A literature review of evidence on cleaning products and occupational risks for asthma

Prepared by the Health and Safety Executive
Occupational asthma is a debilitating illness, caused by exposure to hazardous substances in the workplace. The UK cleaning sector employs nearly half a million people using a variety of products and processes that have the potential to cause respiratory diseases.

A review of the published scientific literature was undertaken to summarise evidence about cleaning products that may increase the risk of occupational asthma. The overall breadth, consistency and quality of the evidence were assessed.

There were few high quality studies and only three related specifically to the UK cleaning sector. From the available evidence, there was consistent evidence that certain types of cleaning work were associated with an increased risk of developing asthma and/or experiencing respiratory symptoms consistent with asthma, both new cases and exacerbations of pre-existing conditions.

An excess of asthma and respiratory symptoms were reported in studies of healthcare workers and domestic cleaners; this excess may reflect a selection bias for studies favouring these populations.

A broad spectrum of cleaning products was reported to cause respiratory symptoms, particularly chlorine-liberating agents and bleaches. Spray application of cleaning products was also associated with increased risk for respiratory disease.

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A literature review of evidence on cleaning products and occupational risks for asthma

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KEY MESSAGES

1. There is evidence that acute inhalation exposure to cleaning product constituents and persistent low level exposures from routine cleaning tasks may be linked to the development of occupational asthma, exacerbation of pre-existing asthma (and potentially other respiratory conditions) and also the development of irritant symptoms in those without asthma.

2. An excess of asthma and of respiratory symptoms compatible with asthma were described in studies of healthcare workers and domestic cleaners. This excess in healthcare workers and domestic cleaners may reflect a selection bias for studies favouring these populations.

3. A broad spectrum of cleaning products was reported to elicit respiratory symptoms in exposed cleaners, in particular chlorine/bleach products. Use of spray delivery devices for cleaning products was associated with an increased risk for respiratory tract exposure and respiratory symptoms.

4. Due to the variability in diagnostic approaches, symptom reporting, clinical testing and frequent absence of exposure monitoring, it is more difficult to establish consistent evidence about specifically which cleaning products or their constituents, or cleaning tasks, cause occupational asthma.
EXECUTIVE SUMMARY

Occupational asthma (OA) is a debilitating illness caused by exposure to hazardous substances in the workplace. The UK cleaning sector employs approximately half a million people across a broad range of settings and uses a variety of products and processes, some of which may have the potential to cause or exacerbate respiratory diseases such as asthma.

A review of the published scientific literature was undertaken to summarise evidence about cleaning products, their ingredients, and cleaning processes that may increase the risk of occupational asthma and respiratory symptoms of asthma.

Fifty-nine papers were identified through a structured search of the literature published between 1994 and 2014. The review included evidence about the risks for occupational asthma, and symptoms characteristic of asthmatic responses, attributed to exposure to chemical or biological cleaning agents. The breadth, consistency and quality of this evidence were assessed. In addition, specific details concerned with respiratory disease and cleaning work, such as the circumstances of exposure (i.e., cleaning processes and products used) and other risk factors were considered.

- There were few high quality studies and only three related specifically to the UK cleaning sector.
- There was consistent evidence that certain types of cleaning work were associated with an increased risk of developing asthma and/or experiencing respiratory symptoms consistent with asthma, both new cases of disease as well as exacerbations of pre-existing conditions. However, variability in diagnostic approaches, symptom reporting and clinical testing across studies meant that it was difficult to establish specifically which cleaning products, constituents or other factors caused OA or elicited asthma symptoms.
- Cleaners were subject to both acute and chronic inhalation exposures to cleaning product constituents. These chronic exposures may be linked to the development of OA but there was consistent evidence that acute exposures exacerbated pre-existing asthma or elicited irritant and obstructive respiratory disorders.
- An excess of asthma and respiratory symptoms was reported in studies of healthcare workers and domestic cleaners. Chemical irritants such as chlorine/bleach were frequently reported to elicit respiratory symptoms in exposed cleaners. Spray application of cleaning chemicals was also associated with an increased risk for respiratory disease.
- The length of time working in the cleaning industry and an allergic predisposition to common environmental allergens were considered factors contributing to the risk of respiratory symptoms compatible with asthma.
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1. INTRODUCTION

1.1 BACKGROUND

There is evidence of an association between cleaning and the development of occupational asthma (OA) and respiratory symptoms compatible with asthma, particularly in certain sectors, i.e., healthcare and domestic cleaning. Research provided evidence for an association between exposure to cleaning products and new onset adult asthma in Great Britain (GB). In a cohort study of ~10,000 individuals born in 1958, the prevalence of new onset adult asthma by age 42 was about twice as high among those ever working in cleaning-related jobs than those only ever having worked in office-based jobs (Ghosh et al, 2013). The authors of the study reported the risk was over 60% higher in those having been 'ever' exposed to cleaning and disinfecting products than those unexposed.

An association between occupational exposure to cleaning agents and new onset adult asthma has been previously highlighted in the European Community Respiratory Health Survey (ECRHS) and a subsequent follow-up survey (Zock et al, 2001 and 2007). In contrast, in GB, data from 'The Health and Occupation Research Network-Surveillance of work-related and occupational respiratory disease’ (THOR-SWORD) suggested that the relative risk amongst "cleaners and domestics" for new onset occupational asthma is relatively low. For example, during the period 2008-2010 the average annual incidence was estimated to be 0.9 per 100,000 for cleaners and domestics compared to 66 per 100,000 in spray painters and 61 per 100,000 in bakers and flour confectioners.

Factors that may explain the difference between the GB data and the study by Ghosh et al, 2013 may include the relative power of the 1958 cohort study to identify an association compared to SWORD; it is also considered likely that significant under-reporting of respiratory disease by cleaners leads to many cases going unrecognised within occupational ill health reporting schemes.

Overall, therefore, the evidence currently available indicates that cleaning or exposure to cleaning products may be associated with the development of OA. Cleaners are present across all workplaces and it is not known if this association with OA is general to all cleaners or may be focussed on some cleaning work or certain cleaning products. Furthermore, it is not known if OA in some cleaners is hidden because they work in a sector where work-related illness is not readily associated with cleaning in their profession.

The cleaning industry in the UK is a growing sector with current estimates placing the workforce at around 450,000 employees. It accounts for work in domestic, health care, industrial, food, buildings and other settings with operations ranging from self-employed and SME cleaning companies to large multinational cleaning service providers. The diversity of the industry extends to the processes and products used. As technology and businesses continue to develop, the cleaning industry will also need to adapt.
Research Aim

The purpose of this review was to summarise the published evidence around whether or not cleaning product ingredients or cleaning processes increase the risk of developing occupational asthma and/or experiencing respiratory symptoms compatible with asthma.

The intention was to clarify the strength of the evidence for an association between cleaning and OA and whether this association applies to all types of cleaning activities or for particular work practices.

This review provides a short summary of the published evidence about asthma and reported respiratory symptoms attributable to work with cleaning agents. It considers data and other information from a relevant range of workplaces and population health studies identified using specific search criteria.

If a relationship between cleaning and OA is identified, this information could help to underpin future research, to identify whether there are practical solutions to minimise any risks identified, or whether cleaning processes could be altered to reduce exposure and therefore risks for occupational asthma.

1.2 ASTHMA AND ASTHMA-LIKE SYMPTOMS

This review includes evidence about risk of developing OA and symptoms characteristic of asthmatic responses which can be attributed to exposure to chemical or biological agents in cleaning products. Other types of respiratory disease attributable to cleaning chemicals have not been included in the review. Asthma is defined in terms of a combination of symptoms such as wheeze, breathlessness, chest tightness and cough, particularly if these symptoms are worse at night and in the early morning, or are present during exercise, following exposure to allergens or cold air, or after taking aspirin or beta blockers. A history of atopy (predisposition to develop allergy to common environmental allergens such as pollen or dust mites), and/or a family history of asthma and/or atopic disorders are also relevant. Typically, serial peak expiratory flow (PEF) measures are variable in asthma. Therefore resting lung function, such as the forced expiratory volume in one second (FEV$_1$), may either be normal or abnormal. Consequently, there is no single diagnostic lung function test for asthma. An increase in eosinophils (white blood cells that play a pivotal role in immune development and asthma) in the peripheral circulation is common (Scottish Intercollegiate Guidance Network (SIGN) 141: British guideline on the management of asthma. A national clinical guideline: October 2014).

OA is clinically characterised by the presence of variable airflow limitation and bronchial hyper-responsiveness due to causes and conditions encountered in an occupational environment and not outside the workplace (Bernstein et al, 1993). The condition can appear after a long period of exposure (long latency; for example 10 years of flour dust exposure) but exposure to certain chemicals and irritant substances can result in the onset of asthma without latency, so called acute irritant induced asthma (formerly termed reactive airway dysfunction syndrome).

Occupational hazards may also aggravate pre-existing asthma; for example non-specific factors such as cold or dry air, exertion, or dust and fumes. This latter situation is termed work aggravated asthma (WAA) and both OA and WAA are types of work-related asthma. Whether lower dose irritant
exposure causes asthma is far more controversial and requires further work before developing a more definitive stance (Fishwick et al, 2008 and Baur et al, 2012).

Occupational respiratory irritants include many low molecular weight volatile chemicals but also dusts and powders. Studies of cleaners have reported increased risks for respiratory disease and proposed a link to new cases of asthma (Kogevinas et al, 2007; Mäkelä et al, 2011) or the exacerbation of pre-existing asthma (Arif et al, 2012; Fishwick, 2014). Some authors have also suggested that some cleaning chemicals cause irritant-induced OA (Massin et al, 2007; Mäkelä et al, 2011), acute irritant-induced asthma (sometimes also referred to as reactive airways dysfunction syndrome or RADS) (Quirce et al, 2010), as well as chronic bronchitis (Medina-Ramon et al, 2005). Although not the subject of this review, it has been suggested that chronic obstructive pulmonary disease (COPD) may be a long term outcome from these exposures (Medina-Ramon et al, 2005). This is an area that requires further work before developing a more definitive stance.

It has been suggested that late onset asthma can be linked to the use of microbial enzymes in cleaning products (Schweigert et al, 2000; Adisesh et al, 2011). These have gained increasing use because of their value in destroying pathogens and removing biological contaminants whilst reducing the environmental impact associated with chemical cleaning agents. Certain types of chemical cleaning and disinfectant agents have been considered as potential asthmagens, such as quaternary ammonium compounds, reactive biocidal agents (e.g., formaldehyde, chloramine-T) as well as colours and scents added to cleaning products. Chemical agents which have been associated with airway irritancy include detergents and surfactants, biocidal chemicals and strongly acid or alkaline solutions (Baur et al, 2012).

The studies described in this review also include cases studies of physician diagnosed asthma where a range of respiratory symptoms have been reported. Although these symptoms may be consistent with asthma, they do not always support a firm diagnosis of the condition. Therefore, for the purposes of this report, the term “asthma symptoms” refers to respiratory symptoms consistent with those observed in asthma cases (sometimes referred to as “asthma-like”), but might not necessarily be asthma. Furthermore, as causation of asthmatic disease is often difficult to establish, the terms “elicit” and “trigger” with regard to symptoms consistent with asthma, have been used where causation is not clear.
2. METHODOLOGY

A structured literature search was undertaken with a focus on key search terms relevant to the research question. A search strategy using broad and specific terms was applied (Table 1) and searches of the literature were carried out using combinations of terms. The searches were based upon proximity of the terms irrespective of their order within the document.

Table 1. Specific terms and combinations used to search the published literature.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Broad terms</th>
<th>Narrow terms</th>
<th>Specific terms</th>
<th>Specific terms</th>
<th>Specific terms</th>
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</thead>
<tbody>
<tr>
<td>Ill health (respiratory) in cleaners</td>
<td>Clean*</td>
<td>Cleaning, Clean</td>
<td>Work-related</td>
<td>Health care</td>
<td>Healthcare professionals</td>
</tr>
<tr>
<td>Health</td>
<td>Respiratory Irritant Sensitiser</td>
<td>Irritant-induced Asthma</td>
<td>Bronchial hyper-responsiveness (BHR)</td>
<td>Asthma-like BHR</td>
<td>Immunoglobulin E (IgE)</td>
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<td>Allergens</td>
<td>Chemically induced</td>
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<td>Peak Expiratory Flow (PEF)</td>
<td>Exposure Products Agents Sensitiser</td>
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<td>Dust, Spray</td>
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<td>Airborne, Exhaust</td>
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<td>Smoke, Ammonium compounds</td>
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<tr>
<td>Cleaning products and activities</td>
<td>Clean*, Product*</td>
<td>Activit*</td>
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*Denotes where a truncated term and wildcard used

Searches of the web-based databases, PubMed, ISI Web of Knowledge, and TOXNET were carried out for the years 1994-2014. Additional sources included the search engines Google and Google Scholar. Appropriate references (including abstracts) were identified and exported to Endnote™ (version 9.0) reference management database. This collection of references was then exported to TxtViz™ (version 6.1.14), a bibliographic and textual mapping tool used to identify key references.
Abstracts for peer-reviewed papers published between 1994 and 2014 were identified, and a short-list of papers was selected for full review by consensus decision amongst the research team. Principles of a full systematic literature review were followed, where the emphasis was placed on papers deemed to be relevant to the research purpose; where possible, ‘review papers’ to broaden the number of studies were included as efficiently as possible. A data extraction template (Appendix Section 7.1) was applied to ensure consistency in the information gathered from each publication. The quality of the evidence was rated using a system based on the SIGN (Harbour, 2001) which addressed some of the inherent problems with occupational health studies and identified knowledge gaps to inform future research (Section 7.2).

A total of 2,659 potential references were identified from these combined searches after duplicates were identified and removed in Endnote™. The clustering analysis softwareTxtViz™ was used tobrigate all of these papers into sets of studies with related content (based on key terms and concepts in the abstracts and titles). A total of 97 papers were identified that related to the subject of the review but, on closer examination of the abstracts, only 59 related directly to exposure and respiratory disease and occupation in cleaning (and use of cleaning products).

Of the 59 papers selected for this review, 21 focussed on recognised risk factors and were scrutinised further in order to extract detailed clinical findings. Only 4 pertinent reviews were identified, one of which was systematic; the remainder included different types of research studies. A schematic of the search, sift and review process is provided in Figure 1.
Figure 1: Schematic of the search, sift and review process of the published literature related to asthma and respiratory symptoms attributable to working with cleaning agents.
3. OVERVIEW OF THE EVIDENCE

Fifty-nine papers published between 1994 and 2014 were selected for review. The majority were individual cross-sectional studies concerned with the risks of developing asthma and symptoms compatible with asthma from occupational exposure to cleaning products and chemicals, or from working in different cleaning industries/sectors. Of the four review papers included, one by Baur et al (2012) was based on a systematic approach and summarised findings from 474 studies covering 188 cleaning agents.

The studies identified in the review presented here included research from the UK, Europe, USA, Canada, South Africa and Asia but most of these studies were focussed on specific parts of the cleaning industry. Some of the reviews concentrated on large population epidemiological studies describing risk factors across a broad range of cleaning activities in several countries or regions of the world.

Although the evidence reviewed described various cleaning sector/job types, the evidence could be categorised broadly into three areas of cleaning work:

- **Domestic cleaners**: Those workers employed to clean in the domestic/household environment
- **Healthcare workers (HCW)**: Those conducting cleaning duties in the health care setting, including cleaning and disinfection tasks in hospitals and care homes
- **Other/mixed cleaning**: Cleaning environments not included under the other two categories (e.g., office, education, industrial cleaning).

Figure 2 illustrates the proportion of the literature reviewed for each of these areas of cleaning work, and Figure 3 the distribution of publications by geographical region. Figure 4 illustrates the quality of evidence identified for each of the main areas of cleaning work based on the modified SIGN scoring criteria. The majority of papers reviewed represented cohort, population or case studies that described limitations or challenges in terms of study design and execution. As such, there were few high quality studies based on the criteria applied. The only paper achieving the highest grade (1) of evidence was the systematic review by Baur et al (2012) which included studies undertaken in the cleaning industry. There were a further 18 papers which were assigned a quality rating of 2 using a system based on the SIGN (Harbour, 2001).

The review and analysis of these papers identified some key themes. Twenty-one of the fifty-nine publications selected focussed on at least one of the key themes: cleaning as an occupation (n=9), healthcare workers (n=2), the use of bleach (n=10), and use of spray formulations (n=5). From this sub-selection of papers, seven reported physician-diagnosed asthma, eight reported a mix of physician-diagnosed (including some clinical tests) and self-reported conditions, and five were based on self-reported symptoms only. A summary of the clinical findings presented in these particular studies has been included in the Appendix (Section 7.3) to provide a view of the range of different methods that have been used to define respiratory ill health (such as self-reported symptoms, physician-diagnosed, specific inhalation challenge tests, etc.).
Figure 2: The proportion of studies (papers identified and included for review = 59) for each of three cleaning sectors (number, %).
Finding 1: Evidence base.

The current published literature covers the broad spectrum of cleaning activities but studies specifically focussed on domestic cleaners and healthcare workers were more common. There were very few GB specific studies (n = 3) with most research undertaken in the USA and Europe (in particular, Spain).
4. KEY FINDINGS

4.1 ASTHMA AND ASTHMA-LIKE SYMPTOMS

Asthma, wheeze and shortness of breath related to exposure to cleaning products were explored in the majority of studies, with additional reference to other respiratory symptoms such as nasal burning and dry cough linked to workplace exposures. However, in the large population studies, the authors frequently referred to inconsistencies in the diagnosis and reporting of symptoms as limitations that may have led to errors in estimation the number of cases (Kogevinas et al, 1999; Karjalainen et al, 2002; Zock et al, 2007; Arif et al, 2011; Vizcaya et al, 2011 Baur et al, 2012).

Although the range of respiratory symptoms reported in many cases was consistent with asthma, they were not sufficient for a firm diagnosis of the condition. Therefore, the term “asthma symptoms” has been used to refer to respiratory symptoms consistent with asthma cases, but which may not necessarily have been asthma. This variability in diagnosis and reporting of symptoms or disease reflects the variation in study designs described in the literature.

Other conditions reported to result from exposure to cleaning products included Work-Associated Irritable Larynx Syndrome (WILS) (Hoy et al, 2010), and acute irritant-induced asthma (Rosenman et al, 2003; Reinisch et al, 2001).

In the subset, there were 21 papers that offered evidence related to the risk factors: cleaning as an occupation, being a healthcare worker, use of bleach and the use of sprays. Of these, 7 papers described physician-diagnosed asthma, 5 described self-reported symptoms and diseases only, and 8 papers self-reported conditions subsequently diagnosed using specific tests (e.g., lung function tests, IgE tests, skin prick test, bronchial challenge tests, Section 7.3). Whilst physician-diagnosed cases of asthma provided the strongest evidence, studies based on self-reported symptoms contributed to the overall evidence about respiratory symptoms compatible with asthma in those working as cleaners.

The systematic review by Baur et al (2012) included evidence from other occupational circumstances that the use of cleaning agents was associated with an increased prevalence of asthma. The strongest evidence level (allocated a two star grading based on a modified Royal College of General Practitioners (RCGP) SIGN grading) was found for work with chlorine gas and ‘off-gassing’ of chlorine gas and risk for OA and COPD. Moderate evidence was also found that exposure to glutaraldehyde and cleaning agents (not specified) were relevant occupational risk factors but insufficient evidence was found linking work as a cleaner with an increased prevalence of asthma.

de Fatima et al (2007) reported a prevalence of 11% and 35% for asthma and rhinitis respectively in a population of 341 cleaners in Brazil. This estimate was based on the application of a validated respiratory symptom questionnaire (Medical Research Council) as well as lung function tests, clear definitions of asthma and OA as well as other relevant symptoms. A US population-based study, confirmed a prevalence of 12% for physician-diagnosed asthma cases linked to exposure to cleaning agents (Rosenman et al, 2003). Kogevas et al (2007) and Ghosh et al (2013) reported associations between cleaning and higher risk of adult onset asthma. In the study by Kogevas et al (2007), asthma was defined by the participant either having an asthma attack or using asthma medication.
12 months before their interview. Bronchial hyper-reactivity by methacholine challenge was also assessed.

Earlier studies by Reinish et al (2001) and Rosenman et al (2003) also reported that cleaning products commonly aggravated pre-existing asthma conditions. The study undertaken by Rosenman et al (2003) reported cases of asthma between 1993 to 1997 from state-based work ill-health reporting surveillance schemes in California, Massachusetts, Michigan and New Jersey. They found that 12% of confirmed cases of work-related asthma were associated with exposure to cleaning products, of which 80% were new cases and 20% attributed to work aggravated asthma. About a fifth of the new cases of disease were consistent with acute irritant-induced asthma. The majority of these cases worked in medical settings (39%), schools (13%), or hotels (6%), as janitor/cleaners (22%), nurse/nurses' aides (20%), or clerical staff (13%). The study by Reinish et al (2001) identified an average annual reporting rate of 625 per million for work-related asthma in janitors and cleaners compared with 25 per million for all workers in California (based mostly on historical medical records and follow up interview of 945 cases).

Orriols et al (2006), based on physician diagnoses, reported an association between asthma symptoms and acute inhalation of cleaning chemicals. Acute exposure to cleaning agents (e.g., following a chemical spill or gas leak) and bronchial hyper responsiveness (BHR) symptoms were also reported by Delclos et al (2007) using an internationally validated asthma symptom questionnaire supplemented with questions on physician-diagnosed asthma and age at asthma diagnosis.

Similarly, Kogevinas et al (1996) found associations with wheezing and airway whistling from exposure to cleaning chemicals based on self-reported symptoms, lung function tests, and bronchial provocation tests using methacholine. Exposure to irritant cleaning products was found to aggravate pre-existing obstructive lung disorders and lower airways symptoms were more common in cleaners on working days than on non-working days (Medina-Ramon et al, 2006).

Finding 2: Lung disease.

There is consistent evidence that occupational exposure to cleaning products is associated with an increased risk of reported asthma and/or “asthma symptoms”. Cleaners are potentially subject to inhalation of chemicals in some cleaning products linked to a risk of acute irritant-induced asthma.

4.2 WORK PRACTICES (TYPES OF CLEANING, JOBS OR INDUSTRY PRACTICE)

In the various studies reviewed, the prevalence of disease within populations of professional cleaners was compared with control groups (typically comprising non-cleaning occupations) to investigate the risk factors associated with work-related asthma.

The prevalence of work-related asthma in cleaners was 3.7% compared to 2.9% in management, secretarial and clerical occupations (Arif et al, 2003). However, this elevated increase was not statistically significant, and other occupations had a much higher prevalence, for example 11.9% in
agriculture-related occupations. The relative risk of asthma in cleaners versus non-manual workers across 13 countries was 1.7 (95% Confidence Interval (CI) 0.9-3.2) (Kogevinas et al, 2007). In Spain, comparing indoor (private) home cleaners with office workers, the prevalence ratio for asthma symptoms or using asthma medication was 3.3 (95% CI 1.9-5.8) and for asthma symptoms or medication plus bronchial hypersensitivity was 5.0 (95% CI 1.9-13). In other types of cleaners included in this study (including those working in schools, shops and hospitals) the prevalence of symptoms was similar to the reference group (Zock, 2001). Medina-Ramon et al (2003) compared Spanish cleaners with subjects who have never been professional cleaners and reported a prevalence rate for work-related respiratory symptoms of 12% versus 5% for those who had never worked in cleaning. Amongst the groups studied, a statistically significant risk for asthma and chronic bronchitis was observed in subjects cleaning in hospitals and other healthcare centres (odds ratio (OR) 2.5 (95% CI 1.1 to 5.8) and OR 2.2 (95% CI 1.0 to 4.8) respectively).

Hospital cleaners and HCW carrying out cleaning duties represented the group most frequently investigated by researchers, along with domestic cleaners (contract paid commercial cleaning work in a domestic setting). A study of HCW across 10 European countries revealed that 6% reported new onset adult asthma during a 9-year period, compared to 5% of the referent group (Mirabelli et al, 2007). Delclos et al (2006) and Kim et al (2013) both reported a high prevalence of respiratory problems in HCW (up to 33% population attributable risk). Studies of US HCW (including physicians, nurses, occupational therapists and respiratory therapists) and demonstrated an increased risk for asthma symptoms with exposure to cleaning agents (Delclos et al, 2007; Arif et al, 2012).

It is recognised that the cleaning activities carried out by HCW are varied, ranging from janitorial duties in hospital wards to specific disinfection procedures for hospital surgical equipment. Delclos et al (2007) reported a strong association between asthma and hospital instrument cleaning as well as general cleaning duties in the healthcare setting. In a cross-sectional survey of HCW, Arif et al (2003) reported an increased risk of physician-diagnosed work-related asthma associated with instrument cleaning. However, in only a few cases were specific HCW roles cited in the research, such as radiologists, nurses and endoscope operators. In the broader context, Pechter et al (2005) reported that nurses were at a high risk of developing work-related asthma as a result of exposure to cleaning products; 24% of all cases of work-related asthma amongst nurses (74/305) were linked to cleaning agents. In addition, combinations of cleaning tasks in the hospital setting were linked to greater risk estimates of asthma or symptoms compatible with asthma amongst HCW.

Industry-specific exposures and practices may be important in considering risks for respiratory disease. For example, Mäkelä et al (2011) reported that some chemicals such as isocyanates caused OA in cleaners in an industrial plant where they were used in the production process. Those workers engaged in equipment cleaning were at a more significant risk of developing asthma and wheeze.

BHR, wheezing and airway whistling were associated with work as a caretaker, cleaner and window cleaner (Kogevinas et al, 1996). In a study by Reinisch et al (2001), the highest rates of OA were in janitors and cleaners in a study of 945 cases of work-related asthma in California, with an annual reporting rate of 625 per million (the rate amongst managerial/professional groups was calculated to be 12 per million).
Finding 3: Working practices and risk

Respiratory symptoms were prevalent in workers across a broad range of cleaning sectors, however, HCW and domestic cleaners were frequently cited as the most at-risk group. This may in part reflect a focus of health research in HCW populations. In most cases, specific details regarding the cleaning tasks or processes associated with an excess of symptoms were not investigated or reported.

4.3 CLEANING PRODUCTS (CHEMICALS, AGENTS AND APPLICATION METHODS)

This literature review focussed on the respiratory health consequences of exposure to cleaning products and did not explore in depth the chemicals and compounds routinely used in the cleaning products. There is some evidence to suggest that the use of chemical cleaning products is linked with OA, work-related respiratory symptoms and/or adult-onset asthma. Several studies reported that exposure to cleaning products was associated with an increased risk of OA (Kennedy et al, 2000; Kogevinas et al, 2007) and adult-onset asthma (Le Moual et al, 2004).

In some of the studies reviewed, the authors explored the relationship between respiratory health and exposure to specific chemicals agents. The information provided on the frequency of use and exposure to chemicals, was predominantly based on self-reported information. Some authors referred to certain classes of cleaning agent as respiratory irritants (e.g., chlorine and ammonia) and others as respiratory sensitisers (e.g., benzalkonium chloride, chloramine, chlorhexidine, formaldehyde and glutaraldehyde) (Tarlo et al, 2008). In a series of challenge tests conducted by Mäkelä et al (2011), OA symptoms were triggered by chemicals commonly used in cleaning products and on industrial sites where cleaners were indirectly exposed e.g., ethanolamines, chloramine-T, hexamethylene diisocyanate, phenylmethane diisocyanate and nickel sulphate.

Agents cited in the wider literature as relevant hazards included bleaches, hydrochloric acid and ammonia. Off-gassing of chlorine and chloramines from bleach were the most frequently self-reported agents identified as causing respiratory symptoms in cleaning workers. de Fatima et al (2007) described exposure to chlorine accounting for 14% of all reported upper airways symptoms in a study of non-domestic cleaners.

Reports on respiratory disease and symptoms attributed to exposure to specific types of cleaning product are presented below. In some instances, the information relates to a single reported case. They have been included for completeness as examples of specific exposures that may be relevant to current industry practice but often underreported in the scientific literature.

Bleach (Sodium hypochlorite): In a US study that considered approximately 1900 physician-confirmed work-related asthma cases that occurred between 1993 and 1997, when the causative chemical was identified this usually involved disinfectants in cleaning products (38% of cases), with bleach comprising 22% (Rosenman et al, 2003). In a further study between 1993 and 2000 from the same data collection program, 9.6% of the cases of new-onset asthma associated with the use of cleaning products were attributed to bleach (Mazurek et al, 2008).
Medina-Ramon et al (2005) reported an association between the use of bleach, degreasers and sprays, and work-related lower respiratory tract symptoms, increasing with duration of exposure (length of working day); they reported an OR of 5.6 for daily cleaning time in excess of 8 hours (95% CI 1.7-19). Specific inhalation challenges with bleach resulted in significantly greater falls in FEV₁ compared to placebo challenges (Sastre et al, 2011). In a study of HCW across 13 European countries, a significantly increased relative risk (2.16, 95% CI 1.03-4.53) of new-onset asthma was observed with the use of ammonia and/or bleach more than once per week (Mirabelli et al, 2007).

In France, 175 workers in the food industry performing cleaning and disinfecting activities developed irritant respiratory symptoms following exposure to either trichloramine (nitrogen trichloride) or chlorine (Massin et al, 2007).

**Quaternary Ammonium Compounds (QACs):** QACs are chemical components used in a large proportion of disinfectant products. QACs have been linked to the development of OA and work-related respiratory symptoms in a number of case studies (Bernstein et al, 1994; Burge et al, 1994; Purohit et al, 2000; Rosenman et al, 2003). Specific inhalation challenges in mainly professional cleaners and HCW showed that in patients who demonstrated a positive reaction (>20% fall in FEV₁), 65% were induced by cleaning products containing QACs. A further 18% of the positive challenge tests were induced by cleaning products that contained glutaraldehyde (Vandenplas et al, 2013).

**Chloramine-T:** Chloramine-T is included in HSE’s Asthmagens Compendium (HSE 2001), with sufficient evidence that exposure induces asthma. It has a harmonised classification as a respiratory sensitiser at the EU level (HSE, 2001). Chloramines have been linked with respiratory symptoms compatible with asthma in HCW (Arif et al, 2012) and in two individual case studies of professional cleaners chloramine-T was implicated as causative in cases of OA and rhinitis and confirmed by skin-prick tests and bronchial-specific inhalation challenges (Kujala et al, 1995; Mäkelä et al, 2011).

**Volatile Organic Compounds (VOCs):** VOCs have been associated with irritant-induced and occupational asthma. In a small study of 44 patients, 50% of whom were professional cleaners and 36% HCW, of those with positive inhalation challenge reactions, 18% were induced by glutaraldehyde (Vandenplas et al, 2013). Work-related respiratory symptoms and OA (confirmed by diagnostic tests) were reported in smaller studies and individual case studies to be induced by ethanolamines (Savonius et al, 1994; Mäkelä et al, 2011).

**Solvents:** Individual case studies have reported OA and work-related respiratory symptoms. For example, in a worker in a dry cleaning factory, specific inhalation challenge tests confirmed that perchloroethylene was involved (Boulet, 1988). Another case in the US involved a dry-cleaning worker exposed to perchloroethylene who later developed hypersensitivity pneumonitis (Tanios, 2004).

**Polishes, degreasers and waxes:** these were also cited in a number of papers as putative agents. In a study of non-domestic cleaners by Obadia et al (2009), waxing floors, spot cleaning carpets, oiling furniture, and cleaning tiles and grout all were reported to increase work-related asthma symptoms. In addition to this, Medina-Roman et al (2006) reported that lower airway symptoms amongst cleaners were associated with exposure to diluted bleach, degreasing sprays and air fresheners. Zock et al (2001) also described a higher prevalence of asthma in those ‘ever exposed’ to polishes.
compared to those ‘never exposed’; the relative risk factors were estimated as 4.3 (95% CI 2.2-8.7) and 2.3 (95% CI 0.9-5.8) respectively.

**Acids:** Acids (and alkalis) are used to dissolve grease and used in drain and pipe cleaning products and for specialised cleaning activities. Individual case studies showing links to asthma and asthma symptoms have been reported with use of phosphoric and hydrochloric acid for degreasing engines and cleaning swimming pools (Quirce and Barranco, 2010; Boulet, 1988), use of sulphuric acid for washroom cleaning (Boulet, 1988) and hydrofluoric acid as a rust stain remover (Franzblau and Sahakian, 2003). The presumed mode of action of acids is as airway irritants exacerbating the onset or provocation of asthma symptoms.

**Ammonia:** Although ammonia is known to be an ocular and nasal irritant and is present in various domestic and commercial cleaning products (Fedoruk *et al*., 2005), little evidence has been published linking it directly with asthma and symptoms compatible with asthma. Rosenman *et al* (2003) reported that ammonia was implicated in 7% of work-related cases of asthma, where the chemical component was specified. In a case study of a hospital cleaner that developed irritant-induced asthma and rhinitis and work-related symptoms, pulmonary challenge tests confirmed ammonia and alkaline detergents to be the cause (Quirce *et al*., 2000).

**Ethylenediaminetetraacetic Acid (EDTA):** A study was undertaken in France of 28 patients with rhinitis, with or without asthma, working as cleaners or healthcare professionals and exposed to aerosolised cleaning agents. Nasal provocation tests with EDTA were positive in 37% of the patients (half of whom were cleaners). However, the authors suggested the incidence of EDTA-induced rhinitis and asthma was probably severely underestimated. EDTA is often a component in cleaning products alongside other potential known allergens which are often considered to be responsible but without further investigation (Laborde-Casterot *et al*., 2012).

**Biological agents (enzymes):** A paper by Adisesh *et al* (2011) reported several cases of HCW from UK hospitals exposed to biological cleaning agents (enzymes) which were considered to have caused the development of occupational asthma.

**Use of cleaning products in sprays:** Cleaning processes and cleaning product delivery methods may be an important factor in altering the risk of exposure. For example, the generation of aerosols of liquid, or powder, using compressed gases or spray devices (Medina-Roman *et al*., 2005; Laborde-Casterote *et al*., 2012). Other factors that increase the risk of inhalation include volatile constituents, vapours and gases released from interactions between the chemicals in the products and particularly when they react with soliant on surfaces they are applied to. Other types of equipment can generate aerosols including automated mopping systems, fume delivery devices and compressed liquid hoses used for deep cleaning operations.

**Frequency of use of cleaning products:** In a study investigating the use of cleaning products at least once a week, consistent positive associations were observed between asthma and use of cleaning sprays. For example a relative risk of 1.49 (95% CI 1.12-1.99) for using any spray and 1.71 (95% CI 1.22-2.39) for using air-freshening sprays compared to 0.94 (95% CI 0.64-1.38) for use of liquid multi-use cleaning products (Zock *et al*., 2007). Application of cleaning chemicals in aerosols and spray formulations were also associated with a greater risk of asthma symptoms and rhinitis (Laborde-
Casterote et al., 2012). In several European studies in cleaners, HCW and subjects cleaning in their own homes, the use of cleaning sprays increased the risk of asthma or asthma symptoms (Neilsen et al., 1999; Mirabelli et al., 2007; Zock et al., 2007).

**Perfumed products:** In studies based on self-reported data, perfumed products were often cited as causing respiratory issues amongst cleaners. However, this observation may in part be a result of recall bias, with cleaners more likely to recall using highly perfumed or strong smelling products.

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**Finding 4: Cleaning products**

A wide range of cleaning products is reported to cause respiratory symptoms in exposed cleaners. Volatiles such as chlorine or chloramines from bleach (along with other substances) have been identified as irritants which provoke inflammation, airway reactivity and exacerbation of pre-existing asthma. These agents are more commonly identified as hazards in studies of cleaners. Although their role in causing asthma is unclear from the available evidence, there is stronger evidence to support their contribution to respiratory disease in general in cleaners. Certain chemicals (such as Chloramine-T) and high molecular weight enzyme allergens are identified as asthmagens but most of the evidence about them comes from small case studies of cleaners with respiratory illness. The method of dispensing cleaning products is an important consideration, with aerosol and spray formulations associated with increased risk of respiratory exposure.

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**4.4 OTHER RISK FACTORS**

Besides chemicals constituents in cleaning products, a number of additional risk factors were also cited in the literature reviewed.

The formulation processes and application of products are important factors with respect to risk of exposure (e.g., pouring of chemicals and aerosol/spray application). Poor labelling of hazardous products (by manufacturers/suppliers) and a lack of user knowledge and training are contributory risk factors. Additionally, inappropriate mixing of incompatible cleaning products may lead to the generation of respiratory hazards (Rosenman et al., 2003) and acute inhalation of mixed chemical cleaning products is associated with respiratory symptoms (wheezing) in professional cleaners (Vizcaya et al., 2011). A small number of studies have reported cases where bleach has been mixed with an acid and the resultant exposure to irritant gases (chlorine) has caused symptoms compatible with asthma. Table 2 highlights a number of cases describing work-related symptoms associated with mixing cleaning chemicals.
Table 2: Case studies of mixing chemical cleaning products

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Cleaning activity</th>
<th>Mixture</th>
<th>Diagnosis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Household cleaning</td>
<td>Bleach with hydrochloric acid</td>
<td>Acute irritant-induced asthma (RADS)</td>
<td>Deschamps (1994)</td>
</tr>
<tr>
<td>55</td>
<td>Household cleaning</td>
<td>Bleach with hydrochloric acid</td>
<td>Acute irritant-induced asthma (RADS)</td>
<td>Gorguner (2004)</td>
</tr>
<tr>
<td>1</td>
<td>Cleaning worker</td>
<td>Bleach with malic acid and sulphamic acid</td>
<td>Work-exacerbated asthma</td>
<td>Mapp (2000)</td>
</tr>
<tr>
<td>1</td>
<td>Cleaning</td>
<td>Bleach with phosphoric acid</td>
<td>Diagnosed work-exacerbated asthma</td>
<td>Centers for Disease Control (1991)</td>
</tr>
</tbody>
</table>

In a small number of studies, gender was cited as a risk factor. Reinsch et al (2001) proposed that non-occupational domestic exposures were more common in females and have an additive effect on occupational exposures, resulting in a higher prevalence of symptoms. By contrast, in some industries, acute exposures were thought to be more prevalent in males tasked with heavy lifting and pouring of cleaning chemicals (and therefore more prone to exposures from spillages). It is possible, though, that these differences relate to gender-oriented societal roles in workplaces and domestic settings rather than intrinsic gender-specific differences in sensitivity.

In addition, cleaners operating in the domestic setting and exposed to dust mite and moulds, may show increased susceptibility to high molecular weight allergens when also occupationally exposed to chemical cleaning products. Work-related asthma and wheeze were more likely to occur in atopic individuals. Arif et al (2003) noted a non-significant association between atopy and the prevalence of work-related asthma. Kogevinas et al (1996) observed a higher risk of asthma in atopics working with cleaning products, however, this observation was also not statistically significant.

The prevalence of work-related asthma and rhinitis amongst cleaners in Brazil was reported by de Fatima et al (2007) to be 3% for domestic cleaners who had worked less than a year and 41% for those who had worked as a non-domestic cleaner for 6.5 years or more, and followed a significant linear trend.

Some of the risk factors reported in the papers reviewed are perhaps of less relevance to the present day in that these exposure risks are either on the decline or non-existent. For example, there has been a decline in the use of potent sensitisers such as glutaraldehyde previously used in cleaning disinfectant products. However, the introduction of biological cleaning agents (such as microbial industrial enzymes) to replace chemical hazards, may create a new risk scenario for
cleaners since some of these enzymes are asthmagens. General improvements in working conditions (in particular the healthcare setting) were also referenced as factors helping to reduce risks.

### Finding 5: Other Risk Factors

The length of time working in the industry may increase the risk of developing symptoms and there may be a greater risk to those who undertake regular domestic cleaning duties with exposure to other chemicals and protein allergens e.g., house dust mites. Atopy may also be associated with an increased prevalence of work-related respiratory symptoms in cleaners.

### 4.5 LIMITATIONS OF THIS REVIEW

Most studies reviewed for this report were not specifically focussed on the cleaning industry. The majority reported findings from large epidemiological studies encompassing a broad spectrum of occupations and exposures, including cleaners and cleaning products. Therefore, this evidence is limited in its relevance to cleaning as an occupation and the extent to which it provided meaningful data on exposure to specific cleaning products or chemicals. In a study of cleaners in the healthcare sector by Arif et al (2012), nurses were the second most populous group investigated but ‘day to day’ they undertook a broad range of duties of which cleaning may have been a small component; consequently their exposure to cleaning products may have been limited.

This literature review is focussed on asthma and reported respiratory symptoms consistent with asthma in cleaners. However, not all of the available studies had this focus: some were less specific and relied on participants either to recall their symptoms experienced years previously, or the authors amalgamated diagnostic information from historical medical records. The authors of these studies recognised their findings were subject to diagnostic inconsistencies, which were even more problematical in large population studies across different countries and regions (ECRHS, 2004). Only a few papers reviewed here described physician-diagnosed asthma, the majority were population cohort studies based on self-reported symptoms subsequently categorised as asthma by the authors (e.g., as occupational, new-onset or work-aggravated asthma). In some cases studies, self-reported symptoms were followed up and tests undertaken to confirm the diagnosis of asthma or relevant disease symptoms. However, the respiratory tests undertaken or the weighting of the results varied between studies making an assessment of the prevalence of disease challenging. Work by Fishwick et al (2008) to prepare a UK Standards of Care for OA was in part a response to earlier findings suggestive of diagnostic inconsistencies in the GB and a need for a more accurate standardised approach to assessing cases of OA.

Where the study design was dependent on self-reported disease or symptoms, issues of recall bias and potential misreporting and misrepresentation of the findings were limitations. This applied to workers exposed to cleaning chemicals and products, the cleaning tasks undertaken, duration and frequency of use of the products. The results of a study of exposure to household cleaning products by Zock et al (2007) suggested an element of over-reporting by those exposed to highly perfumed cleaning products but the relationship between use of perfumed products and increased risk of
asthma was not established. This may be due to a greater awareness of perfume and its association with respiratory symptoms.

In all of the papers reviewed, exposures were implied on the grounds of job type or category (using Standard Occupational or Industrial Classification codes: SOC/SIC, or other matrices of exposure). Some of the studies were limited by small population size with a focus on a limited number of cleaning industry sectors (e.g., an emphasis of research amongst HCW groups in USA and Europe).

Many of the studies investigating ill-health in cleaners were based on self-reported information and the numbers of cleaning agents listed in the survey questionnaires was often small which may have led to misclassification of exposures. Furthermore, the circumstances in which many of these cleaning products were used (e.g., confined spaces, limited ventilation, delivery using sprays) were unknown. Direct exposure monitoring data typically was not collected or used in combination with health measurements. Although “spray” delivery systems were cited, this is a broad term and may not account for differences in exposure between aerosols, pump and foam “sprays”.

Many studies were subject to the inherent weaknesses in occupational health studies such as bias due to the ‘healthy worker’ effect (Neilsen et al, 1999), small test populations, and difficulties in establishing representative control or well defined reference population groups. In addition, the potential for socio economic and lifestyle factors to confound results of studies by impacting on symptoms and work attribution as a result of multiple chemical or organic exposures in the home may be important (Reinisch et al, 2001).

Other possible limitations in these studies included the transitory nature of employment in parts of the cleaning industry resulting in poor response rates and difficulty following participants in longitudinal studies. Geographical or cultural differences may also have influenced cleaning practices with an associated impact on exposure.

**Finding 6: Study limitations and design**

The evidence was limited by challenges synonymous with occupational health research: small sample sizes in specific groups, suitability of reference ‘control’ populations, ‘healthy worker’ effects and recall bias through self-reporting. Diagnostic inconsistencies, variable health reporting schemes and confounding (health) factors were also cited as limitations.

### 4.6 KNOWLEDGE GAPS

The lack of clarity on the biological mechanisms by which respiratory disease results from exposure to cleaning products was commented on by many authors, in particular whether the symptoms reported were irritant in nature or due to immunological sensitisation. Although specific components of cleaning products were cited as hazards, knowledge is weak in this area. Furthermore, there is little knowledge about the impact of using mixed/diluted products and how this may affect the toxic potency or risk of exposure. Information around the frequency and impact of improper or misuse of cleaning chemical products was not available through the published literature.
Knowledge of specific exposures and practices was lacking and as with any industry, changes in trends, practices and the evolution of chemical products were in constant flux. Such important information can only be obtained from the industry itself. This requires engagement with the UK cleaning industry and those manufacturing and supplying cleaning products to gain a clear understanding of these issues.

Future research in this area would benefit from accurately measured exposure data and consistent use of accurate diagnostic criteria in reporting schemes for occupational respiratory disease. Similarly, the design of job exposure matrices that account for the variety and subtleties within the cleaning industry are required to help identify exposures to specific groups of cleaners.

The current evidence suggests an association between certain types of cleaning work and chemicals in cleaning products and the risk for developing OA or symptoms compatible with asthma.

**Finding 7: Knowledge gaps**

The mechanism by which cleaning products cause asthma or elicit symptoms consistent with asthma, is still unclear for most cleaning product ingredients that have been linked to these outcomes. There is evidence that in some cleaning products, chemicals cause irritant reactions in the airways and symptoms of asthma, or they may aggravate pre-existing asthma. Some chemicals or biological agents may also be sensitisers and cause asthma but the evidence for this is mostly based on small case studies and inhalation challenge tests. However, for many cleaning products containing mixtures of chemicals, the link between causative agent(s) and asthma and asthma symptoms is less clear. Similarly, there is less well developed evidence that low dose exposure to irritant chemicals causes asthma.

Deficiencies in diagnostic approaches and health definitions, reporting schemes and limited job exposure matrices all contribute to the lack of clear evidence on this topic.
5. MAIN CONCLUSIONS

- The published research (1994-2014) on risks for asthma and reported respiratory symptoms compatible with asthma in cleaners, focussed mostly on domestic cleaners and HCW. Only a small number of these studies were considered high quality based on their design because of the inherent limitations in studying ill health in occupational groups compared to the general population. Only three studies conducted in the UK were identified through this review (two of which described case reports from the healthcare setting) with most undertaken elsewhere in Europe or the USA.

- The published research was consistent in reporting that occupational exposure to cleaning products was associated with increased risk for reporting asthma and symptoms compatible with asthma. However, most studies were based on self-reporting of symptoms and exposure and therefore the strength of link between OA and exposure to specific chemicals or cleaning products was not always clear. There was stronger and more consistent evidence that exposure to chemical irritants in cleaning products can elicit respiratory symptoms and exacerbate pre-existing asthma and these mechanisms add to the overall burden of respiratory disease in cleaners.

- Cleaners can be subject to both acute and long-term exposure to chemicals. The use of certain cleaning product delivery systems (e.g., sprays) was associated with an increased risk of exposure which could cause irritant symptoms, exacerbate existing asthma and potentially trigger acute irritant-induced asthma.

- Emission of volatile chemicals such as chlorine from cleaning/disinfection products can occur when these products are not used properly, leading to similar outcomes.

- Chronic exposure to some cleaning products may be more important in considering allergic sensitisation or asthma, but specific evidence about the mechanisms applying to chemical allergens is limited.

- Asthma and symptoms consistent with asthma have been reported in studies that considered workers operating across a broad range of cleaning sectors, however, HCW and domestic cleaners were consistently reported to be at risk, an outcome that may reflect bias towards studying these working groups.

- Specific details about cleaning tasks and processes associated with asthma or asthma symptoms were not commonly reported and most studies categorised workers in broad terms (e.g., the type of cleaning work undertaken or cleaning product used in circumstances of either domestic or professional cleaning/disinfection work).

- A broad range of chemical ingredients in cleaning products has been reported as airway irritants or allergic sensitisers. Chlorine liberating agents and bleaches were commonly recorded as respiratory irritants and identified in studies of cleaners, although their role in causing asthma and associated health end points is unclear. However, their contribution to respiratory disease in general in cleaners is based on consistent evidence. Chemicals such as chloramine-T and high
molecular weight industrial enzymes are recognised asthmagens but evidence about these agents mostly comes from small case studies of cleaners.

- The method of using and applying cleaning products may add to the risk for asthma and respiratory symptoms compatible with asthma. There is some evidence that the application of cleaning products using spray delivery systems increases the risk for respiratory tract exposure and disease.

- The studies reviewed identified other factors that may contribute to the risk for asthma and respiratory symptoms. The length of time working in the industry; exposures outside of work as a result of domestic cleaning duties and co-exposure to common environmental allergens (e.g., house dust mites, moulds) may also be important risk factors. Atopy has been associated with an increased risk for developing work-related asthma and respiratory symptoms in cleaners.

- The mechanisms by which cleaning chemicals cause asthma or symptoms compatible with asthma are still unclear for most product ingredients. There is evidence to support some chemicals irritating the airway, and aggravating pre-existing asthma. There is evidence that certain chemicals are asthmagens but usually based on small cases studies.

- For many cleaning products containing mixtures of chemicals the link between the reported disease, symptoms, and causative agent(s) is less clear. Similarly, there is less evidence that low-dose exposures to irritant chemicals cause asthma. However, high exposures to certain cleaning agents can cause acute irritant induced asthma.
6. REFERENCES


Boulet LP. (1988) Increases in airway responsiveness following acute exposure to respiratory irritants. Reactive airway dysfunction syndrome or occupational asthma? *Chest*; 94: (3) 476-481.


7. APPENDICES

7.1 DATA EXTRACTION FORMS

Cleaning Products and Occupational Risks for Asthma and ‘Asthma-Like’ Respiratory Disease

Stage 1.1 To summarise published evidence about asthma and ‘asthma-like’ disease attributable to work with cleaning chemicals.

This summary will include peer-reviewed published studies that have examined whether occupational asthma and ‘asthma-like’ disease can be attributed to exposure to cleaning agents or to occupation as a cleaner. Studies over the last 20 years as well as numbers of reviews (including systematic reviews and meta-analysis of data) will be included; however, given the few systematic reviews other narrative reviews and larger primary studies will be accessed to help assess the strength of the published evidence. The summary will focus on:

- The types of asthma and ‘asthma-like’ disease attributable to work with cleaning agents (excluding asthma conditions made worse by these chemicals).
- The types of cleaning agents, or cleaning work, that have been linked to asthma and asthma-like conditions.
- The strength of the relationship reported (i.e., risk factors and confidence estimates).
- The quality of the studies (the methodology used, the size of the study population, comparison with non-exposed ‘comparator’ populations).
- Where studies have investigated other respiratory disease outcomes and suggest sufficient evidence of a causal relationship, these outcomes will be noted as areas for potential investigation in future.

Asthma/Asthma-like conditions

Asthma

Acute irritant-induced asthma (also termed reactive airways dysfunction syndrome; RADS)

Chronic bronchitis and chronic obstructive pulmonary disease (COPD)

Respiratory irritancy, including hyper reactive airway responses as result of chemical activation of neurosensory pathways

Inclusion/Exclusion criteria

Studies within the last 20 years only (1994 to the present) will be included

Relevant reviews, primary studies and narrative reviews will be considered

Relevant papers from UK, Europe and worldwide will be considered

Studies focussed on disease linked to exposure to chemicals/products that are no longer used (e.g., glutaraldehyde) will be excluded.

Details of the paper examined (Include author, title, year of publication, journal title, pages)

<table>
<thead>
<tr>
<th>Date completed:</th>
<th>Summary completed by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of</td>
<td>Systematic review with meta-analysis of data</td>
</tr>
<tr>
<td>review / summary paper</td>
<td>Systematic review</td>
</tr>
<tr>
<td>------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>1</td>
<td>Are the studies summarised addressing only occupational risk factors for asthma/like conditions?</td>
</tr>
<tr>
<td>2</td>
<td>What types of occupational risk factors were examined by the studies reviewed?</td>
</tr>
<tr>
<td>3</td>
<td>If this is described as a systematic review or meta-analysis is the methodology used clearly stated (e.g., Cochrane, SIGN etc.) in the methods section of the paper?</td>
</tr>
<tr>
<td>4</td>
<td>Is the review methodology used clearly described?</td>
</tr>
<tr>
<td>5</td>
<td>Have criteria for exclusion / inclusion of studies been stated clearly?</td>
</tr>
<tr>
<td>6</td>
<td>How many separate studies were included in the review / summary?</td>
</tr>
<tr>
<td>7</td>
<td>What is the range of size of the populations that were studied (give lower and upper boundary for the range of studies reported)?</td>
</tr>
<tr>
<td>8</td>
<td>Were the majority of the studies of large (&gt;10,000), medium (1000-10,000) or small cohorts (&lt;1000)?</td>
</tr>
<tr>
<td>9</td>
<td>What were the comparison control groups (state if not included); were these internal occupation control groups (e.g., non-exposed) or external general population controls?</td>
</tr>
<tr>
<td>10</td>
<td>What occupations/cleaning practices were included?</td>
</tr>
<tr>
<td>11</td>
<td>What were the characteristics of the populations studied (male only, male/female, young, elderly)?</td>
</tr>
<tr>
<td>12</td>
<td>Were the studies mainly carried out in the UK, Europe and US or other countries?</td>
</tr>
<tr>
<td>13</td>
<td>What was the main conclusion(s) of the review in terms of the evidence for CVD caused by risk factors (preferably occupational, or if general risk factors are these relevant to occupation)?</td>
</tr>
<tr>
<td>14</td>
<td>Were risk estimates summarised and if so what was the size of these risk estimates (if only a few studies reviewed summarise risk estimates here, alternatively add page and table reference to data summarised in the paper)?</td>
</tr>
<tr>
<td>15</td>
<td>Does the review describe the summary findings in terms of the strength, weight, or sufficiency of evidence?</td>
</tr>
<tr>
<td>16</td>
<td>Do the authors identify caveats that need to be considered when interpreting the results of these studies? If so what were identified as the major caveats?</td>
</tr>
<tr>
<td>17</td>
<td>Were any significant knowledge gaps identified?</td>
</tr>
<tr>
<td>18</td>
<td>Were the risk factors regarded as historical (ie, declining) current, or part of a growing upward trend in risk?</td>
</tr>
</tbody>
</table>
| 19 | Other factors that may need to be considered  
a) Where a study reported or presented evidence related to types of respiratory disease other than asthma or asthma like, what were these?  
b) No relevant systematic reviews identified but recent narrative reviews available what were the main conclusions (*some of the questions above cannot be answered if the review was not systematic*)?  
c) No review(s) identified but a large single study relevant to an occupational risk factor identified (*in which case describe methodology and results in relevant sections above*) |
| 20 | Other references/links  
List any other papers/links/references highlighted in the paper that may be of value to the review (these can be checked against the original “sift” of papers for the topic for completeness). |
7.2 EVIDENCE RATING

Papers reviewed were assigned an evidence rating using a modified version of the Scottish Intercollegiate Guidelines Network (SIGN) for describing levels of evidence presented in each paper. This simplified rating (scaled between 1-4 in order of decreasing quality of evidence) was applied to identify those findings that were well supported by the evidence presented.

SIGN defines the quality of evidence as: “the extent to which confidence in an estimate of the effect is adequate to support recommendations”. These quality criteria can be applied to the following:

1. The design of the study (e.g., non-analytic studies, case reports; case control or cohort studies, systematic reviews of case control or cohort or studies, meta-analyses of such studies, and the results of randomised controlled studies).

2. The likelihood that the results of these studies were confounded or biased (as a result of insufficient power, or poor design).

Other factors that were relevant in ranking the papers were:

3. The size of the populations studied.

4. The characteristics of the study population(s) (and controls if included).

5. The nature of the intervention and follow up period in the study.

6. The nature of the outcome measures (quantitative or qualitative) and any measurable effect size that resulted from the intervention.

- I: systematic review or meta-analysis of RCTs, or at least one RCT.
- II: at least one well-designed controlled or quasi-experimental study without randomisation.
- III: well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, case-control studies and case series.
- IV: expert committee reports, opinions and/or clinical experience of respected authorities (also, non-systematic reviews).
## 7.3 EVIDENCE SUMMARY

Subset of the reviewed literature focussed on cleaning as an occupation, health care workers, the use of bleach and the use of sprays

<table>
<thead>
<tr>
<th>Process</th>
<th>Asthma or asthma-like symptoms as stated in paper</th>
<th>Self/Physician-diagnosed, diagnostic tests</th>
<th>Type of study</th>
<th>Population size and controls</th>
<th>Summarised findings</th>
<th>Reference</th>
<th>Country of study</th>
<th>Evidence rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleaning as an occupation</td>
<td>Work-related asthma (WRA) and work-related wheeze (WRW). Cough and shortness of breath SOB not included. Distinction between work aggravated asthma (WAA) or new onset asthma not made.</td>
<td>Physician-diagnosed WRA and self-reported WRW</td>
<td>Cross-sectional population based survey.</td>
<td>5,022 (WRA; 188 cases analysed) and 4,573 (WRW; 454 cases analysed). Office workers as Referent group. Part of NHANES III 1988-1994. Exposures defined using SOC codes.</td>
<td>For cleaners, prevalence of WRA estimated at 3.7% and significant elevation in prevalence of WRW 25.6%. Odds ratio (OR) of 2.37 (95% CI 0.53-10.58) and 5.44 (95% CI 2.43-12.18) respectively. Equipment cleaning significantly associated with a higher risk of WRA compared to referents, and increased risk of WRA was associated with health-related occupations: Relative Risk (RR) 4.9%, OR 1.38 (95% CI 0.54-3.53).</td>
<td>Arif (2003)</td>
<td>USA</td>
<td>3</td>
</tr>
<tr>
<td>WRA. Cases classified as new onset (asthma with known sensitiser or from exposure to unknown sensitiser, and RADS) or WAA.</td>
<td>Physician-diagnosed (from Doctors First Reports – DFRs). No objective health measurements made.</td>
<td>Retrospective case series.</td>
<td>945 cases of WRA in California of which 444 followed up. Exposures defined using SIC codes.</td>
<td>Janitors and cleaners have highest rate of WRA out of 31 occupations specified (annual rate of WRA 625 per million workers). 4.7% of WRA cases (WAA or new onset) were associated with exposure to cleaning materials. However, 50% of new onset asthma cases resulted from exposure to unidentified</td>
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<td>USA</td>
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<tr>
<th>Process</th>
<th>Asthma or asthma-like symptoms as stated in paper</th>
<th>Self/Physician-diagnosed, diagnostic tests</th>
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<th>Population size and controls</th>
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<tr>
<td>Adult onset asthma.</td>
<td><strong>Physician-diagnosed</strong> new adult onset asthma (presence of at least cough, wheeze, dyspnea, nocturnal cough/wheeze and reversible airways obstruction.</td>
<td>Case control.</td>
<td>521 cases of new asthma. 932 controls (no reported asthma).</td>
<td>Cleaners amongst the 28 occupational groups studied. For female cleaners, the risk of asthma was significantly increased: OR 1.42 (95% CI 0.81-2.48) compared to professional, administrative, clerical and management controls.</td>
<td>Jaakola (2003)</td>
<td>Finland</td>
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<td>Asthma (asthma or woken with SOB in the last 12 months, or on asthma medication).</td>
<td><strong>Self-reported</strong> respiratory symptoms, and objective tests (bronchial responsiveness and IgE) in those reporting respiratory symptoms.</td>
<td>Retrospective cohort analysis (based on cases identified in Spanish ECHRS population).</td>
<td>From 2654 subjects, 67 indoor cleaners vs 1272 professionals, clerical and admin workers (controls).</td>
<td>Overall prevalence of asthma was 1.7 times higher than controls (95% CI 1.1-2.6). RR of asthma symptoms amongst private home cleaners was 3.3 (95% CI 1.9-5.8). RR for asthma symptoms plus bronchial responsiveness was 5.0 (95% CI 1.9-13.0). 62% of private home cleaners reported Work-related (WR) symptoms. Use of polishes associated with higher prevalence ratio of asthma vs referents. However, small numbers of cleaners studied and authors emphasise these findings relate to the Spanish cohort only.</td>
<td>Zock (2001)</td>
<td>Spain</td>
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<td><strong>Asthma</strong> (attack in the last 12 months or taking asthma meds).</td>
<td>Self-reported asthma confirmed by challenge tests.</td>
<td>Prospective study (follow-up of cross-sectional ECRHS populations).</td>
<td>6837 participants eligible (358 cleaners).</td>
<td>12 cases of asthma reported amongst cleaners. RR of asthma in cleaners vs non-manual workers was 1.7 (95% CI 0.9-3.2). Cleaning included as a “high asthma risk occupation” for which a significant excess RR (2.5) was observed. Exposure to low molecular weight agents/irritants in cleaning products accounted substantially for occurrence of OA observed.</td>
<td>Kogevinas (2007)</td>
<td>European countries</td>
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<td><strong>Current asthma, adult onset asthma, chronic bronchitis, rhinitis and WR respiratory symptoms.</strong></td>
<td>Self-reported asthma symptoms.</td>
<td>Cross-sectional with follow up.</td>
<td>4521 respondents of which 593 currently employed as domestic cleaners.</td>
<td>25% of asthma cases in the study group were attributed to domestic cleaning work with cleaners showing an excess risk for all respiratory outcomes. In female domestic cleaners vs women who had never worked in cleaning, asthma prevalence was increased: OR 1.46 (95% CI 1.1-1.92). Former domestic cleaning work was strongly associated with asthma, OR 2.09 (95% CI 1.7-2.57). A statistically significant risk for asthma (OR 2.5 (95% CI 1.1-5.8)) and chronic bronchitis (OR 2.2 (95% CI 1.0-4.8)) was observed in subjects cleaning in hospitals and other healthcare</td>
<td>Medina Ramon (2003)</td>
<td>Spain</td>
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<td>Rhinitis and asthma symptoms; work-related/work-aggravated and new onset.</td>
<td>Self-reported symptoms recorded via questionnaire. Cases defined between new onset and WAA/rhinitis. Atopy determined by skin prick tests.</td>
<td>Cross-sectional study or Brazilian cleaners in non-domestic setting.</td>
<td>341 cleaners (workers exposed to other vapours dusts, gases and fumes (VDGF), including hospitals, bars, nightclubs and industrial plants, excluded). Self-reported frequency of exposure recorded.</td>
<td>Cleaning related airway symptoms reported by 56% of all exposed workers. 11% had WRA and 35% WR rhinitis, with risk of work-related disease increasing significantly (p=0.0018) with years employed as a cleaner, for females, for atopics and for those who had reported a previous inhalation incident. The men with asthma/rhinitis symptoms had significantly more cleaning-related airway symptoms than the reference group. There was a higher risk of rhinitis in women (OR 2.07, 95% CI 1.20-3.70). Exposure to chlorine accounted for 14% of all reported associations with upper airways symptoms.</td>
<td>de Fatima (2007)</td>
<td>Brazil</td>
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<p>| Healthcare workers (physicians, nurses, occupational | WRA symptoms, work-exacerbated asthma and occupational | Self-reported symptoms and physician-diagnosed. WR defined as wheeze/SOB while at | Cross-sectional survey (Doctors, nurses, occupational therapists and | 3650 (from a total of 5600 Healthcare Professionals.). Self-reported exposure in longest job held. | No increased risk of OA reported, however, odds of WRA symptoms was significantly elevated (OR 3.9 (95% CI: 1.7-9.3)) with exposure to cleaning products as a general | Arif (2012) | USA | 3 |</p>
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<td>therapists and respiratory therapists)</td>
<td>asthma.</td>
<td>work that improved away from work.</td>
<td>physiotherapist s).</td>
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<td>purpose cleaner. Risk of WRA symptoms increased from 2.64 to 5.37 if exposure frequency increased from 1 per week to 1 per day for cleaning agents. Note: no “cleaners” included, however nurses second most populous group, therefore exposures to cleaning products possibly low.</td>
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<td>WRA symptoms, work-exacerbated asthma and occupational asthma.</td>
<td></td>
<td>Cross-sectional survey.</td>
<td>3650 (from a total of 5600 healthcare professionals).</td>
<td>Reported asthma was significantly associated with medical instrument cleaning (OR 2.22 (95% CI 1.34-3.67) and general cleaning (OR 2.02, 95% CI 1.2-3.4), in addition to latex glove use and aerosolised medication. BHR related symptoms were associated with general cleaning (use of cleaning products on building surfaces) OR 1.63 (95% CI 1.21-2.19).</td>
<td>Delclos (2007)</td>
<td>USA</td>
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<tr>
<td>Use of sprays</td>
<td>WRA and work-related rhinitis (with or without asthma).</td>
<td>Physician-diagnosed (nasal provocation test against EDTA) and asthma symptoms, Pulmonary Function Tests, skin prick tests,</td>
<td>Case series.</td>
<td>28 patients (10 cases of WRA/rhinitis were associated with use of cleaning products).</td>
<td>10 cases reported of WRA and/or rhinitis associated with positive NPT to EDTA. These cases were cleaners or healthcare workers who used spray</td>
<td>Laborde-Casterote (2012)</td>
<td>France</td>
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<td>IgE.</td>
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<td>formulations of cleaning products</td>
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<td></td>
<td>Case definitions of asthma/rhinitis not described.</td>
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<td>Authors suggest that the incidence of EDTA-induced occupational rhinitis and asthma is probably severely underestimated, and when present in aerosolized products, EDTA or EDTA salts should be considered to be a possible cause of work-related rhinitis and asthma.</td>
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<td>New onset asthma. (SOB/attack of asthma).</td>
<td><strong>Self-reported</strong> new-onset asthma (based on symptoms, medication and IgE).</td>
<td>Prospective population-based cohort study (ECRHS).</td>
<td>332 healthcare workers, 2481 controls (admin/professional occupation).</td>
<td>6% of HCW reported new onset asthma. Significant increased RR (1.85, 95% CI 0.76-4.5) among nursing-associated professionals, personal care providers (RR 2.3, 95% CI 1.03-5.14), and hospital technician (RR 4.63, 95% CI 1.87-11.5). Increased risk observed for HCW using ammonia/bleach at work (a RR of 2.16 (95% CI 1.03-4.53). The RR of new onset asthma for those using any spray cleaning products was reported as 2.36 (95% CI 0.99-5.64).</td>
<td>Mirabelli (2007)</td>
<td>10 European Countries</td>
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<tr>
<td>New onset Asthma (asthma-like symptoms, wheeze, SOB,</td>
<td><strong>Physician-diagnosed and self-reported</strong> current asthma, symptoms (asthma)</td>
<td>Multi-centre longitudinal population-based study</td>
<td>3503 involved in domestic cleaning. Exposures based on weekly use of cleaning sprays associated with asthma symptoms or use of medication (RR 1.49 (95% CI 1.12-1.99) and wheeze (RR 1.39)</td>
<td>Mirabelli (2007)</td>
<td>10 European Countries</td>
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<td>asthma attack, medication.</td>
<td>attack/woken with SOB in the last 12 months) and/or use of medication. FEV₁, methacholine challenge and atopy also recorded.</td>
<td>(ECRHS).</td>
<td>self-reported use and frequency. Control group were those who never used cleaning products (or less than 1 per week).</td>
<td>(95% CI 1.06-1.80). Incidence of physician diagnosed asthma was higher for those using sprays at least 4 days per week (RR 2.11 (95% CI 1.15-3.89). Point estimates for the associations between any spray use and asthma varied only slightly (&lt;5%), and RRs for current asthma and wheeze remained statistically significant. Cleaning products in non-spray formulations were not associated with asthma.</td>
<td>Neilsen (1999)</td>
<td>Denmark</td>
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<tr>
<td></td>
<td>Symptoms associated with asthma, rhinitis, bronchitis and atopy.</td>
<td><strong>Self-reported</strong> asthma (attack of wheeze in the last 12 months).</td>
<td>Prospective longitudinal study.</td>
<td>1011 female cleaners in nursing homes, schools and public offices. Self-reported exposure.</td>
<td>36% of the cleaners used sprays and the RR of developing symptoms in that group was increased for those who continuously used sprays throughout the study period (Asthma OR 3.0 (95% CI 0.9-10.0), bronchitis OR 3.2 (95% CI 1.0-10.4).</td>
<td>Medina-Ramon (2006)</td>
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<tr>
<td>Air fresheners/atomisers</td>
<td>Asthma or bronchitis symptoms.</td>
<td><strong>Physician-diagnosed and Self-reported</strong> (asthma as an attack of SOB in the last 12 months, bronchitis as cough and/or sputum).</td>
<td>Cross-sectional study of domestic cleaners.</td>
<td>Panel comprised of 51 (from a larger cross-sectional study of domestic cleaners.</td>
<td>Lower respiratory tract symptoms more common on working days, and significantly associated with use of bleach, degreasing/atomisers and air fresheners (OR for lower respiratory tract symptoms of 7.8 (95% CI 2.6-24) was reported). This was increased by duration of</td>
<td>Medina-Ramon (2006)</td>
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<td>Bleach</td>
<td>Rhinitis and asthma symptoms; work-related/work-aggravated and new onset.</td>
<td><strong>Self-reported symptoms</strong> recorded via questionnaire. Cases defined between new onset and WAA/rhinitis. Atopy determined by skin prick tests.</td>
<td>Cross-sectional study of Brazilian cleaners in non-domestic setting.</td>
<td>341 cleaners (workers exposed to other VDGF, including hospitals, bars, nightclubs and industrial plants, excluded). Self-reported frequency of exposure recorded.</td>
<td>Cleaning related airway symptoms reported by 56% of all exposed workers in the study. 11% had WRA and 35% WR rhinitis, with risk of work-related disease increasing with years employed as a cleaner, for females, for atopics and for those who had reported a previous inhalation incident. Exposure to chlorine accounted for 14% of all reported associations with upper airways symptoms. Among the men, a significant association between the use of ammonia and WRA/rhinitis was identified (OR 6.7 (95% CI 1.6-28.1).</td>
<td>de Fatima (2007)</td>
<td>Brazil</td>
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<tr>
<td>WRA (work-exacerbated or reports from physicians)</td>
<td>Physician-diagnosed; Case series.</td>
<td>1915 cases of work-exacerbated</td>
<td>62% of all WRA cases classified as OA, 20% were WAA, 18% RADS.</td>
<td>Rosenman</td>
<td>USA</td>
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<td>new onset occupational asthma</td>
<td>partially linked to reimbursement for medical services. Hospital discharge records reviewed coded for 'respiratory conditions due to chemical fumes/vapours'. Telephone questionnaire; medical records reviewed for pulmonary function tests.</td>
<td>asthma/occupational asthma. Self-reported exposures.</td>
<td>12% of all cases of WRA attributed to cleaning product exposures. Of the cleaning products identified, the most common were irritants such as acids, ammonia, or bleach; and disinfectants such as formaldehyde, glutaraldehyde, and quaternary ammonia compounds. Inappropriate mixing of incompatible components was reported to be the cause in 4% of the reported cases of WRA. Of the cases where a chemical component was specified, 22% attributed to exposure to bleach. However information on the specific use situations was not collected.</td>
<td>(2003)</td>
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<td>WRA/WAA/new-onset asthma and RADS.</td>
<td>Physician-diagnosed reports, telephone questionnaire follow-up.</td>
<td>2995 cases from within the educational services sector.</td>
<td>Janitors, cleaners, and housekeepers represented one of the groups with the most reports of asthma (n 31; 11.7%). This group also cited a link between cleaning product exposure and their symptoms (74.2%). Of the cases of new-onset asthma associated with the use of cleaning products, 9.6% were attributed to bleach.</td>
<td>Mazurek (2008) USA 3</td>
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<td>New-onset asthma.</td>
<td>Self-reported; interviewer-administered questionnaires about respiratory symptoms and asthma therapies. New onset asthma if symptoms reported since baseline (Attack of asthma, SOB, asthma meds). Atopy determined by skin prick tests.</td>
<td>Prospective, population-based cohort study. Longitudinal study with fixed cohort (ECRHS I-II).</td>
<td>332 nurses, and 2481 professional/admin controls. Self-reported exposures.</td>
<td>No significant increased RR for new-onset asthma among all nursing/related occupations. However, elevated RRs of asthma among nurses who reported using ammonia and/or bleach cleaning products more than once per week; RR 2.16 (95% CI 1.03-4.53).</td>
<td>Mirabelli (2007)</td>
<td>13 European Countries (28 study centres)</td>
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<td>Asthma/ COPD/Bronchial hyper-responsiveness.</td>
<td>Self-reported; confirmed by lung function and allergy testing. Atopy determined by skin prick tests.</td>
<td>Population-based survey, nested case-controlled study.</td>
<td>43 female domestic cleaners.</td>
<td>Work-related lower respiratory tract symptoms were predominantly associated with exposure to bleach, degreasers and sprays. Two thirds of reported accidents related to the mixing of cleaning products involving bleach. Significant associations between LRTSs and working day, increased by duration of exposure (OR 5.6 for daily cleaning time &gt;8hrs, 95% CI 1.7-19). The use of bleach, either diluted or undiluted, was reported more frequently by cases compared to controls.</td>
<td>Medina-Ramon (2005)</td>
<td>Spain</td>
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<td>in a strong and significant association with a high level of exposure (OR 4.9), as well as an exposure-response trend.</td>
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<td>Bronchial hyper-responsiveness, lower respiratory tract symptoms.</td>
<td>Self-reported symptoms plus 2 week panel study, completing diary of self-measured peak expiratory flow readings 3 times per day, confirmed by lung function testing. Atopy determined by skin prick tests.</td>
<td>Case-controlled study nested within a large population based cross-sectional survey.</td>
<td>43 female domestic cleaners.</td>
<td>Lower respiratory tract symptoms more common on working days, and significantly associated with use of bleach, degreasing/atomisers and air fresheners (OR for lower respiratory tract symptoms of 7.8 (95% CI 2.6-24) was reported). This was increased by duration of exposure (OR 5.6 for daily cleaning &gt;8hrs, 95% CI 1.7-1.9). BHR was present in 31% of participants. (Part) Irritant mechanism of health effect from exposure to cleaning products in the domestic setting was hypothesised. Use of diluted bleach associated with respiratory symptoms; OR 4.4 (95% CI 1.8-11) and also symptoms the next day; OR 2.8 (95% CI 1.2-6.6).</td>
<td>Medina-Ramon (2006)</td>
<td>Spain</td>
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<td>Chlorine</td>
<td>Bronchial hyper-responsive, Specific inhalation challenges with bleach</td>
<td>Physician-diagnosed. Specific inhalation challenges with bleach</td>
<td>Case control study with single blind</td>
<td>13 cleaning employees, 3 non-symptomatic controls</td>
<td>The data suggest that subjects with or without BHR manifest an exaggerated, non-specific FEV₁</td>
<td>Sastre (2011)</td>
<td>Spain</td>
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<td>responsiveness.</td>
<td>with subsequent FEV$_1$, BHR and fractional exhaled nitric oxide objective tests.</td>
<td>challenge testing.</td>
<td>from allergy outpatient clinic.</td>
<td>decrease following bleach (chlorine gas) inhalation at a chlorine-concentration level of 0.4 ppm, which is below the 8-hr permissible occupational exposure level. Significantly greater falls in Forced respiratory volume (FEV$_1$) in cleaners compared to placebo challenges.</td>
<td>Massin (2007)</td>
<td>France</td>
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<td>Trichlor amine (nitrogen trichloride)</td>
<td>Irritant respiratory symptoms.</td>
<td><strong>Self-reported</strong> confirmed by inhalation challenge tests and spirometry.</td>
<td>N=175 workers in food industry exposure to nitrogen trichloride and aldehydes whilst cleaning and disinfecting.</td>
<td>A significant concentration-response relationship was found between eye, nasal, and throat symptoms of irritation—but not chronic respiratory symptoms—and exposure levels or exposure duration. The prevalence rates for irritant symptoms tended to increase with increasing exposure levels: for the exposure index and for exposure duration, a statistically significant exposure-response relationship was found for all symptoms.</td>
<td>Massin (2007)</td>
<td>France</td>
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<td>Disinfectants</td>
<td>WRA (work-exacerbated or new onset occupational asthma).</td>
<td>Case series.</td>
<td>1915 cases of work-exacerbated asthma/occupational asthma.</td>
<td>12% of all cases of WRA attributed to cleaning product exposures. Of the cases where a chemical component was specified, the most commonly involved class of cleaning products were disinfectants in 10% of cases.</td>
<td>Rosenman (2003)</td>
<td>USA</td>
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<td>Process</td>
<td>Asthma or asthma-like symptoms as stated in paper</td>
<td>Self/Physician-diagnosed, diagnostic tests</td>
<td>Type of study</td>
<td>Population size and controls</td>
<td>Summarised findings</td>
<td>Reference</td>
<td>Country of study</td>
<td>Evidence rating</td>
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<td>WRA symptoms, work-exacerbated asthma and occupational asthma.</td>
<td>Self-reported symptoms and physician-diagnosed.</td>
<td>Cross-sectional survey (doctors, nurses, occupational therapists and physiotherapists).</td>
<td>3650 (from a total of 5600 healthcare professionals. Self-reported exposure in longest job held.</td>
<td>Odds of BHR-related symptoms significantly greater when exposed to general cleaning products and disinfectants: OR of 1.57 (95% CI 1.11-2.21). Odds of WRA symptoms was elevated 3.9 (95% CI 1.7-9.3). For exposure in any job, the odds of WRA symptoms were significantly elevated for bleach, cleaners/abrasives, toilet cleaners, detergents and ammonia glutaraldehyde/ortho-phtaldehyde, chloramines and ethylene oxide). Significantly elevated odds of WEA were observed for exposure to bleach, factor 2 and formalin/formaldehyde. Exposure to chloramines was significantly associated with an almost fivefold elevated odds of OA.</td>
<td>Arif (2012)</td>
<td>USA</td>
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A literature review of evidence on cleaning products and occupational risks for asthma

Occupational asthma is a debilitating illness, caused by exposure to hazardous substances in the workplace. The UK cleaning sector employs nearly half a million people using a variety of products and processes that have the potential to cause respiratory diseases.

A review of the published scientific literature was undertaken to summarise evidence about cleaning products that may increase the risk of occupational asthma. The overall breadth, consistency and quality of the evidence were assessed.

There were few high quality studies and only three related specifically to the UK cleaning sector. From the available evidence, there was consistent evidence that certain types of cleaning work were associated with an increased risk of developing asthma and/or experiencing respiratory symptoms consistent with asthma, both new cases and exacerbations of pre-existing conditions.

An excess of asthma and respiratory symptoms were reported in studies of healthcare workers and domestic cleaners; this excess may reflect a selection bias for studies favouring these populations.

A broad spectrum of cleaning products was reported to cause respiratory symptoms, particularly chlorine-liberating agents and bleaches. Spray application of cleaning products was also associated with increased risk for respiratory disease.

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