	1 exhaled breath **	Gender; consumption of coffee, leeks, or garlic; not smoking; heavy alcohol use; season; temperature
[55]	Test facility	2021	North America	Pilot study to characterize the baseline of exhaled breath of a healthy cohort	7	GC × GC-qMS/FID	ND	2 h fast, sit isolated for 10 min before beginning, lifestyle questionnaire
[56]	Test facility	2015	Europe	Identify, quantify, and analyse VOCs present in the breath of IBD patients and controls	18	SIFT-MS	2 L exhaled breath	Medication; environmental factors; diet (fasting); pregnancy; pro/prebiotics
[57]	University classroom	2016	North America	Calculate emission factor per person, quantify source of VOCs indoors from materials, people and outdoors	>85	PTR-MS	5 min intervals	Age; activity; health status; emotional state; recalibration of measuring devices; steady state continued monitoring after departure
[57]	University (art gallery)	2019	North America	Transport, emission, deposition, and transformation of chemicals	300	quadrupole PTR-MS	2 h	HVAC system; food; alcohol
[14]	Test facility	2012	Europe	Assess the effects of smoking on the composition of exhaled breath	115	GC-MS	Single exhalation	Exposure to pollution and indoor-air contaminants; correlation with exposure to smoking, time since sample is collected
[38]	Cinema	2017	Europe	HVOC emissions from audiences as a function of time	8300	PTR-TOF-MS	2.75 h	Chemosignals, emotions; diabetic status; well mixing air; ozone; food consumed during; position

ND = No data.

cases.

Further, 30% of investigations did not report number of samples taken. For those that did, the median number of samples was 55 per study. 90% of studies included less than 245 samples. Samples were collected either: consecutively, only once, repeated another day or replicated at some other time. Studies that pooled or averaged sample data did not account for potential variation amongst sampling times.

3.2. Data sampling method and collection

3.2.1. Sampling method

For sample collection, 28% of tests used breath collection bags, 50% of these bags were Tedlar, others types included Nalophan, Quintron and Mylar. Gas Chromatography-mass spectrometry (GC-MS) is regarded as the gold standard for sampling HVOCs in the literature [58]. GC-MS was used as the standalone method in 60% of the sampled investigations, or with Solid phase-microextraction (SPME-GC-MS), thermal desorption (TD-GC-MS) or time of flight mass spectrometry (ToF-GC-MS). Proton transfer reaction mass spectrometry (PTR-MS) was also a common method and was used in 25% of studies. Methodologies vary for breath and skin sampling; with 32% of studies measuring both skin and breath emissions, the remainder studied either one or the other type of emission. Fig. 2 presents a discrete breakdown of the sampling methods used.

3.2.2. Species identification

Retention time (RT) and Spectral library match was the most frequent stated method used for identifying VOC species, with 25% of the studies identifying VOCs using both procedures. Unfortunately, 42% of the sampled papers did not define how they identified VOCs. The most commonly used spectral libraries were NIST and/or AHMS; 42% of papers referenced these.

Of all the VOCs identified across studies, only a select portion were reported in the papers, and there were various criteria used for which species were listed, dependent on the hypotheses tested by each study. In 25% of the papers, the most frequently detected VOCs in their samples were those that were listed (e.g. >50% presence in samples, top 60 detected VOCs etc.). In 21% of the papers, it was not specified what criteria were required to be met for the VOC species to be listed. In 17% of the studies, a minimum frequency of occurrence in the samples of VOCs was required for a species to be listed. The listing criteria used are shown in Fig. 3.

The median number of VOCs identified per study was 94 species. The smallest number of species identified in a paper was 6 compounds. 28% of studies reported less than 50 species, 39% of papers reported between 50 and 200 species; 10% of papers reported more than 200 species and 21% of papers did not report the total number of VOCs identified. The paper which identified the most species used only retention time for VOC identification. Refer to Table 3 for a summary of dataset and sampling information.

3.2.3. VOC metrics reported

Emission rates per VOC per person were only reported in 45% of papers. Limit of detection was reported in less than 40% of papers. Retention time was reported just over 20% of the time. There were on average 3 data metrics available per VOC per study. Almost 90% of papers listed standard deviation of VOC species found. Please see Fig. 4 for a summary of the metrics presented in the sampled papers.

There were two broad categories for experimental setup: being room sampling and direct breath and skin sampling. Ambient conditions are relevant to both, but were largely unreported, which may impact sample HVOC outcomes. Most studies had considerable gaps in the presented information related to experimental setup, such as room size, cleaning schedules, window positions, ambient temperature and humidity, and ambient/unoccupied VOC concentrations.

3.3. Controls and contributing factors

HVOC causal factor identification was all or part of the objective for 28% of the studies reviewed. Only 28% of the papers did not identify factors which contributed to HVOC variability, with most papers discussing factors contributing to the HVOC data regardless of whether it was part of their main objective. Tang [61] and Mochalski [39] were often referred to for previously published HVOC emission results. The factors (Fig. 5) were assigned tiers as per the frequency of incorporation and depth of discussion in the studies under 4 criteria; i) sample analysis; ii) occupant related factors; iii) test conditions & iv) sampling techniques. The most discussed causal factors in papers were occupant and test conditions related. Only 10% of the papers used a combination of testing methods and provided commentary on their selection of methods other than to validate their selection. Still, sampling and analysis methods are considered important factors because of how varied they are in the literature and how differently they have been applied. There were a range of commonly attributed potential contributors amongst the

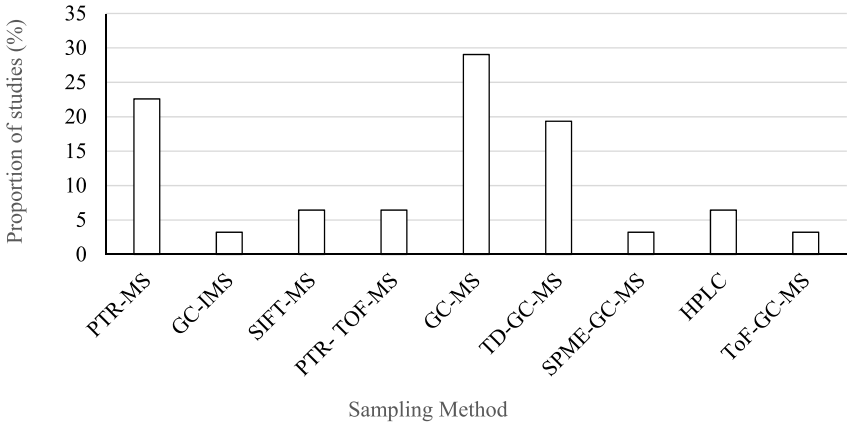

Fig. 2. Summary of Sampling methods used.

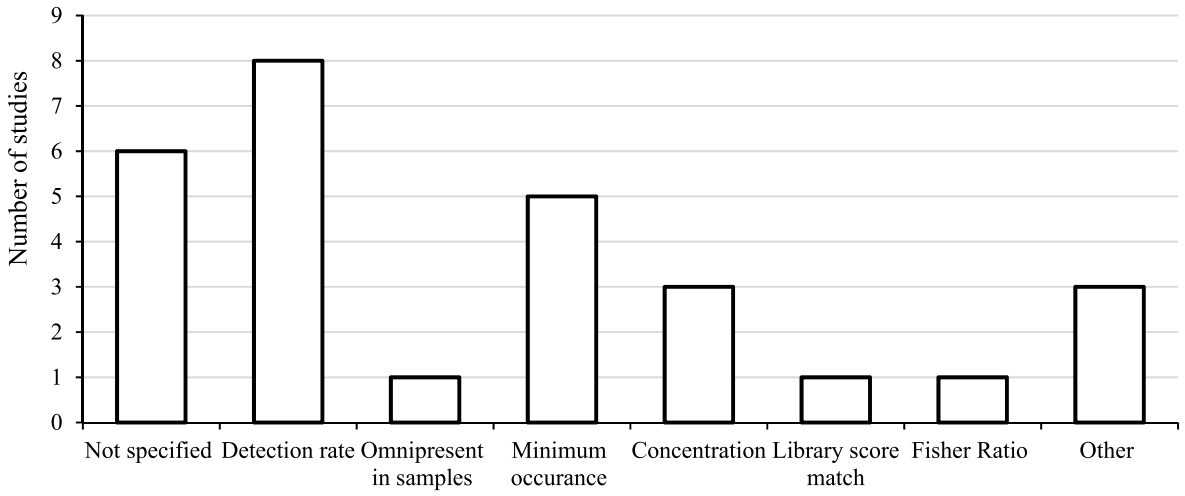

Fig. 3. Criteria for which VOCs were listed.

Table 3
Summary of Dataset and Sampling information per study.

Ref	Type	#Occupants	Method	Test Duration	n Samples	n VOC species
[21]	Chamber	4	PTR-ToF-MS	Half day and full day	25	68
[39]	Test facility (skin only)	31	SPME-GC–MS	30 min	31	64
[40]	Chamber	14	GC-MS and HPLC	56 min	56**	143
[5]	Test facility	20	TD-GC-MS	30 min	20**	43
[41]	Chamber	14	GC-MS	40 min	200**	38
[42]	Test Facility	117	TD-GC-MS	ND	117	60
[23]	Chamber	14	GC-MS	4 min breath; 56 min skin	56	42
[43]	Test facility	1	GC-MS & HPLC	ND	8**	11
[59]	University	150**	TD-GC-MS; room samples	30 min	97**	89
[44]	Residence	NA	PTR-TOF-MS; room samples	10 h	15**	249
[45]	Residence (dormitory)	30**	TD-GC-MS; room samples	10 h	20**	94
[46]	Chamber	11	GC-IMS	1 h skin; 1 h whole body	77**	35
[9]	Residence	26**	GC-MS: room samples	24 h	653	119
[47]	Test Facility	10	PTR-MS	30 min	10**	NA
[48]	Test Facility	7	PTR-MS & GC-MS	15 min	49	NA
[49]	Test Facility	16*	TOF-GC-MS	1 exhaled breath	29	1179
[50]	Hospital	55*	TD-GC-qMS; room samples	ND	245	328
[51]	Test Facility	101*	TD-GC-MS	5 min	190	134
[52]	Test Facility	55*	SIFT-MS	1 exhaled breath	55	NA
[53]	Test Facility	17*	PTR-MS	1 exhaled breath	17	503
[54]	Test Facility	154*	GC-MS	1 L exhaled air	154	195
[30]	Test Facility	1147	GC-MS	1 exhaled breath **	1447	15
[55]	Test Facility	7	GC × GC-qMS/FID	ND	105	65
[56]	Test Facility	18**	SIFT-MS	2 L exhaled breath	18	6
[60]	University	85**	PTR-MS; room samples	5 min intervals	18	ND, ions
[57]	University (Gallery)	300	quadrupole PTR-MS; room sample	2 h	24	ND
[14]	Test Facility	115	TD-GC-MS	single exhaled breath	115	162
[38]	Cinema	8300	PTR-TOF-MS; room sample	2.75 h	28050	13

Table 3: Summary of dataset and sampling information; *Healthy controls, **Calculated, ND=No data.

sampled papers, though there were varying conclusions regarding the extent to which they were significant.

3.3.1. Sample analysis

The level of detail provided on sample analysis was generally lacking across the board. The well-mixing assumption, Henry's law and ventilation assumptions were referenced in several papers but in all cases only stated as assumptions or equations for use in further modelling. Stated instrumental limits of detection were varied across both species and study, possibly for reasons relating to the sampling method or target range of mass spectra. Descriptions of per person and per room volume area emissions were generally vague, with a consistent absence of information regarding the number of people per room, room dimensions, duration of occupation and positioning of sampling equipment within the sample room.

3.3.2. Occupant related factors

Most occupant-associated factors incorporated in the studies were related to occupant demographics, behaviour or health status. 7% of studies detected differences in emissions between genders, the impact of oral bacteria, personal care products, coverage of clothing worn and the influence of medication. 10% of studies noted effects related to toxin or environmental exposure. It was commonly concluded that personal care products make a large contribution to emissions, thus more than 50% of the studies included a limitation on the use of personal care products prior to experiments. A smaller number of studies limited personal care product use to 2 days prior to testing whilst others did not restrict personal care use. There was a consensus that time since application did influence concentration of the VOCs commonly associated with soap, deodorant, and perfume. 3% of studies tested the influence of time since application, producing findings that showed VOC emissions associated with personal care were reduced in the afternoon when compared to the

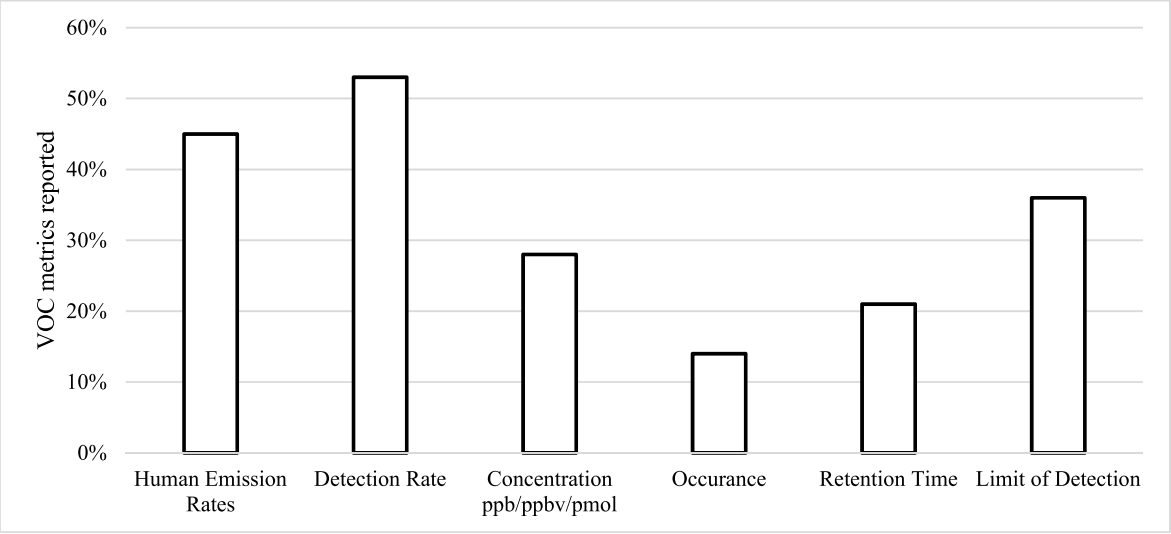

Fig. 4. Published metrics per VOC.

Fig. 5. Diagram of tiered factors, based on frequency of research themes, contributing to HVOC emission variation.

morning. 14% of studies detected correlations between skin exposure (i.e. reduced clothing coverage) and increased VOC emissions. It was concluded in 14% of studies that alcohol consumption influences emissions. Oral bacteria were discussed in several studies as a factor contributing to variation in HVOCs which could be related to length of time since eating. 7% of studies addressed nutrition specifically; one study [30] assessed the effect of diet directly and found that only select foods had a correlation with emissions (coffee, leek, garlic). Another found that nutrition had no effect on emissions [47]. The studies that had participants eating and cooking whilst sampling (7%) detected a correlation between these activities and increased VOC emissions, though interestingly there are geographic considerations for the effects of cooking because the oils and foods used in some countries are vastly different to others and hence are not general in nature. Overall, 14% of papers discussed diet as a factor, but most papers included information on hours of fasting prior to testing, which ranged from zero to 12 h prior. 21% of papers referenced smoking, with 3% of studies comparing a non-smoking group to a smoking group, and other studies either standardising time since last smoke or simply noted that smokers were in the control group and no further distinction was made. Time since last cigarette ranged from zero to 2 h.

3.3.3. Test conditions

Details on the general test conditions were somewhat scant for the studies using health controls, as they generally did not account for or describe situational dynamics. Ozone was often stated to be a significant factor in indoor emissions within those papers which addressed it; the presence of ozone was discussed in 15% of the studies papers and there was an established understanding that more ozone equated to more oxidation products. Generally, HVOC tests where the subject was seated included a period of resting before sampling, although the time allowed for this varied amongst studies. There was variation in the time utilized for HVOC emissions to reach steady state, along with variation in the length of sampling time after the occupant had left the room; only 10% of studies continued monitoring room conditions after the occupant had left and the duration of continued sampling was 0–1.5 h 10% of studies agreed that there were effects on VOCs when humans move during sampling. The materials in the sampling room, dust and cleanliness were addressed in several papers, which emphasises the need for both the elimination of these effects, along with ambient VOC testing to reduce background effects when testing HVOC emissions. Amongst the existing literature, only 7% of papers considered the influence of outdoor air quality.

3.3.4. Sampling techniques

Sampling techniques were varied and how they were maintained and operated varied significantly. Only 10% of studies referred to instrument calibration. Almost all papers reported the airflow rate in their sampling tubes, although the rates varied considerably. The time until offline samples were analysed varied between 2 and 12 h, and sample incubator temperature was not consistently reported. 10% of studies discussed the downfalls of single exhalation breath testing and accounted for the dead-air collected in differing ways.

3.4. General trends in VOCs detected

Aldehydes were the most common group identified, followed by ketones and alkanes. Isoprene was the most occurring VOC. 412 VOC species were only identified once in the metadata review. The following section reviews the top 20 unique species and the chemical groups identified (Fig. 6).

Of the top 20 occurring VOC species recorded in the metadata, 3 are listed on the American Agency for Toxic Substances and Disease Registry (ATSDR) – acetone, benzene, and styrene [62].

3.4.1. Comparison to compendium data

It is clear from our analysis that acetone and isoprene are the standout VOC emissions from humans. It is also clear that the HVOCs identified in more recent work correlate closely with those previously published in the compendium [31]. Comparison between the current metadata and the 2014 compendium dataset is present in Fig. 7 and Table 4.

The most frequent chemical groups of HVOCs listed in the compendium for breath and skin emissions were similar – with alkanes, alkenes, and aldehydes dominating emissions from both sources. This result is indicative that sampling indoor air from occupied spaces will produce similar findings to direct/isolated tests such as chamber testing and direct exhalation sampling. Hence, more repeatable and large-scale experiments are likely to provide greater efficiency for future HVOC emissions testing.

4. Discussion

4.1. Considerations regarding main study characteristics

A targeted approach enables the identification of specific compounds compared to experimental reference or control samples, but will overlook less abundant or body metabolized compounds [57]. Many papers reviewed were focused on targeted VOCs. There was limited data and discussion on untargeted VOCs in 35% of the papers whose objective was not to survey HVOC emissions, especially in the studies using healthy controls.

The literature is dominated by two general methodological directions to study HVOCs: one prioritizing larger datasets and general conditions, and the other focusing on individual occupants, often targeted at specific biomarkers for disease states. The current literature mainly uses chamber experiments and controlled conditions for examining HVOC emissions. This approach may not fully characterize HVOC emissions in densely occupied indoor environments with numerous confounding factors, and may not be scalable. However, it is hoped that by pooling these experiments, it might be possible to establish baseline human emissions. Emission rates averaged across a significant number of individuals could minimize the influence of each participant's unique behaviours [27,38]. Small sample size studies are likely to be inadequate to characterize HVOC emissions within a population subset due to the many variables affecting limited samples. Dataset size has been a significant limitation for HVOC testing, especially given the lack of replicated tests and the limited repeatability of many studies. Hence, the lack of standardized conditions across these groups hinders effective

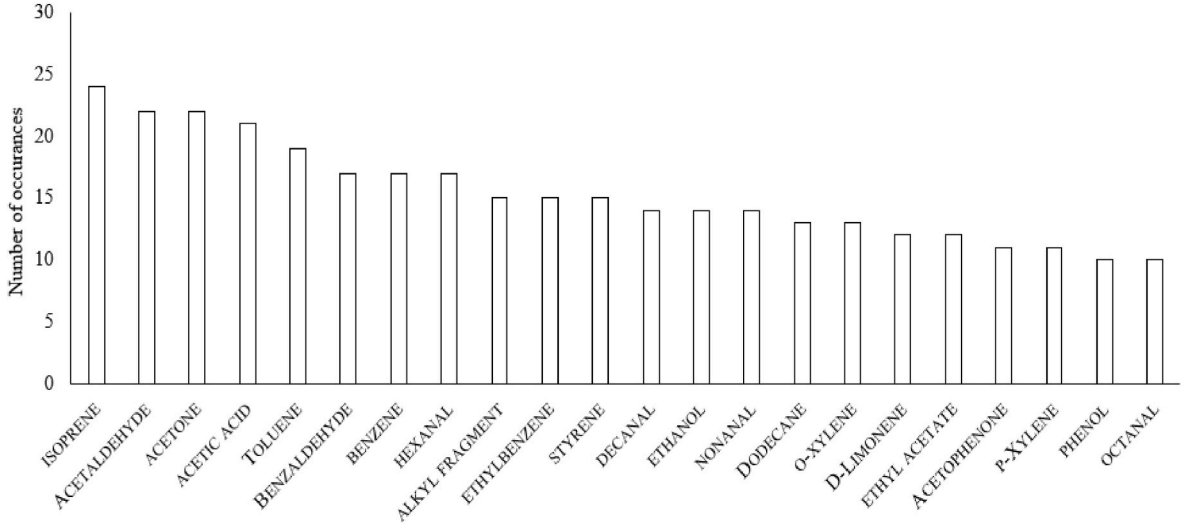

Fig. 6. Top 20 VOC species collected in the metadata, ranked by number of instances.

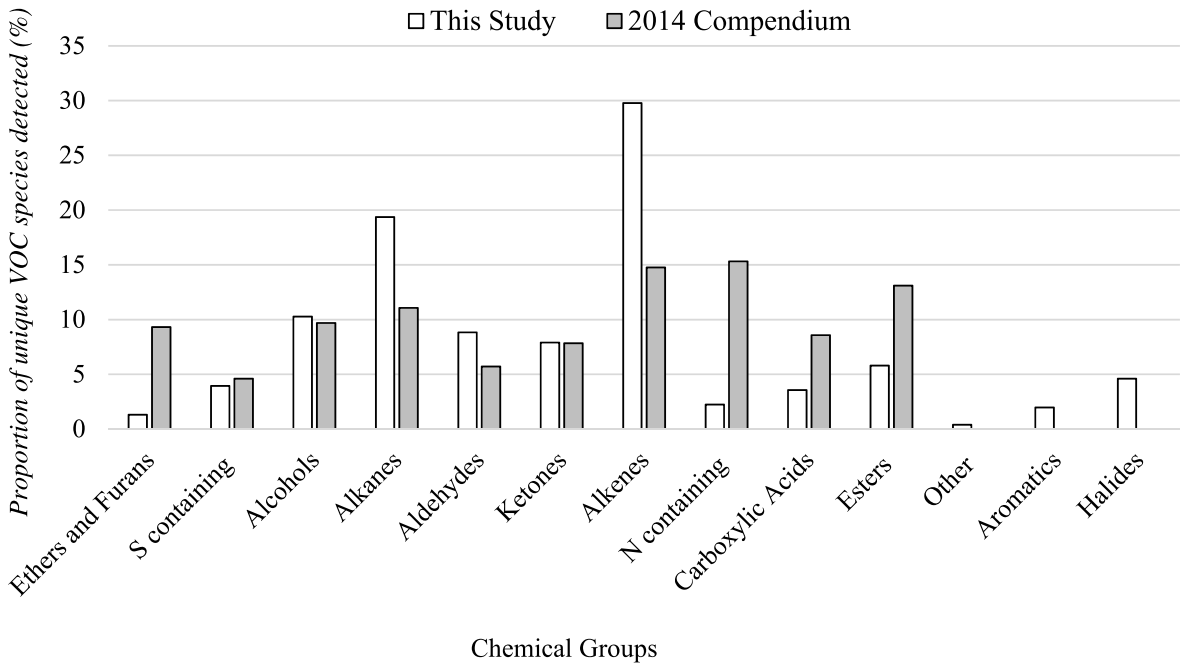

Fig. 7. Comparison of chemical groups as percentages, current study and 2014 compendium [31].

Table 4
Comparison between the current metadata and the 2014 compendium dataset [31].

Comparison between this metadata and the compendium dataset		
	This study	2014 Compendium
Year published	2023	2014
VOC emissions included (for the review purposes)	indoor total emissions, skin emissions, whole body emissions, breath only emissions	skin and breath
Source references for each VOC	yes	no
Number of instances reported available	yes	no
VOCs assigned several chemical groups where necessary	yes	yes

Comparison between this metadata and the compendium dataset		
	This Study	2014 Compendium Results *Skin and Breath only
Total number of VOC instances reviewed	1684	1089
Total number of unique VOCs reported	763	ND
% instances	Alkenes, 28.9% Alkanes, 16.9% Aldehydes, 15.4% Alcohols, 10.7%	ND
Total unique VOCs in study	Alkenes, 29.7% Alkanes, 19.36% Alcohols, 10.27% Aldehydes, 8.82% Other, 31.85%	N-containing, 15.2% Alkenes, 14.69% Alkanes, 11% Alcohol, 9.6%

VOCs listed in the compendium were manually counted according to their chemical groups which had been double qualified by retention time and mass spectra.

comparison and integration of findings. It is clear that the number of occupants, number of samples, frequency and samples and replication of samples within treatments limit the capacity of most existing research to provide generalized findings. Moreover, quantitative sampling of densely occupied conditions has not been adequately performed to date, with none of the studies included in this review testing such phenomena. Changes in the number of occupants in a space and occupant density are factors which are known to influence HVOC concentrations, but the lack of consistency in reporting the occupancy status of sampled indoor environments is inconsistent across the literature.

There is also inconsistency in the literature in identifying specific VOCs in samples, especially the dominant and potentially hazardous ones, leading to a general lack of understanding of the most frequently emitted HVOCs, and their concentrations in spaces with specific occupation rates, along with emission rates per person. An overview of the relationship between experimental approach, number of studies, the number of occupants in a sample space, the number of samples collected and the number of VOCs identified is shown in Table 5. The less controlled studies generally had the most occupants and samples, but identified more varied VOCs. Meanwhile, test facility studies that typically provided less room and general conditions information identified more VOC species.

4.2. Considerations regarding data sampling method and collection

The methods used for HVOC sampling in the field have remained largely unchanged for several decades. It may thus be worthwhile to

Table 5
Overview of the reviewed studies based on experiment type and number of occupants and samples (NA: not available).

Type of study	Proportion of studies	Median no. of occupants (range)	Median no. of Samples (range)	Median no. of HVOC species (range)
Chamber	25.8%	11 (4–14)	82 (25–200)	65 (35–143)
Test Facility	48.3%	218 (1–1447)	157 (8–1447)	203 (6–1179)
Uni, residence, other	25.8%	894 (NA–8300)	3640 (18–28050)	111 (NA–249)

extend the scope of future reviews back another 15 years to see if more data is appropriate for inclusion, given the sampling methodologies have remained mostly consistent. Although several new methods have emerged, unfortunately no data collected using these methods met the criteria for inclusion in this review. Differences between sampling methods influence experimental efficacy because of the variables inherent to each method. There is an acknowledged shortcoming with comparisons of different breath sampling procedures due to the lack of consideration of the various methods' effects [57,63]. The chosen analytical method influences the detectable VOCs. For instance, proton transfer reaction mass spectrometry (PTR-MS) is highly sensitive to certain compounds but cannot efficiently detect most light and medium-chain alkanes or formaldehyde [14,64]. Likewise, Tedlar (polyvinyl fluoride, Dupont) bags have been shown to be formaldehyde permeable, so emission samples in these sample bags would be expected to decline in concentration through time, which would cause underestimates when analysis is prolonged [65], as is normally the case for offline methods such as GC-MS [66].

Whilst GC-MS is the gold standard approach, usage may be limited by the restrictive requirements to control more variables and the inherently long profiling time, along with the high cost of the instrumentation. Some papers outside the scope of this review, compared different testing methodologies and proposed standard procedures, although these have apparently not been commonly taken up. It is likely that there is not a more consistent, controlled methodical approach across the HVOC literature due to the considerable variation in testing locations. For example, chamber experiments are typically more rigorous and consistently controlled than room scale research. Experimental setup can significantly influence the detected VOC levels in different environments. Geographical factors such as temperature, humidity and outdoor ozone and VOC levels, along with project-specific factors such as position and height of samplers; how often samples are taken, sampling duration; how often samplers are recalibrated and room and building ventilation all influence indoor VOC levels, and descriptions of these factors must be included in research papers to facilitate robust comparisons. Few studies in the existing literature measure or record building ventilation rates, which clearly directly influence indoor VOC concentrations, and which may vary substantially with time within buildings [67]. Skin secretion studies are susceptible to interference from personal care products [68,69], and the surface chemistry of building materials, which is in turn influenced by temperature and humidity, is a critical aspect of VOC analysis [70]. The presence of dust and other particulate matter and VOCs from pets and plants, and the "background air problem" make both data collection and interpretation challenging in *in situ* studies, causing variability in background air quality in different settings [69,71]. It is thus recommended that a 'blank', or occupant-free analysis of air samples should be included in any HVOC emission sampling procedure to identify baseline VOC patterns and identify potential confounding emissions [69].

Additional, comparable research is essential to create a robust basis for understanding HVOCs indoors. Many studies consider the presence and absence of VOCs in correlation with diseases and controls [68] However it is understood that many of the VOCs previously thought absent are still present in healthy subjects [72,73], only at very low concentrations [74]. Hence, the focus is shifting from presence or absence to the concentration levels of VOCs [50]. Hence, a database of metrics to both identify HVOCs and compare their concentrations between subjects with different health states, with an inclusion of the variability recorded, would be of significant value.

4.3. Considerations regarding controls and contributing factors

There are complex challenges in attributing definitive sources in HVOC studies due to the coexistence of both primary and secondary sources and often neglected components like alkanes in some studies [75]. Standards for validating HVOC metabolites are crucial; it is possible that there may be mistaken assignations in original publications, especially concerning isomers. A significant gap exists in validating compounds present in the human volatilome, emphasizing the need for proper validation in line with existing metabolomic standards [68]. The human *exposome*; the environment in which humans live, is highly individual, and the associated compounds can undergo conversion in our bodies, contributing to a wide range of differences in the human volatilome. Volatile constituents can be naturally produced (endogenous) or exogenous when they are produced by an interaction with external exposure, such as by inhalation or contact [75]. The likelihood of different exposure levels to the same compounds among individuals further complicates this scenario [68]. It is established knowledge that the variability in human breath HVOCs and associated biomarkers can result from differences in sampling methodologies, inherent human variability, complex compound interactions in breath, and confounding signals from comorbidities [21]. Since the severity of an illness has been shown to correlate to a change in HVOCs [76], it is thus essential that a standard definition of 'healthy' as regards HVOCs be defined; stress, mood, sleep, microbiome, and gut health have all been noted in literature as factors which affect the metabolome and hence, HVOC emissions [77].

Some secondary human-related VOC emissions may not fall within the top 20 VOCs but are still worth noting. Human skin oil and lipids are characterised by a high proportion of squalene ($C_{30}H_{50}$) a semi volatile VOC which is readily oxidised within indoor environments [78]. Squalene is transferred to surfaces such as bedding, furniture and flooring through direct physical contact, here it reacts with ozone producing secondary oxidation products including 4-oxopentanal (4-OPA) and 6-methyl-5-hepten-2-one (6-MHO) which is known to cause skin and airflow irritation at a concentration range of 0.3–0.5 ppm [79]. Liu et al. [80] investigated the impact of squalene ozonolysis within a 350 m^3 100 year old timber house (floor area ~140 m2) and a low occupancy level (2 occupants), and indoor ozone concentrations within 2–4 ppb. During occupancy 6-MHO production reached a rate of 0.056 ppb/h, and once the room was vacated the rate of 6-MHO production was maintained at 0.045 ppb/h for the first hour and then 0.023 ppb/h for ~130 h after. It was concluded that 'off-body' skin flakes and oil is a more significant contributor to secondary oxidation that 'on-body' VOCs. Alongside squalene the oxidation of *cis*-hexadec-6-enoic acid (which makes up to 6% of skin surface lipids by weight) has also been observed as a major contributor to 6-MHO and 4-OPA production within simulated office spaces [81]. The ozonolysis of these secondary human VOCs and the emitted products have significant human exposure implications. it is important to recognise that the health effects which are associated with ambient indoor ozone may coincide with these products of indoor ozone chemistry [82].

4.4. Considerations regarding real world application; emission rates and skin/ozone reactions

The findings of the current study reveal the presence of both endogenous and exogenous VOCs, with more VOC species detected in indoor environment studies than in those specifically examining breath and skin samples, as expected. However, the current literature still lacks sufficient data to accurately discern the role of the indoor environment on *in situ* HVOC samples. To better elucidate the relationship between indoor occupants' emissions and their environment, more studies that include replicate testing of indoor spaces with and without occupants would providing a strong baseline for comparison.

It is evident that the more hazardous VOCs present in the volatilome would rarely cause indoor air to exceed toxic levels. Despite significant research since the publication of the compendium [31], there are clear parallels between this review and the previous work, in terms of the prevalence of chemical groups and the consistent detection of acetone and isoprene as the two most common HVOCs. The emissions of these compounds do not pose significant toxicity risks. It is nonetheless

suggested that further research be targeted towards identifying circumstances, if any, where HVOCs can accumulate to levels where they may become toxic, along with further developing our understanding of the role they have in TVOC and IAQ levels. This is of course dependent on emission rates of VOCs. Recent work by Wang [83] demonstrated that in the absence of ozone, individuals emitted an average of 2180 ± 620 μg per hour per person, primarily from exhaled substances. Tang recently published emission rates from several VOCs measured in a classroom, and determined the emission rates per person of acetone at 106 μg per hour per person, acetic acid at 329 μg per hour per person, isoprene 162 μg per hour per person, and monoterpenes at 187 μg per hour per person. Stönner [38] and colleagues determined the emission rates of selected gaseous species from individuals seated in a cinema, with comparable results: acetone at 419 μg per hour per person, acetic acid at 205 μg per hour per person, isoprene 166 μg per hour per person, and monoterpenes at 201 μg per hour per person, with the prominent difference being emitted ethanol in the cinema was double that recorded in the classroom at 216 μg per hour per person, which was hypothesised to be due to evening alcohol consumption. As stated previously, human emissions of VOCs are strongly dependent on ozone level [81,84]. In ozone-rich environments (approximately >35 ppb), the overall emission rate from the body has been shown to double, primarily due to VOCs resulting from reactions between skin surface lipids and ozone, which are particularly influenced by relative humidity [85]. Many dermally emitted VOCs originate from the reactions of ozone with reactive constituents in skin lipids, in addition to the metabolic processes within the human body [86]. For example, ozonolysis of squalene forms acetone, 6-MHO, and geranyl acetone as the major first-generation volatile products, and 4-OPA as a key second-generation product [83,87].

Although not widely recognized, a potentially important source of ozone-reactive compounds in regularly occupied spaces is human skin oil, both on occupants and on nonoccupant surfaces [88]. Better defining the occurrence of ozone chemistry with skin oil on occupant and nonoccupant surfaces furthers our understanding of the ways in which occupant emissions influence human chemical exposures indoors [89–91]. Further, human emission rates of certain nitrogen-containing compounds can increase in ozone-rich environments [83,92]. These compounds likely created from reactions between emitted ammonia and ozonides formed from skin/ozone interactions [93]. Interestingly, the emission rates of volatile organic compounds (VOCs) shows weak correlation with ammonia emission rates in ozone-free conditions conducted at moderate temperatures [83].

These findings depict the typical human emission rates of individuals in real-life settings, applicable for assessing indoor air quality and designing buildings [94,95]. When considering the potential exposure impact, and thus considering the health implications of the emission rates, fundamental knowledge of various factors, including, gas-surface interactions, indoor atmospheric reactions, environmental influences on human exposure, and the toxicity of these emerging pollutants is required. Comprehensive information on these aspects is presently unavailable, and is worthy of continued research [80].

5. Conclusion

This paper presents a review of human emitted volatile organic compounds based on the literature published since 2010. Twenty-eight papers were included, resulting in the production of metadata for HVOC and compared to the 2014 compendium [31]. The review highlights several issues:

Human VOC emissions test results are lacking. More experiments using larger datasets with consistent experimental set-up information that report the following are needed (in no particular order).

- o Total number of compounds identified
- o VOCs identified by both mass spectral library and retention time with CAS number and chemical group
- o Concentration or emission data along with statistical metrics for variability
- o Clear methodology stating at minimum i) number of total occupants ii) number of samples iii); Information on sampling area including i) number of persons in room ii) area of room iii) general description of ventilation
- o Test ambient air quality: Preliminary ozone, NOx and formaldehyde readings before and after testing
- o Robust replication and disclosure of the number of samples taken. More data which is comparable will allow further characterisation of HVOC emissions

It is proposed that the factors identified in this report will be developed by researchers experimenting in this space and a standard is developed to facilitate a more transferrable and consistent research methodology. It is further proposed that subsequent research includes more densely populated indoor environments such as offices, gyms, retirement homes and schools, the spaces commonly most occupied, and most susceptible to IAQ problems resulting from high HVOC concentrations.

CRediT authorship contribution statement

Peter. J Irga: Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Gabrielle Mullen:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Robert Fleck:** Writing – review & editing, Conceptualization. **Stephen Matheson:** Writing – review & editing, Visualization. **Sara. J Wilkinson:** Writing – review & editing, Supervision, Project administration. **Fraser. R Torpy:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors have declared no conflict of interest, financial or otherwise.

Data availability

No data was used for the research described in the article.

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