Indoor PM2.5, VOCs and asthma outcomes: A systematic review in adults and their home environments

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Abstract

Introduction: As the amount of time people spend indoors increases globally, exposure to indoor air pollutants has become an important public health concern. Asthma is a complex disease caused and/or exacerbated by increased exposure to diverse chemical, physical and biological exposures from multiple indoor and outdoor sources. This review aims to investigate the relationship between increased indoor PM and VOC concentrations (i.e. objectively measured) and the risk of adult asthma in higher-income countries.

Methods: Eleven databases were systematically searched on the February 1, 2019 and again on the February 2, 2020. Articles were limited to those published since 1990. Reference lists were independently screened by three reviewers and authors were contacted to identify relevant articles. Backwards and forward citation chasing was used to identify further studies. Data were extracted from included studies meeting our eligibility criteria by three reviewers and assessed for quality using the Newcastle-Ottawa scale designed for case-control and cohort studies.

Results: Twelve studies were included in a narrative synthesis. We found insufficient evidence to determine the effect of PM2.5 on asthma in the indoor home environment. However, there was strong evidence to suggest that VOCs, especially aromatic compounds, and aliphatic compounds, were associated with increased asthma symptoms.

Discussion & conclusion: Although no single exposure appears to be responsible for the development of asthma or its associated symptoms, the use of everyday products may be associated with increased asthma symptoms. To prevent poor health outcomes among the general population, health professionals and industry must make a concerted effort to better inform the general population of the importance of appropriate use of and storage of chemicals within the home as well as better health messaging on product labelling.

1. Introduction

The prevalence of asthma among children and young people has been well documented (Asher et al., 2006; Pearce et al., 2007; Lai et al., 2009), but fewer studies have investigated asthma in adulthood. While rates vary (BLF, 2019; Mukherjee et al., 2016), it is thought that around 10% of adults have doctor-diagnosed asthma in the United Kingdom (U.K.). This represents one of the higher prevalence rates in the world (Netuveli et al., 2005) and poses a significant economic and societal burden (Takaro et al., 2011; Salo et al., 2014). Asthma is a complex heterogeneous disease characterised by airway inflammation, which can be caused and/or exacerbated by increased exposure to diverse chemical, physical and biological exposures (Sharpe et al., 2015b). Chemical, physical and biological exposures within the home are a public health concern as the amount of time people spend indoors increases. For example, Europeans now spend 89% of time indoors (McGratha et al., 2017). Around 70% of this time is in the home environment (Klepeis et al., 2001; Schweizer, 2007; Torfs et al., 2008), which increases to around 90% in vulnerable populations such as the very young, the infirm and the elderly (Torfs et al., 2008; Spalt et al., 2016).

The interaction between indoor biological agents such as house dust mites and mould has been well documented (Sharpe et al., 2015a).
Fewer studies have investigated the potential impact of indoor particulates (PM2.5 and PM10) and volatile organic compounds (VOCs) such as formaldehyde (WHO, 2010). The concentrations of indoor PM and VOCs are largely dependent on resident behaviours (e.g. cooking, heating and environmental tobacco smoke), the presence of damp and mould (presence of microbial VOCs) and the reintroduction of chemicals into the home environment (e.g. new furnishings and building products (Sharpe et al., 2014). Increased exposure to indoor PM and VOC concentrations are thought to increase the risk of asthma (Arif and Shah, 2007a; Kwon et al., 2018; Guarnieri and Balmes, 2014; Hulin et al., 2012) and can enhance the bronchial responsiveness to other allergens in sensitised individuals (Casset et al., 2006). However, prior studies have reported inconsistent evidence between formaldehyde and VOCs and risk of asthma (Hussain et al., 2019; Patelarou et al., 2015). The risk of childhood asthma and interest in these exposures (e.g. particulates increases oxidative stress and inflammation in the lungs (Mir, 2007)), has led to a number of prior reviews investigating elevated PM and VOCs and childhood asthma (Kelly and Fussell, 2015; Patelarou et al., 2015; Dick et al., 2014; Al-daghri et al., 2013). Fewer studies have focused on the interaction between indoor PM and VOCs and asthma in adulthood. Furthermore, prior studies have used a variety of proxy measures of indoor air quality (Jaakkola and Knight, 2008), rather than objective measures. To our knowledge, no prior studies have systematically reviewed studies concerning the indoor concentrations of elevated PM and VOCs (objectively measured) in higher income countries and the development and/or exacerbation of asthma in adulthood, which is the focus of this study. This is of public health interest because it provides an opportunity to inform future health intervention strategies.

2. Methods

2.1. Search strategy

In accordance with our study protocol (PROSPERO reference: CRD42018110070), electronic searches of 11 databases were conducted on the February 1, 2019 and again on the February 2, 2020. Searches were conducted across 11 databases (Cochrane Library (Wiley), MEDLINE (via the OVID platform), AMED, Web of Science, Scopus, Environment Complete (EBSCO), GreenFile (EBSCO), EMBASE (via the OVID platform), British Nursing Database, Applied Social Sciences Index and Abstracts (ASSIA), ScienceDirect and the TRIP Database). The World Health Organization (WHO) and the Department for Environment Food and Rural Affairs (DEFRA) were also searched. The search string included the following terms related to respiratory health; asthma, wheeze, cough, dyspnea, bronchitis, bronchial hyperactivity and bronchial spasms; and the following pollutants/exposures, particulate, PM2.5, PM10, volatile organic compounds, formocresols and benzene. To fully understand the impact of indoor air quality on respiratory health, a systematic review of studies using objective measures of indoor air quality were needed. Observing this gap in the literature, we updated our protocol to include studies that used only objective measures of indoor concentrations of PM and/or VOCs. The full search strategy is available on PROSPERO reference: CRD42018110070.

Forward and backward citation searches were conducted alongside contacting all authors of included studies to identify additional studies. The screening process was managed in Endnote version X8.2 (Thomas Reuters, New York, NY) and recorded using the PRISMA guidelines. Articles were independently screened by three team members (C.A.P., R.A.S and K.M) at title and abstract. The full text of articles meeting the inclusion criteria were obtained and screened by the three reviewers. Where there was any disagreement, a fourth reviewer (T.T) was consulted, and any discrepancies resolved through discussion.

2.2. Eligibility criteria and study selection

Included articles consisted of those reporting associations between the indoor home environment and objective measures of PM and VOCs exposure and risk of developing and/or the exacerbation of asthma (Fig. 1). The populations investigated encompassed adults aged over 18 years and both sexes. Studies deemed eligible for the analysis comprised:

1. Original peer-reviewed journal articles publishing primary data
2. English language studies
3. Cohort; case-control studies; randomised control trials; non-randomised control trials; cluster-randomised trials and cross over trials
4. Studies published in 1990 or later (due to rise in publications in this area of research after this date)
5. Investigation of the indoor home environment
6. Studies which identify objective measures of PM and/or VOCs and report level of risk as Odds Ratio or Relative Risk (crude and adjusted models)
7. Studies with outcomes of asthma ever and/or asthma symptoms in the last 12 months (including wheeze, whistling in the chest or a dry cough), doctor-diagnosed asthma (e.g. peak flow or spirometry), and initiation/development of asthma requiring newly diagnosed cases of asthma by a physician or doctor.

2.3. Data extraction

Relevant study and participant characteristics were extracted using a data extraction, which was adapted from the Cochrane guidelines for systematic review (Furlan et al., 2009). The data extraction form was subsequently used to populate data synthesis tables developed using the PROGRESS plus framework, which applies equity when reporting findings (O’Neill et al., 2014).

2.4. Quality assessment

Included studies were assessed for quality by two review authors (C.A.P, R.A.S) using the Newcastle-Ottawa Scale (NOS) (Wells et al., 2009) customised for cross-sectional studies (Herzog et al., 2013). This scale assesses population selection, study comparability, and ascertainment of exposure and outcomes, to yield a maximum of ten points for cross-sectional studies (Herzog et al., 2013). A maximum of five points can be awarded for selection, two for comparability and three for the outcome. It was decided a priori that if disagreements persisted a third review author (KM) would be consulted. Studies were independently assigned an overall score out of 10. Consensus on the risk of bias scores was reached by two review authors (C.A.P, R.A.S) and a third reviewer was not required. Detailed notes on the decisions made with reference to the quality scoring for each paper is available from the authors on request.

3. Results

3.1. Synthesis

Due to significant heterogeneity, we provide an overarching synthesis of 12 studies that met our inclusion criteria; (Arif and Shah, 2007b, Balmes et al., 2014, Billionnet et al., 2011, Hulin et al., 2013, Jarvis et al., 1996, Levesque et al., 2001, Norback et al., 1995, Frisk et al., 2009; Simoni et al., 2002, 2004, Wieslander et al., 1997, Dales and Cakmak, 2019).

3.2. Risk of bias of individual studies

Included studies varied in terms of assessed NOS quality (Table 1). The majority were deemed medium quality according to the NOS, which suggests potential inclusion of bias. There is also significant heterogeneity between studies and therefore, the potential for reporting bias, resulting from studies collecting and reporting data inconsistently. For
this reason, studies were prioritised according to their quality rating score and considered as low (<4), medium (5–7) and high (>8) quality. All 12 studies included studies measured VOCs (Simoni et al., 2002, 2004, Frisk et al., 2009, Levesque et al., 2001, Hulin et al., 2013, Billionnet et al., 2011, Bentayeb et al., 2013, Norbäck et al., 1995, Arif and Shah, 2007b, Wieslander et al., 1997, Dales and Cakmak, 2019); only one study measured just PM (Balmes et al., 2014). Studies have been grouped in our synthesis according to those reporting;

- Increased risk of spirometry-diagnosed asthma through exposure to particulate matter or VOCs
- Increased risk of self-reported asthma through exposure to particulate matter or VOCs
- Increased risk of asthma symptoms through exposure to particulate matter or VOCs

3.3. Study and participant characteristics

Three studies were performed before 1999 and nine after this time. Included studies were from five countries and included cross-sectional, cohort and case-control design methodologies (Table 1). Two studies were conducted in the USA, three in France, three in Sweden, two in Canada and two in Italy. Not all studies reported whether they had investigated rural or urban environments.

The characteristics of the participants were generally reported in detail across the studies (Table 1). The participants were all adults as defined by the inclusion criteria with the exception of the (Levesque et al., 2001 and (Dales and Cakmak, 2019)) study which included adult and child pairs, however, due to the focus of this review, only data relating to adults was considered. Recruitment was generally a random sample of the population designed to be representative of the general population. Six studies reported on ethnicity; however, this was not consistent across the studies. No studies reported any religion, disability or time-dependent relationships. Social-economic status (SES) was recorded in seven studies and reported in six. We grouped education and employment with SES as health opportunities, outcomes and SES are generally closely linked. Six of these studies reported on education and employment.

3.4. Study design characteristics of included studies

Eleven studies were cross-sectional, and one study was a case-control study with one day follow up. Recruitment, funding and statistical analyses differed between studies. Significant heterogeneity between study designs including the defined exposure and outcomes prevented the use of meta-analysis (described below).

In total, three studies measured PM 2.5 (Table 2). The study by Levesque et al. (2001) measured PM10. In terms of PM monitoring techniques, similar techniques were utilised in two of the studies (active sampling with Dorr Oliver type pre-selector) (Simoni et al., 2002) (Simoni et al., 2004), in one study sampling was via nephelometer and recorded three measurements of 3-min duration. Where VOCs were measured these were generally broken down into aldehydes, hydrocarbons and glycol ethers. VOC concentrations were monitored with reasonable consistency across studies in both duration and sampling location. For 10 studies, VOCs were measured continuously in either the bedroom or living room for one week with the exception of Wieslander et al. (1997) and Arif and Shah (2007a, 2007b). Measures were collected via one measurement in the bedroom over 2 h and by personal exposure over 48–72 h in these cases. Sampling techniques for the VOCs
were similar and consisted of diffusive sampling. While all studies measured concentrations of PM and/or VOCs, all studies (Levesque et al., 2001; Wieslander et al., 1997) reliably assessed the interaction between PM or VOC concentrations and health outcomes measured.

All studies used self-administered questionnaires to obtain data on the various health-related of interest. The majority of the health-based measures of respiratory health; the Mini Wright peak flow meter for PEF and an EasyOne Spirometer for FEV1. A reduction in per cent predicted FEV1 is suggested to be more closely related to the incidence of chronic respiratory symptoms in the general population than other measures of lung function impairment (Jakeways et al., 2003), and therefore a useful measure in this review.

 Objective measurements of the independent variables were used in six studies. Three studies examined formaldehyde separately from other included VOCs. Three studies also recorded temperature and relative humidity in the properties.

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**Table 1**

Summary of participant characteristics of included studies.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Study population</th>
<th>Non-respondents</th>
<th>Urban/rural, region</th>
<th>% Female</th>
<th>Ethnicity</th>
<th>SES</th>
<th>% Current Smokers</th>
<th>Current Asthma %</th>
<th>Final quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frisk et al. (2009)</td>
<td>Sweden</td>
<td>Adults aged 19–54 y</td>
<td>No details</td>
<td>Orebro</td>
<td>63</td>
<td>Not reported</td>
<td>Occupation</td>
<td>24</td>
<td>No details</td>
<td>2/10</td>
</tr>
<tr>
<td>Levesque et al. (2001)</td>
<td>Canada</td>
<td>Adults aged 23–52 y</td>
<td>No details</td>
<td>Within 50 km Quebec</td>
<td>86.5</td>
<td>No details</td>
<td>Family income recorded but not reported</td>
<td>No details</td>
<td>No details</td>
<td>4/10</td>
</tr>
<tr>
<td>Alrif and Shah (2007b)</td>
<td>USA</td>
<td>Adults aged 20–59 y</td>
<td>No details</td>
<td>No details</td>
<td>51.2</td>
<td>Non-Hispanic whites, Mexican, Americans, Non-Hispanic blacks, Other race/ethnicity</td>
<td>13.7% below the poverty line</td>
<td>26.8</td>
<td>12.3</td>
<td>4/10</td>
</tr>
<tr>
<td>Norback et al., 1995</td>
<td>Sweden</td>
<td>Adults aged 20–44 y</td>
<td>14 who didn’t attend medical investigation, 12 who were unreachable, 14 refused exposure measurements</td>
<td>Urban, Uppsala</td>
<td>72</td>
<td>No details</td>
<td>No details</td>
<td>No details</td>
<td>No details</td>
<td>6/10</td>
</tr>
<tr>
<td>Simoni et al. (2002)</td>
<td>Italy</td>
<td>Adults aged 15–72 y</td>
<td>No details</td>
<td>Po River Delta</td>
<td>51.4</td>
<td>No details</td>
<td>No details</td>
<td>No details</td>
<td>No details</td>
<td>6/10</td>
</tr>
<tr>
<td>Simoni et al. (2004)</td>
<td>Italy</td>
<td>Adults aged 15–72 y</td>
<td>No details</td>
<td>Urban, Pisa Rural, Po Delta Uppsala</td>
<td>50.9</td>
<td>No details</td>
<td>No details</td>
<td>No details</td>
<td>No details</td>
<td>6/10</td>
</tr>
<tr>
<td>Wieslander et al. (1997)</td>
<td>Sweden</td>
<td>Adults aged 20–44 y</td>
<td>Non-responders did not differ from participants in age, gender and smoking status</td>
<td>Urban, Suburban, Rural, Northern California, 19 regions</td>
<td>73.5</td>
<td>Non-Hispanic white 58.9%</td>
<td>High school education</td>
<td>7.9</td>
<td>41.4</td>
<td>6/10</td>
</tr>
<tr>
<td>Balmes et al. (2014)</td>
<td>USA</td>
<td>Adults aged 18–50 y</td>
<td>Non-responders were younger and more likely smokers</td>
<td>Urban, Suburban, Rural, Northern California, 19 regions</td>
<td>52</td>
<td>French 96%</td>
<td>Education</td>
<td>27</td>
<td>No details</td>
<td>6/10</td>
</tr>
<tr>
<td>Bentayeb et al. (2013)</td>
<td>France</td>
<td>Adults aged 15–89 y</td>
<td>No details</td>
<td>74 municipalities, 19 regions</td>
<td>52.1</td>
<td>French 96%</td>
<td>Employed 47.9% Higher education 52.25% 83.9% Household income above $1000 96.1% educated greater than high school</td>
<td>27</td>
<td>8.6</td>
<td>8/10</td>
</tr>
<tr>
<td>Billionnet et al. (2011)</td>
<td>France</td>
<td>Adults aged 15–89 y</td>
<td>No details</td>
<td>74 municipalities, 19 regions</td>
<td>52.1</td>
<td>French 96%</td>
<td>Employed 47.9% Higher education 52.25% 83.9% Household income above $1000 96.1% educated greater than high school</td>
<td>27</td>
<td>8.6</td>
<td>8/10</td>
</tr>
<tr>
<td>Dales and Cakmak (2019)</td>
<td>Canada</td>
<td>Adults aged 17–19 (children measured in the study but excluded from this analysis)</td>
<td>No details</td>
<td>Two sites in each of Atlantic Canada, the Prairies, and British Columbia, and four sites in Quebec, and six in Ontario.</td>
<td>50.9</td>
<td>Caucasian 76.5%</td>
<td>Household income above $1000 96.1% educated greater than high school</td>
<td>No details</td>
<td>9.3</td>
<td>8/10</td>
</tr>
<tr>
<td>Hulin et al. (2013)</td>
<td>France</td>
<td>Adults aged 26–60 y</td>
<td>Were younger, more of foreign nationality, and lower educational level</td>
<td>Urban, rural, periurban</td>
<td>51.6</td>
<td>Nationality</td>
<td>Recorded but not reported</td>
<td>26.2</td>
<td>8.4</td>
<td>9/10</td>
</tr>
</tbody>
</table>

Norbäck et al., 1995). The same sampling techniques were utilised for all measurements of respiratory health; the Mini Wright peak flow meter for PEF and an EasyOne Spirometer for FEV1. A reduction in per cent predicted FEV1 is suggested to be more closely related to the incidence of chronic respiratory symptoms in the general population than other measures of lung function impairment (Jakeways et al., 2003), and therefore a useful measure in this review.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>Study size</th>
<th>Follow up</th>
<th>Exposure of interest</th>
<th>Exposure measurement</th>
<th>Definition of asthma</th>
<th>Outcome measure</th>
<th>Final quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frisk et al. (2009)</td>
<td>Cohort</td>
<td>49</td>
<td>13 months</td>
<td>Temp &amp; RH Co2, No2, Formaldehyde ETS, 15 respiratory allergens (not stated other than pets)</td>
<td>Diffusion sampling</td>
<td>A physician-diagnosed asthma, current use of asthma medicine, attacks of breathlessness and episodes of wheezing</td>
<td>Self-assessment diary, FEV1 and vital capacity (V. C.), Histamine provocation test, Blood samples, PEF, SFT</td>
<td>2/10</td>
</tr>
<tr>
<td>Balmes et al. (2014)</td>
<td>Cross-sectional</td>
<td>549 Interview 302 Home visit 707 Pisa</td>
<td>N/A</td>
<td>Particulate Matter 2.5</td>
<td>Nephelometer</td>
<td>No clear definition</td>
<td>Spirometry, questionnaire</td>
<td>Symptom diary, PEF</td>
</tr>
<tr>
<td>Simoni et al. (2004)</td>
<td>Cross-sectional</td>
<td>Pisa 707 Po Delta 383</td>
<td>N/A</td>
<td>PM2.5, No2</td>
<td>Passive sampling</td>
<td>Chronic bronchitic and/or asthmatic symptoms (i.e., sputum from the chest, shortness of breath, attack of shortness of breath, and wheeze) without the presence of fever and the reported presence of infection.</td>
<td>PEFF</td>
<td>6/10</td>
</tr>
<tr>
<td>Simoni et al. (2002)</td>
<td>Cross-sectional</td>
<td>383</td>
<td>N/A</td>
<td>Respirable suspended particulate (RSP) (&lt;2.5μg/m3), NO2</td>
<td>Passive sampling</td>
<td>Chronic bronchitic and/or asthmatic symptoms (i.e., sputum from the chest, shortness of breath, attack of shortness of breath, and wheeze) without the presence of fever and the reported presence of infection.</td>
<td>PEFF</td>
<td>6/10</td>
</tr>
<tr>
<td>Levesque et al. (2001)</td>
<td>Case-control</td>
<td>89</td>
<td>1 day</td>
<td>CO, NO, HCHO, PM10. Used self-reported presence of fumes in assessing health outcomes.</td>
<td>Gillian HFS 113 pump/Diffusion monitoring</td>
<td>Asthma defined as complicated lower respiratory tract illness which also included wheezing or respiratory difficulties, medical diagnoses of pneumonia, bronchitis or asthma attacks.</td>
<td>Questionnaire</td>
<td>4/10</td>
</tr>
<tr>
<td>Hulin et al. (2013)</td>
<td>Cross-sectional</td>
<td>897</td>
<td>N/A</td>
<td>Total VOcs: 4 aldehydes (acetaldehyde, acrolein, formaldehyde, hexaldehyde), 12 hydrocarbons (benzene, 1,4-dichlorobenzene, ethylbenzene, n-decane, n-undecane, styrene, tetrachloroethylene, toluene, trichloroethylene, 1,2,4-trimethylbenzene, m/p-xylene, o-xylene), and 4 glycol ethers (2-butoxyethanol, 2-butoxyethylecetate, 1-methoxy-2-propanol, 1-methoxy-2-propylacetate).</td>
<td>Passive diffusion sampling</td>
<td>A positive response to: &quot;Have you had an attack of asthma in the last 12 months?&quot; or &quot;Are you currently taking medicines for asthma?&quot; and &quot;Have you been woken by an attack of shortness of breath at any time in the last 12 months?&quot;</td>
<td>Questionnaire</td>
<td>9/10</td>
</tr>
<tr>
<td>Billionnet et al. (2011)</td>
<td>Cross-sectional</td>
<td>1612</td>
<td>N/A</td>
<td>20 VOCs including 4 aldehydes, 12 hydrocarbons ad 4 glycol ethers</td>
<td>Radial diffusive sampling</td>
<td>As suggested by ECRHS: (i) having an asthma attack in the last 12 months; (ii) having been woken by an attack of shortness of breath in the last 12 months; and (iii) currently using asthma medicine</td>
<td>Questionnaire</td>
<td>8/10</td>
</tr>
<tr>
<td>Bentayeb et al. (2013)</td>
<td>Cross-sectional</td>
<td>1012 Individuals 490 Homes</td>
<td>N/A</td>
<td>Aldehydes: formaldehyde, acetaldehyde, acroleine, hexaldehyde. - Aromatic hydrocarbons: benzene, toluene, m/p-xylene, o-xylene, 1,2,4-trimethylbenzene, ethylbenzene, styrene. - Aliphatic hydrocarbons: n-decane, n-undecane; halogenated hydrocarbons:</td>
<td>Radial diffusive sampling</td>
<td>No clear definition</td>
<td>Questionnaire</td>
<td>6/10</td>
</tr>
</tbody>
</table>

(continued on next page)
Table 2 (continued)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>Study size</th>
<th>Follow up</th>
<th>Exposure of interest</th>
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<th>Definition of asthma</th>
<th>Outcome measure</th>
<th>Final quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norback et al., 1995</td>
<td>Cross-sectional</td>
<td>154</td>
<td>N/A</td>
<td>trichloroethylene, tetrachloroethylene, 1,4-dichlorobenzene; Glycol ethers: 1-methoxy-2-propanol, 2-butoxy ethanol, 2-butoxyethylacetate, 1-methoxy-2-propylacetate.</td>
<td>Direct reading instrument based on light scattering/ Diffusion sampling</td>
<td>Attacks of asthma during the past 12 months, nocturnal breathlessness in the past 12 months, or current use of asthma medication.</td>
<td>Blood samples, Interviews, SPT, FEV1, PEF, Methacholine challenge</td>
<td>6/10</td>
</tr>
<tr>
<td>Arif and Shah (2007b)</td>
<td>Cross-sectional</td>
<td>9965 Interview 9282 Physical exam 669 Exposure monitoring</td>
<td>N/A</td>
<td>Benzene Chloroform Ethylbenzene Tetrachloroethene (TCE) Toluene, trichloroethene, o-xylene, m,p-xylene, 1,4-dichlorobenzene, and methyl tertiary butyl ether (MTBE)</td>
<td>Personal exposure via a passive monitoring device</td>
<td>Positive response to the question “Has your doctor or other health professional ever told you that you have asthma?”</td>
<td>PEF</td>
<td>4/10</td>
</tr>
<tr>
<td>Wieslander et al. (1997)</td>
<td>Cross-sectional</td>
<td>Interview, blood tests, SPT, bronchial provocation 699 Q aire building characteristics, occupation, and symptoms 562 Subsample 62</td>
<td>N/A</td>
<td>Temperature, Humidity, VOCs, Formaldehyde</td>
<td>Passive sampling</td>
<td>A combination of bronchial hyper-responsiveness (BHR) and at least one symptom related to asthma. Symptoms related to asthma were recorded when subjects reported in previous 12 months: (1) wheezing or whistling in the chest or (2) at least one daytime attack of shortness of breath during exercise or while resting; (3) at least one night time awakening because of breathlessness or tightness in the chest</td>
<td>Questionnaire, SPT, FEV1, PEF, Methacholine challenge, blood</td>
<td>6/10</td>
</tr>
<tr>
<td>Dales and Cakmak (2019)</td>
<td>Cross-sectional</td>
<td>2846</td>
<td>N/A</td>
<td>Limonene</td>
<td>Diffusion sampling with Carbopack B 60/80®</td>
<td>Asthma: “We are interested in “long-term conditions” which are expected to last or have already lasted 6 months or more and that have been diagnosed by a health professional. Do you have asthma?”</td>
<td>FeNO FEV1 FVC Questionnaire</td>
<td>8/10</td>
</tr>
</tbody>
</table>

3.5. Results of studies included in our narrative synthesis

3.5.1. Increased risk of asthma through exposure to particulate matter

Conclusive evidence of the relationship between indoor PM2.5 and asthma outcomes in adults is lacking (Table 3). No high-quality evidence was found that measured risk of either development or exacerbation of asthma via a measure of spirometry in relation to exposure to PM2.5. Two medium-quality studies (Simoni et al., 2002, 2004) measured PM2.5 and found that high levels of exposure were associated with increased PEF maximum amplitude and variability. However, the studies primary outcome focus was on indoor pollution and associated acute respiratory symptoms and mild lung function impairment rather than asthma specifically. Although the studies are indicative of lung function changes, assumptions cannot be drawn between exposure to PM2.5 and increased PEF variability in this instance. Only one study of medium quality found that exposure to particulate matter in the kitchen at 21 μg/m3 was associated with increased odds of asthma-like symptoms, this was true in men but not women (Balmes et al., 2014).

3.5.2. Increased risk of asthma through exposure to volatile organic compounds

We found evidence to suggest that exposure to VOCs in the indoor home environment increases the risk of asthma and asthma-related symptoms (Table 3). One study of high-quality evidence (Dales and Cakmak, 2019) identified a 15% (95% CI: 1.14, 1.16) increased risk of asthma via measure of spirometry following a 100% increase in exposure to Limonene, a naturally occurring terpene (aliphatic compound). This may induce sensitisation and had been found to be associated with increased airway hyper-responsiveness in other studies (Norback et al., 1995). One medium quality study found wood and kitchen painting to be associated with an increased risk of asthma symptoms (OR 1.43; 95% CI: 1.01–2.06), bronchial hyper-reactivity, nocturnal breathlessness and current asthma via measure of spirometry. In this case, the most commonly detected compounds were aromatic and aliphatic compounds, aliphatic compounds and TXB (Wieslander et al., 1997).

One study which was deemed to be of high quality and one of low-quality found an increased risk of asthma via measures of self-reported exposure to both aromatic and aliphatic compounds. An
additional two medium quality evidence studies found an increased risk of asthma-like symptoms following this exposure. High-quality evidence indicated that n-undecane and 1,2, 4-trimethylbenzene were significantly associated with asthma (OR 2.02; 95% CI: 1.18–2.85). Using adjusted marginal models, positive associations between asthma and global VOC scores were also observed suggesting the risk of asthma to be 1.07 times higher for exposure to each additional VOC with a high exposure level (OR 1.07; 95% CI: 1.00–1.13). For individuals exposed to five additional VOCs, the risk was increased by 40%. There was no difference reported between sex.

Two specific VOC scores were significantly associated with an increased risk of asthma: aromatic hydrocarbons (OR 1.12; 95% CI: 1.01–1.24) and aliphatic hydrocarbons (OR 1.41; 95% CI: 1.03–1.93) (Billionnet et al., 2011). In contrast, a high quality study by Hulin et al. reported insignificant findings between measured exposures of total VOCs and risk of current asthma (OR 1.01; 95% CI: 0.99–1.03), chronic bronchitis (OR 1.02; 95% CI: 0.99–1.05) and chronic bronchitis like symptoms (OR 1.02; 95% CI: 0.98–1.02).

Arif and Shah (2007a, 2007b) conducted personal exposure monitoring of 669 individuals and found statistically significant odds of physician-diagnosed asthma for individuals exposed to aromatic compounds (OR 1.63; 95% CI: 1.17–2.27). When observing aromatic compounds individually, there was suggestive evidence that Toluene was associated with a 21% increased odds of physician-diagnosed asthma (OR 1.21 95% CI: 0.93–1.58) but the confidence intervals crossed unity. However, the study was deemed to be of a low-quality rating due to the definition used in the study to describe asthma and the outcome measures used.

A medium quality study, using personal exposure monitoring tools (Bentayeb et al., 2013), also identified that individuals without asthma were at increased risk for experiencing symptoms, with a significantly increased risk of asthma (OR 1.12; 95% CI: 0.88–1.48). However, the study was deemed to be of a low-quality rating due to the definition used in the study to describe asthma and the outcome measures used.
increased odds of one to two wheezing attacks observed following exposure to aromatic compounds (adj OR 1.68 95% CI: 1.08–2.61) and chlorinated hydrocarbons (adj OR; 1.50 95% CI: 1.01–2.23) compared to no wheezing. The odds of experiencing three or more wheezing attacks following exposure to benzene were nearly twofold (adj OR 1.85 95% CI: 1.13–3.04) (Arif and Shah, 2007b). The study further suggests a relationship between Toluene and o-xylene (aromatic compounds) and nocturnal breathlessness, a symptom of asthma, in the elderly (Bentayeb et al., 2013). Other VOCs related to increased asthmatic symptoms were formaldehyde but the evidence was limited. One medium quality study found formaldehyde in the bedroom to be associated with nocturnal breathlessness (Norback et al., 1995).

4. Discussion

To our knowledge, this is the first systematic review investigating the links between elevated indoor concentrations of PM and VOCs and risk of asthma in adulthood. The current evidence linking increased indoor concentrations of PM to adult asthma is limited. Despite some mixed findings, this systematic review provides collective new evidence that in adults, aromatic and aliphatic compounds in the indoor home environment are associated with an increased risk of asthma in adulthood. Further, individuals without a diagnosis of asthma or history of respiratory illness are more likely to experience symptoms related to asthma such as wheeze and shortness of breath as a result of exposure VOCs, especially when exposure is at high concentration. We also found PEF variability in relation to respiratory symptoms that could be suggestive of asthma, but the evidence is inconclusive.

The risk of developing and/or exacerbating of asthma depends on a complex interaction between diverse environmental exposures. Resultant outcomes concerning both atopic and non-atopic asthma depends on the timing and extent of exposure resulting from exposure to diverse and overlapping interactions between physical, chemical and biological agents throughout the life course from early childhood into adulthood (Sharpe et al., 2015c). Each of these interactions and the potential impact on health relies on a number of largely modifiable environmental factors including leaks in building fabric, heating and ventilation patterns etc, but also, everyday indoor habits including for example from the presence of environmental tobacco smoke in the homes through to the use and choice of cleaning products (Sharpe et al., 2014). For example, previous authors have already highlighted the dangers of aerosolised domestic cleaning products on respiratory health, noting an increased incidence of asthma following exposure (Buckley, 2007; Zock et al., 2010). To raise awareness of the potential health risks, policymakers and industry alike need to take a more concerted effort in protecting public health by better informing them of the associated health risks by raising awareness and using more explicit health warnings on product labels detailing the importance of adequate ventilation specific to the product.

From a research perspective, there is a need for better exposure measures and case definition of asthma greater adoption of indoor sampling of diverse pollutants, asthma outcomes across the included studies because these were inconsistent and, in some cases, poorly defined. Better case definition must be adopted by future research to enable clearer and more thorough investigations into such vital areas. Furthermore, there is insufficient evidence to determine whether any increased risk of asthma is modified by sex at present. Given that the majority of caregivers are women (Sharma et al., 2016) and individuals spend their day in, means that a meta-analysis approach may not have been appropriate for such a review.

6. Conclusion

While advances in medicine and research mean that the heterogeneity of immunology of asthma is increasingly understood, there is a need for a greater understanding the role of diverse indoor exposures, risk of disease endotypes (Lotvall et al., 2011) and phenotypes (Darveaux and Busse, 2015). In response, this systematic review provides new evidence to suggest that VOCs such as aromatic and aliphatic compounds in the indoor home environment are associated with an increased risk of asthma and asthma-like symptoms (including wheeze) in adults. As noted, individuals are exposed to a complex mix of biological, chemical and physical agents across their life course. To prevent poor health outcomes individuals, health professionals and industry must make a concerted effort to better inform the general population of the importance of appropriate use of, and storage of chemicals, as well as better health messaging on product labelling. This review indicates the need for further investigation on the impacts of indoor air pollution on health and wellbeing using objective measures, and the need for consistency in the reporting of studies to ensure comparability.

CRediT author statement

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Declaration of competing interest

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

References


