Cleaning products and respiratory health outcomes in occupational cleaners: a systematic review and meta-analysis

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ABSTRACT

There is consistent evidence of increased respiratory symptoms in occupational cleaners; however, uncertainty remains on type of respiratory health effects, underlying causal agents, mechanisms and respiratory phenotypes. We aimed to conduct a systematic review and if possible, a meta-analysis of the available literature to characterise and quantify the cleaning-related respiratory health effects. We searched MEDLINE and EMBASE databases and included studies that evaluated the association of any respiratory health outcome with exposure to cleaning occupation or products in occupational cleaners. A modified GRADE was used to appraise the quality of included studies. We retrieved 1124 articles, and after applying our inclusion criteria, 39 were selected for the systematic review. We performed a meta-analysis of the 21 studies evaluating asthma which showed a 50% increased pooled relative risk in cleaners (meta-relative risk (RR)=1.50; 95% CI 1.44 to 1.56). Population-based cross-sectional studies showed more stable associations with asthma risk. No evidence of atopic asthma as dominant phenotype emerged. Also, we estimated a 43% increased risk (meta-RR=1.43; 95% CI 1.31 to 1.56) of chronic obstructive pulmonary disease. Evidence for associations with bronchial-hyper-responsiveness, lung function decline, rhinitis, upper and lower respiratory tract symptoms was weaker. In our systematic review and meta-analysis, we found that working as a cleaner is associated with an increased risk of reversible and even irreversible obstructive airway diseases. All studies lacked quantitative exposure assessment to cleaning products; this would help elucidate underlying causal agents and mechanisms. Exposure control and respiratory surveillance among cleaners is warranted to prevent the associated respiratory health burden. Trial registration number: CRD4201705915.

INTRODUCTION

Occupational cleaners represent a significant proportion of the workforce in developed countries (about 4 million just in Europe), and mostly include 'vulnerable' social categories: women, migrants and low educated subjects.[1] These figures are likely an underestimation given that many in this job sector are self-employed.

In the last decade, a consistent and growing evidence of an epidemic of 'asthma-like' respiratory symptoms among occupational cleaners has been reported worldwide.[2 3] In addition, a recent large population-based study found an increased risk of spirometrically-defined chronic obstructive pulmonary disease (COPD) among cleaners, confirmed in never-smokers.[4]

Cleaners are exposed to a wide range of airborne agents that might contain either respiratory sensitisers or irritants.[5 6] In particular, bleach and disinfectants have been associated with an increased asthma risk. However, most of the evidence is based on self-reported exposure that is likely to be biased towards cleaning agents with pungent odour so the causal agents remain unclear.[7]

In addition, the underlying mechanistic pathways are uncertain. There is no evidence of a classic IgE-mediated allergic asthma phenotype, so alternative pathways ranging from inflammatory to neurogenic have been proposed. Moreover, it is still largely debated whether persistent exposure to irritant agents in cleaning products could trigger and then sustain chronic airway inflammation with subsequent fixed airway obstruction.[5 6]

Key messages

What is already known about this subject?
► There is consistent evidence of increased respiratory symptoms in occupational cleaners worldwide. However, uncertainty remains on type of respiratory health effects, underlying causal agents, mechanisms and respiratory phenotypes.

What are the new findings?
► We evaluated a broad range of respiratory health effects and estimated a 50% increased risk of asthma and 43% of chronic obstructive pulmonary disease among occupational cleaners. No evidence for a typical allergic respiratory phenotype emerged, suggesting that continuous exposure to irritant agents might cause both reversible and irreversible airway obstruction.

How might this impact on policy or clinical practice in the foreseeable future?
► Enhanced exposure control and respiratory health surveillance among cleaners is warranted to avoid the associated respiratory health burden. All studies lacked quantitative exposure assessment to cleaning products; inclusion of such measures in prospective studies would help elucidate underlying causal agents and mechanisms.

Given the uncertainty of causal agents, underlying mechanisms and type of respiratory health effects, we aimed to conduct a broad systematic review and if applicable a meta-analysis of the literature in order to characterise and quantify the respiratory health effects attributable to occupational exposure to cleaning products.

This is an important public health issue, also for the potentially important downstream implications for all end-users of cleaning products during domestic housekeeping, including vulnerable 'bystanders' such as children.

METHODS
Literature search strategy, selection criteria and quality appraisal
We conducted the systematic review following the PRISMA guidelines, and we registered the search protocol in PROS-PERO (CRD42017059150) on 21 March 2017. We searched the electronic bibliographic databases 'Ovid MEDLINE(R) 1946 to 2017' (PubMed) and 'Embase 1947 to 2017' on 24 March 2017. The search was then updated to 31 July 2020. OpenGrey database was also screened to retrieve 'grey literature' using broad, concise search terms covering the domains of 'Occupational cleaning' and 'Respiratory outcomes'. The search strategy used free-text terms which were adapted for each database in combination with 'MeSH' filters where appropriate (online supplementary table S1). All studies examining occupational cleaning and exposure to cleaning products including disinfectants as the exposure and any respiratory disease, symptom or lung function measure as an outcome were eligible for inclusion. Of note, 'cleaning products' is used throughout this paper to designate the broader category of cleaning products and disinfectants. Healthcare workers performing cleaning job tasks were also included. To maximise the number of articles, there were no restrictions on the publication date, and PhD theses captured by the grey literature search were also included. Only articles written in English were included. Case reports, editorials, letters and reviews were excluded. Finally, studies on outdoor cleaners (eg, road cleaners) and cleaners working in industrial/factory settings were excluded as they were likely to have been exposed at workplace to other occupational respiratory toxicants (eg, isocyanates, food respiratory allergens, welding fumes, metals, gas, dusts, diesel exhausts and so on) or to use cleaning agents specific for industrial applications (eg, highly alkaline detergents for heavy industrial soiling). The full list of inclusion/exclusion criteria is in online supplementary table S2. Two authors (OA and SS) independently assessed the retrieved references against the inclusion criteria, and in case of disagreement, consensus was achieved by consulting a third reviewer (SDM). Endnote X7.1 was used as reference management software. Given that virtually the entire evidence in occupational epidemiology comes from observational studies, a modified GRADE system[8] was used for the quality appraisal of the included articles. In particular, we considered 'a priori' as the best study design to assess a causal association a prospective observational cohort instead of a randomised clinical trial because not applicable in this occupational epidemiology context. All the other GRADE criteria were kept as per the original system, including the final scoring classification into high, moderate, low or very low.

Statistical methods for meta-analysis
To quantify the cleaning-related respiratory health effects, we considered for meta-analyses the studies included in the systematic review that showed a high/moderate quality according to the GRADE scoring. We pooled the main reported effect measures between occupational exposure to cleaning products or cleaning occupation and each respiratory health outcome by using fixed-effects[9] or random-effects methods[10] as appropriate based on the Higgins I^2 statistic. Significant within-studies heterogeneity is typically considered to be present if I^2 is $\geq 50\%$.[11] Also, subgroup analyses by epidemiological study type were performed. Pooled risk effect estimates were presented as meta-relative risks (RRs) and 95% CIs. The meta-analysis was performed using the command 'metan' in the statistical software STATA V.15.

RESULTS
From our electronic database search, 1124 articles were retrieved. After removing record duplicates, 712 articles remained eligible for title and abstract screening. Of note, from forward and backward referencing of the removed review articles, we identified three additional records. After abstracts screening, 148 articles remained eligible for full-text article review. After applying our inclusion/exclusion criteria, 39 studies remained to be included in the final qualitative synthesis (figure 1).

Based on our quality appraisal, most of the studies included reached a moderate GRADE score (online supplementary tables S3–S5), the three studies included that were retrieved using OpenGrey scored very low in quality and we decided to not include them in the final systematic review (online supplementary table S6).

We managed to perform a quantitative meta-analysis among 21 high/moderate quality studies evaluating asthma risk and three high quality studies on COPD risk with comparable effect measures (figures 2 and 3, respectively). For the other evaluated outcomes, important differences in both exposure and outcome definition (eg, bronchial-hyper-responsiveness (BHR) defined using self-reported symptoms versus standard methacholine challenge test) prevented us from pooling these studies in a meta-analysis.

Respiratory health outcomes
Asthma
We included in the systematic review 21 studies evaluating associations between asthma and occupational cleaning (and/or exposure to cleaning products) conducted in a broad range of countries (Europe, USA, South America, Canada and New Zealand) in the last two decades (table 1). Thirteen studies were based on general population samples,[12–24] and eight were conducted within workforces.[25–32] The majority used a cross-sectional design. In terms of outcome definition, 'adult-onset asthma' among current or ever cleaners was mainly used as a *proxy* to define 'occupational asthma' or the broader category of 'work-related asthma' outcomes, based on a self-reported doctor's diagnosis or asthma symptoms/medications. Of note, studies evaluating work-exacerbated asthma only were not included. Most of the studies used a standard job-title approach as *proxy* for occupational exposure to cleaning products. Six studies assessed exposure to specific agents included in cleaning products by using an expert-based exposure assessment or a semiquantitative job-exposure matrix approach.[13 17 18 26 27 33] Evidence of a positive exposure-response relationship emerged by using duration of employment as a cleaner or frequency/intensity/duration of cleaning tasks as *proxys* for exposure. Most of these studies were conducted among hospital cleaners and evaluated frequency and intensity of exposure to disinfectants during cleaning tasks.[21 25–27] None actually managed to measure cleaners' personal exposure to cleaning agents, so no
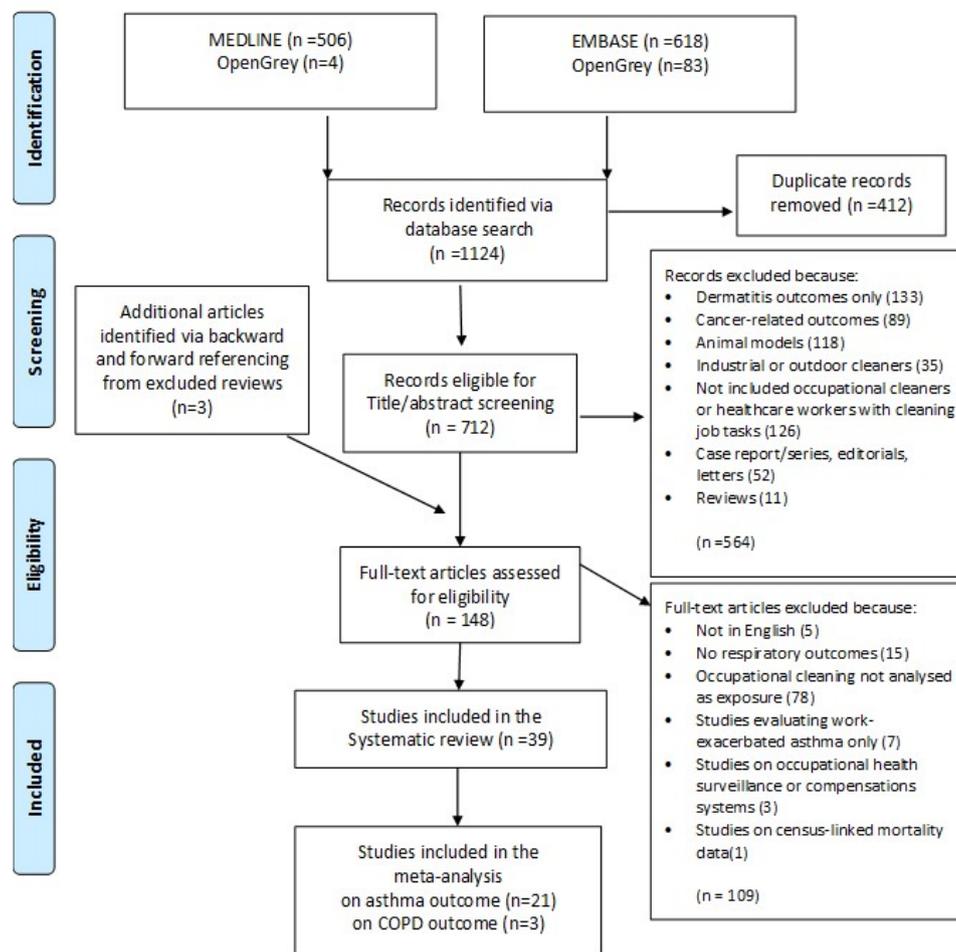
Figure 1 PRISMA flow diagram showing screening and selection of articles related to occupational cleaning and health outcomes resulting from the search in electronic bibliographic databases.

dose-responses based on concentration metrics were evaluated. Both population-based and workforce-based studies found a positive association between occupational cleaning and asthma risk. Among the eight workforce-based studies,[25–32] mainly conducted among hospital healthcare workers, risk estimates were more instable because based on smaller samples. Of note, among healthcare workers emerged positive exposure-response trends for asthma risk and exacerbations for frequency of cleaning tasks, especially when applying disinfectants/sterilising agents.[25] Exposures to ammonia and bleach showed the highest associations with asthma risk both in workforce-based and population-based studies.[19 20] Also, cleaning products in spray format were found more strongly associated with asthma symptoms or asthma exacerbations compared with liquid and powder products. Of note, we did not include in the systematic review a French population-based case-control study that evaluated asthma severity only[33] and a cross-sectional study of cleaners in Brazil because a composite outcome of asthma/rhinitis symptoms was evaluated.[34]

Meta-analysis for asthma outcome
Based on our GRADE quality appraisal (online supplementary table S3), we selected 21 studies on asthma with high/moderate quality score for meta-analysis.

Where studies reported more than one risk effect estimate for asthma, we selected for quantitative summary the one that best-defined occupational asthma: for example, we favoured

the effect estimate for asthma diagnosis after start work among current cleaners over estimates for ever adult asthma diagnosis among ever cleaners.

The population-based studies showed a clear increased risk of asthma among cleaners, irrespective of the study design, with the highest pooled risk estimate among cross-sectional studies (meta-RR=1.53; 95%CI 1.36 to 1.72). Workforce studies found positive, but less stable associations (ie, wider CIs), with the highest pooled risk among cross-sectional studies (meta-RR=1.76; 95%CI 1.33 to 2.34).

Overall, the pooled meta-analysis of the 21 studies, showed a 50% increased risk for asthma (meta-RR=1.50; 95%CI 1.44 to 1.56; I^2=33.7%; p=0.07) (figure 2). Based on the heterogeneity tests between studies, fixed methods were applied to pool the risk estimates.

No evidence of publication bias or small-study effects was detected (Egger's test p=0.23) (online supplementary figure S1).

Bronchial hyper-responsiveness
Among the three studies included in the systematic review that evaluated non-specific BHR as respiratory outcome among occupational cleaners a weak positive association was found (table 2).[23 26 35] In particular, only one study found a clear association with BHR even if assessed using a symptoms score questionnaire instead of an objective a specific bronchial challenge test.[26] One study found an association in ex-smokers only,[22] and one did not find a statistically significant association.[35] Two
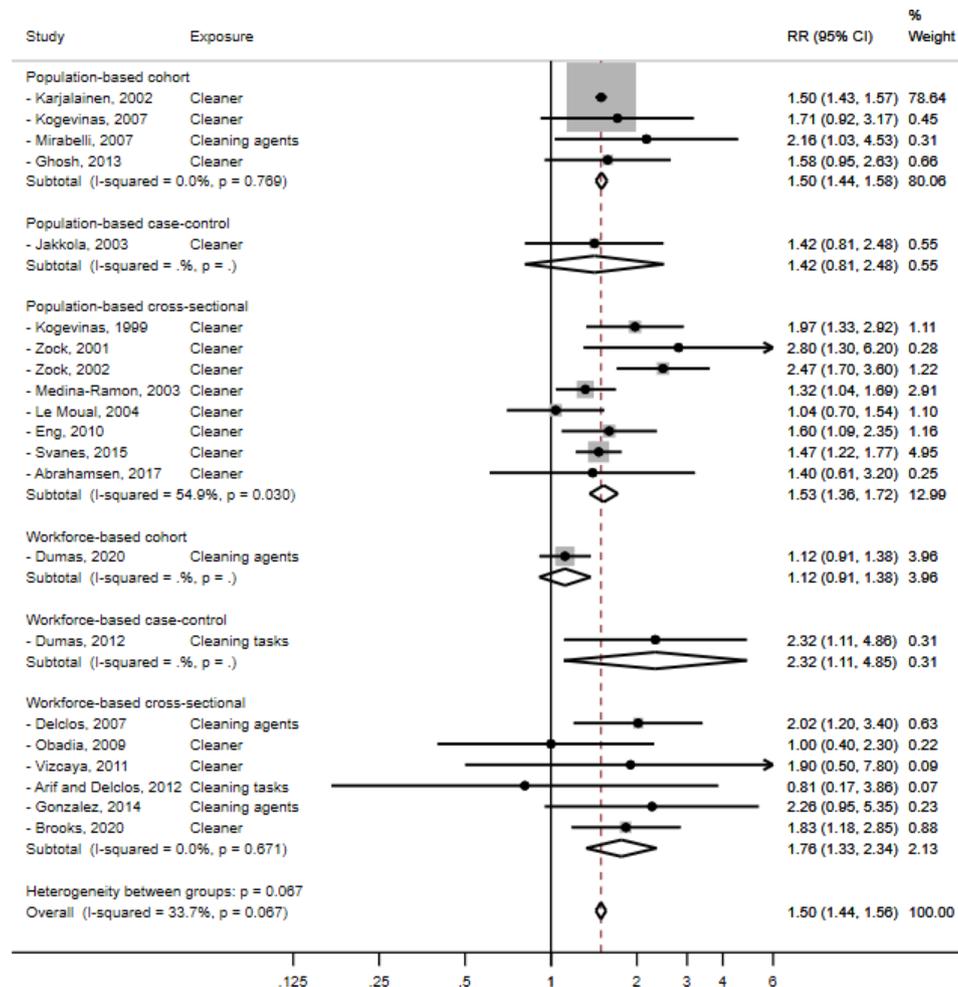
Figure 2 Meta-analysis of 21 studies evaluating the association between occupational cleaning exposure and asthma risk. RR, relative risk.
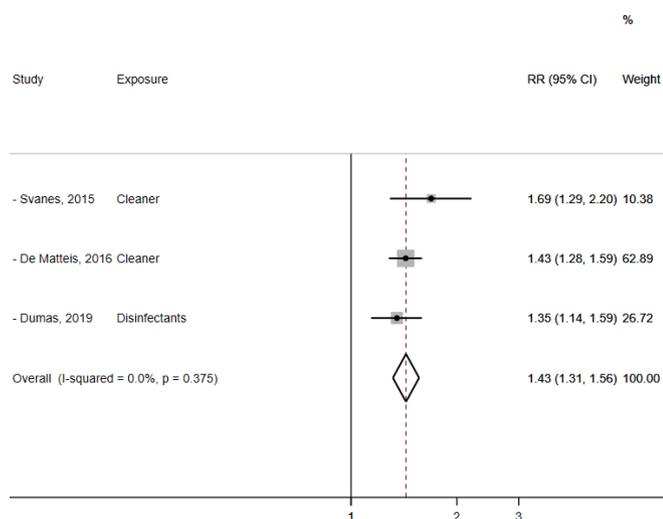

Figure 3 Meta-analysis of three studies evaluating the association between occupational cleaning exposure and COPD risk. COPD, chronic obstructive pulmonary disease; RR, relative risk.

studies included in the systematic review were not included in table 2 because evaluated BHR only in a combined outcome with asthma symptoms.[16 22]

Respiratory symptoms

Eleven studies (five workforce and six population based) investigated as outcomes lower (LRTS) and upper (URTS) respiratory tract symptoms, such as cough, wheeze or chest tightness, and itchy or runny nose, respectively (table 2).[21 24 29 30 35–41] Eight of the 11 studies explored only LRTS and found an increased risk for higher duration of exposure and among those working as cleaners compared with controls. In one study, this increased risk was confined to women although no formal gender interaction was tested,[29] while in another study, there was evidence of a positive exposure-response (OR of wheeze of 1.46; 95% CI 1.18 to 1.83 for exposure between 1 and 4 years and of 1.62 (95% CI 1.34 to 1.96) for exposure >4 years.[21] One cross-sectional study in Spain showed increased risk of LRTS in cleaners, but failed to reach conventional statistical significance.[30] Finally, one study found a significant increase in phlegm (p=0.019) and dyspnoea (p=0.041) suggestive for chronic bronchitis.[35] Three studies assessed also associations with URTS. One study showed a doubled risk for eye/nose/throat symptoms;[40] the second found associations confined only to medium and not high exposures which were attributed by the authors to the healthy worker effect.[36] The third found a significant increase in nasal (p<0.001) and throat symptoms (p<0.05).[38]

Rhinitis

Two population-based studies reported the association of cleaning profession with occupational rhinitis as outcome[19 42] and

Table 1 Summary of epidemiological studies (chronological order) assessing the associations between cleaning occupation, tasks or agents and asthma in population-based and workforce-based studies

Author, year	Country	Period of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% CI in parenthesis)	GRADE score
Kogevinas et al, 1999[16]	26 centres in 12 countries	1992	Population-based survey (ECRHS)	15 637 people randomly selected from the general population (n=443 cleaners)	Asthma was assessed by methacholine challenge test and questionnaire	Age, sex, smoking status, study centre	Cleaning occupation	BHR and asthma symptoms or medications: OR=1.97 (1.33–2.92) Asthma symptoms or medication: OR=1.82 (1.44–2.30)	Medium
Zock et al, 2001[22]	Spain	1998	Population-based cross-sectional (ECRHS)	67 indoor cleaners, 1272 office workers	Questionnaire, blood samples for serum IgE	Age, gender, smoking, study centre	Confirmed cleaners	BHR and asthma symptoms or medications: OR=2.8 (1.3–6.2) Asthma symptoms or medication: OR=1.7 (1.1–2.6) Higher PRs for private home cleaners	Moderate
Karjalainen et al, 2002[15]	Finland	1986–1998	Registry-based cohort	53 708 cleaners, 202 751 administrative managerial and clerical workers	The Medication Reimbursement Register of the SII of Finland and the Finnish Register of Occupational Diseases (FROD)	Age, follow-up period	Female cleaners	WRA: RR=1.50 (1.43–1.57)	High
Zock et al, 2002[23]	11 European countries and three outside Europe	1990–1994	Population-based survey (ECRHS Stage II)	304 cleaners, 4492 office workers	Questionnaire, blood samples for serum IgE	Age, gender, smoking, study centre	Cleaning occupation	Current asthma OR=2.47 (1.7–3.6)	Moderate
Jaakkola et al, 2003[14]	Finland	1997–2000	Population-based case-control	521 asthma cases, 932 controls	Questionnaire	Age, gender, smoking	Female cleaners	OA: OR=1.42 (0.81–2.48)	Moderate
Medina-Ramón et al, 2003[19]	Spain	2000–2001	Population-based cross-sectional	4521 female domestic cleaners, 593 current, 1170 former	Questionnaire	Age, smoking	Current and former cleaning	Ever cleaning for current asthma: OR=1.73 (1.44–2.07) Current cleaner for current asthma: OR=1.32 (1.04–1.69) Current cleaner for current asthma (domestic only) : OR=1.46 (1.10–1.92) Former cleaner for current asthma: OR=2.00 (1.63 to 2.43)	High
Le Moual et al, 2004[18]	France	1975	Population-based survey	404 cleaners, 8428 administrative service workers	Questionnaire ISCO-88 JEM	Age, gender, smoking	Cleaning occupation Generic asthmagens	WRA, cleaning job: OR=1.04 (0.70–1.54) WRA, cleaning agents: OR=2.16 (1.12–4.17)	Moderate
Delclos et al, 2007[26]	USA	2003	Workforce-based cross-sectional	3650 healthcare professionals (862 physicians, 941 nurses, 968 occupational therapists, 879 respiratory therapists)	Questionnaire	Age, sex, race/ethnicity, professional group, years as a health professional ('seniority'), smoking, obesity	Exposure to cleaning agents/tasks Seniority: 10–16 years 17–26 years ≥27 years	WRA Medical instrument cleaning: OR=2.22 (1.34–3.67) General cleaning: OR=2.02 (1.20–3.40) Use of powdered latex gloves between 1992 and 2000: OR=2.17 (1.27–3.73) Administration of aerosolised medications: OR=1.72 (1.05–2.83) OR=2.08 (0.64–6.73) OR=3.37 (1.10–10.26) OR=4.10 (1.39–12.11)	High

Table 1 continued

Author, year	Country	Period of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% CI in parenthesis)	GRADE score
Kogevinas et al, 2007[17]	13 countries	1998–2003	Population-based cohort (ECRHS-II)	6837 (358 of them cleaners)	ECRHS II questionnaire	Age, sex, smoking, centre	Cleaning and caretaking Cleaning products using asthma-specific JEM	Cleaning and caretaking occupation: OR=1.71 (0.92–3.17) Exposure to cleaning products: OR=1.80 (1.01–3.18)	High
Mirabelli et al, 2007[20]	22 centres located in 10 European countries	1998–1999	Population-based cohort (ECRHS-II)	332 nurses or employed in nursing-related job, 2481 professional or administrative workers	Questionnaire ISCO-88	Age, country, sex, smoking, study area	Exposure to cleaning products, cleaning tasks among healthcare workers	New-onset asthma Ammonia and/or bleach: OR=2.16 (1.03–4.53) Liquid multi-use products: OR=1.16 (0.61–2.19) Washing powders OR=1.65 (0.77–3.53) Any products in spray form OR=2.36 (0.99–5.64)	High
Obadia et al, 2009[29]	Canada	Not specified	Workforce-based cross-sectional	566 cleaners and 587 other building workers	Questionnaire	Age, gender, smoking	School or racetrack public building cleaners	OA, males OR=0.93 (0.4–2.3) OA, females: OR=1.00 (0.4–2.3)	High
Eng et al, 2010[12]	New Zealand	2004–2006	Population-based cross-sectional	3055 participants (from a random sample of 10,000)	Telephone survey	Age, gender, smoking, deprivation	Cleaners	WRA, adult onset: OR=1.3 (0.8–2.1) WRA, current: OR=1.60 (1.09–2.35)	Moderate
Vizcaya et al, 2011[30]	Spain	2007–2008	Cross-sectional study on employees of cleaning companies	917 employees of 37 cleaning companies: 761 current cleaners, 86 former and 70 never cleaners (referents)	Spirometry during clinic visit	Age, gender, nationality. smoking status	Cleaning occupation Cleaning products	Current asthma, current cleaners: OR=1.9 (0.5–7.8), former cleaners: OR=1.9 (0.6–5.5) Adult-onset asthma, current cleaners: OR=1.4 (0.4–4.9), former cleaners: OR=2.5 (0.5–12) Use of hydrochloric acid: OR=1.7 (1.1–2.6)	Moderate
Arif and Delclos, 2012[25]	USA	2004–2005	Workforce-based cross-sectional	3650 healthcare professionals	Questionnaire (exposure to cleaning substances) In the longest held job	Age, sex, race/ ethnicity, BMI, seniority, atopy, smoking status	Cleaning agents	WRA symptoms increased in a dose-dependent manner from OR=2.64 (95% CI 0.57 to 12.1) for 1/week exposure to cleaning agents to OR=5.37 (1.43–20.16) for >1/day. For exposures to disinfectants/sterilising agents, WEA increased from 3.75 to 5.06 to 9.02 for at least 1/week, every day and more than once a day, respectively. OA for every day and >1/day self-reported exposure to cleaning agents: 0.81 (0.17–3.86)	High

Table 1 continued

Author, year	Country	Period of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% CI in parenthesis)	GRADE score
Dumas et al, 2012[27]	France	2003–2007	Workforce-based case-control	179 hospital workers, 545 controls, selected from a previous case-control study	Questionnaires, expert assessment and the asthma JEM	Gender, BMI	Among hospital workers: frequency of cleaning tasks: (never,<1, 1–3, 4–7 days/week	In women, for exposure >1 day/week (expert only): OR=1.04 (0.64–1.70); high intensity: OR=1.45 (0.81–2.62) In women, for exposure (expert +JEM) to high intensity cleaning/disinfecting tasks: OR=2.32 (1.11–4.86). Moderate/high exposure to quaternary ammonium: OR=1.93 (0.85–4.40).	High
h, 2013	Great Britain	1991–2000	Population-based cohort	Cleaners unspecified: 156 Domestic helpers and cleaners: 113 Helpers and cleaners in offices, hotels: 516	Interview	Gender, smoking, father's social class, area of residence at 42 years, hay fever/ allergic rhinitis in childhood	Domestic cleaners identified and coded using the ISCO-88 Cleaning products using asthma-specific JEM	Adult onset asthma in cleaners unspecified: OR=1.58 (0.95–2.63) Domestic helpers and cleaners: OR=1.79 (1.02–3.14) Helpers and cleaners in offices, hotels: OR=1.82 (1.34–2.48) Cleaning/disinfecting products: OR=1.67 (1.26–2.22)	High
Gonzalez et al, 2014[28]	France	2006–2007	Workforce-based cross-sectional	543 healthcare workers (94 cleaners)	Questionnaire	Age, gender, smoking, atopy, BMI	Hospital cleaners	WRA, cleaning profession: crude OR=2.38 (0.48–11.85) OA, crude OR=2.33 (0.52–10.44) General cleaning tasks: adjusted OR=2.26 (0.95–5.35)	Moderate
Svanes et al, 2015[21]	Norway, Sweden, Denmark, Iceland, Estonia	2010–2012	Population-based cross-sectional (RHINE III), extension of ECRHS	2138 ever cleaners (from 13499 respondents)	Questionnaire	Age, gender, smoking, educational level, parent's educational level, BMI, centre	Occupational cleaner (ever	OA OR=1.47 (1.22–1.27) Positive trend with duration of exposure	High
Abrahamsen et al, 2017[24]	Norway	February to August 2013	Population-based cross-sectional study	185 cleaners (among 16099 responders)	Questionnaire	Age, gender, area of residence, smoking, home damp/mould, housing conditions	Female and male cleaners JEM	Current asthma: OR=1.4 (0.61–3.2) Physician diagnosed asthma (ever): OR=0.92 (0.51–1.60)	Medium
Brooks et al, 2020[31]	New Zealand	2008–2010	Workforce-based cross-sectional	425 cleaners, 281 reference workers	Questionnaires, bronchodilator	Age, gender, ethnicity, smoking	Cleaners	Current asthma in cleaners: OR=1.83 (1.18–2.85) Physician-diagnosed asthma ever: OR=0.62 (0.42–0.92)	High
Dumas et al, 2020[32]	USA	2009–2015	Workforce-based prospective cohort study (NHSII)	116429 female registered nurses	Questionnaires	Age, smoking status and pack-years, race, ethnicity, and BMI	Disinfectants Sprays for cleaning, disinfection, other JEM	OA Exposure to any disinfectant: HR=1.12 (0.91-1.38) Weekly use of sprays: HR=1.10 (0.76-1.59)	High

ECRHS, European Community Respiratory Health Survey; ISCO, International Standard Classification of Occupations; JEM, job-exposure matrix; NHSII, Nurses' Health Study II; OA, occupational asthma; PR, prevalence ratio; RHINE, respiratory health In northern Europe; WEA, work-exacerbated asthma; WRA, work-related asthma.

Table 2 Summary of epidemiological studies (chronological order) assessing the associations between cleaning occupation, tasks or agents and BHR and UTRS and LTRS

Author, year	Country	Year of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% CI in parenthesis)	GRADE score
BHR									
Zock et al, 2002[23]	11 European countries and three outside Europe	1990–1994	Population-based survey (ECRHS)	304 cleaners, 4492 office workers	Spirometry, methacholine challenge test	Age, gender, smoking, study centre	Cleaning occupation	Case-case analysis: OR=1.60 (p>0.05)	Moderate
Delclos et al, 2007[26]	US	2003	Workforce-based cross-sectional	3650 healthcare professionals (862 physicians, 941 nurses, 968 occupational therapists, 879 respiratory therapists)	Questionnaire, BHR defined as 8-item, symptom-based predictor of PC20, JEM	Age, sex, race/ethnicity, professional group, years as a health professional ('seniority'), smoking, obesity	Exposure to cleaning agents/tasks	Outcome: BHR related symptoms General cleaning: OR=1.63 (1.21–2.19) Cleaning products used on building surfaces: OR=1.74 (1.34–2.26) Instrument cleaning: OR=1.40 (1.09–1.79) Adhesives/solvents/gases in patient care: OR=1.86 (1.42–2.44)	High
Karadzinska-Bislimovska et al, 2007[35]	FYROM	2004–2006	Cross-sectional	Women, 43 cleaners,37 cooks, 45 controls (office workers)	Questionnaire	Smoking, BMI, baseline FEV_1	Female cleaners	Prevalence of BHR higher in cleaners than controls though not statistically significant (30.2% vs 17.7%)	Moderate
LRTS and URTS									
Nielsen and Bach, 1999[40]	Denmark	1989–1991	Workforce-based cohort	1011 female cleaners employed at nursing homes, schools and offices	Questionnaire	Age, smoking	Female domestic cleaners Use of sprayers	Continuous use of sprayers Eye/nose/throat symptoms: OR=2.1 (1.1–3.8) Asthma symptoms: OR=3.0 (0.9–10) Bronchitis: OR=3.2 (1.0–10.4)	Moderate
Medina-Ramón et al, 2005[37]	Spain	2001–2002	Case-control, nested within a large population-based survey	Domestic cleaning women, 40 cases (with asthma and/or chronic bronchitis symptoms, 155 controls)	Questionnaire Lung function, methacholine challenge, serum IgE testing Personal measurements of airborne chlorine and ammonia	Age, smoking, bleach, cleaning products, washing dishes, inhalation accidents, non-domestic cleaning	Female domestic cleaners	Combined outcome: asthma/chronic bronchitis symptoms Bleach use Intermediate exposure: OR=3.3 (0.9–11) High exposure: OR=4.9 (1.5–15)	Moderate
Medina-Ramón et al, 2006[39]	Spain	2001–2002	Population-based cross-sectional panel	43 female domestic cleaners recruited from a previous case-control study	Diary Lung function and allergy testing	Age, respiratory infections, medications	Domestic cleaners	LRTS more common on working days: OR=3.1 (1.4–7.1) LRTS predominantly associated with exposure to diluted bleach, degreasing sprays/atomisers and air fresheners	Moderate
Karadzinska-Bislimovska et al, 2007[35]	FYROM	2004–2006	Population-based cross-sectional	Women, 43 cleaners,37 cooks, 45 controls (office workers)	Questionnaire	Smoking, BMI, baseline FEV_1	Female cleaners	Significantly higher prevalence of phlegm (p=0.019) and dyspnoea (p=0.041) in cleaners compared with the control group	Moderate
Obadia et al, 2009[29]	Canada	Not specified	Workforce-based case control	566 cleaners and 587 other building workers	Questionnaire	Age, gender, smoking	School or racetrack public building cleaners	LRTSs in female cleaners: OR=2.59 (1.6–4.3) LRTSs in male cleaners: OR 1.16 (95% CI 0.7 to 1.9)	High
Wieslander and Norback, 2010[38]	Sweden	Not specified	Population-based cross-sectional	21 hospital cleaners	Questionnaire		Hospital cleaners	Significant increase in nasal symptoms (p<0.001) and throat symptoms (p<0.05) Significant increase in dyspnoea (p<0.01)	Low

Table 2 continued

Author, year	Country	Year of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% CI in parenthesis)	GRADE score
Vizcaya et al, 2011[30]	Spain	2007–2008	Cross-sectional study on employees of cleaning companies	917 employees of 37 cleaning companies: 761 current cleaners, 86 former and 70 never cleaners (referents)	Spirometry during clinic visit	Sex, age, nationality, smoking status	Cleaning occupation	Wheeze without having a cold, current cleaners: OR=1.3 (9 0.5–3.3), former cleaners: OR=2.0 (0.6–6.5) Chronic cough, current cleaners: OR=1.8 (0.7–4.7), former cleaners: OR=1.9 (0.5–7.8)	Moderate
Lee et al, 2014[36]	USA	Not specified	Workforce-based cross-sectional	183 hospital cleaners	Questionnaire, face to face interview	Age, gender, job title	Hospital cleaners. Exposure classified in tasks and cleaning products used	For chemical-related symptoms (respiratory tract, eye, skin, nervous and gastrointestinal systems): *Medium exposure* Cleaning tasks using sprays: OR=3.16 (1.24–8.04) Cleaning toilet bowls or sinks: OR=1.71 (0.72–4.01) Bleach: OR=1.29 (0.55–3.04) Disinfectants: OR=0.67 (0.28–1.62) Liquid multi-use cleaning products: OR=0.83 (0.35–1.95) *High exposure* Cleaning tasks using sprays OR=1.98 (0.87–4.51) Cleaning toilet bowls or sinks: OR=1.96 (0.82–4.69) Bleach: OR=1.68 (0.70–4.01) Disinfectants: OR=0.72 (0.30–1.74) Liquid multi-use cleaning products: OR=2.35 (1.02–5.43)	High
Svanes et al, 2015[21]	Norway, Sweden, Denmark, Iceland Estonia	2010–2012	Population-based cross-sectional (Respiratory Health In Northern Europe, part of ECRHS)	2138 ever cleaners (from 13 499 respondents)	Questionnaire	Age, gender, smoking, educational level, parent's educational level, BMI, centre	Occupational cleaner	Wheeze last 12 months: OR=1.44 (1.27–1.62) Asthma symptoms: OR=1.66 (1.46–1.90) Positive trend with duration of exposure for both outcomes	High
Abrahamsen et al, 2017[24]	Norway	February to August 2013	Population-based cross-sectional study	185 cleaners (among 16 099 responders)	Questionnaire	Age, gender, area of residence, smoking, home damp/mould, housing conditions	Female and male cleaners JEM	Wheezing OR=0.76 (0.47–1.2) Woken with dyspnoea OR=0.63 (0.27–1.4)	Medium
Whitworth et al, 2019[41]	USA	2017	Cross-sectional study	56 Hispanic female domestic cleaners	Questionnaire	Age and ever smoking	Cleaning tasks and agents	Exposure to cleaning tasks was statistically insignificantly associated with BHR symptoms. Exposure to ammonia: OR=7.5 (1.6–35.9). Exposure to solvents and use of sprays for air freshening was also associated with BHR related symptoms	Medium

BHR, bronchial hyper-responsiveness; ECRHS, European Community Respiratory Health Survey; JEM, job-exposure matrix; LTRS, lower tract respiratory symptom; PR, prevalence ratio; UTRS, upper tract respiratory symptom.

one workforce-based assessed associations with the composite outcome rhinitis/asthma[34] (table 3); most have shown small and statistically not significant increased risks. Phenotypes of rhinitis were examined by one study that found increased risk of perennial rhinitis among cleaners, especially women (OR=1.70 (1.09 to 2.64).[42] Similarly in Brazil, female cleaners only had higher risk of a composite outcome rhinitis/asthma (rhinitis defined as self-reported sneezing or runny or blocked nose, without cold or influenza over the past 12 months).[34] Neither of these studies conducted formal tests for gender interaction. Evidence from a cross-sectional study in Spain on current and former cleaners (domestic and non-domestic) showed increased and significant associations with rhinitis only for former domestic cleaners.[19]

COPD

Three studies examined the association between occupational cleaning exposure and COPD risk.[4 21 43] A significant association of working as a cleaner and having spirometrically-defined COPD (ie, forced expiratory volume in 1 s, FEV_1/forced vital capacity, FVC <lower limit of normal, LLN) was found in a recent large population-based cross-sectional analysis of 228 614 people in the UK Biobank study. A 43% risk increase (prevalence ratio, PR=1.43; 95% CI 1.28 to 1.59) was found for cleaning occupation, also confirmed in analyses restricted to never smokers and non-asthmatics.[4] Also, a cross-sectional study of 13 499 Northern European cleaners reported an increased risk of self-reported COPD diagnosis (OR=1.69; 95% CI 1.29 to 2.20).[21] Finally, a very recent workforce-based prospective cohort study among hospital nurses in USA found an increased incidence of COPD (self-reported doctor-diagnosis) for exposure to cleaning products and disinfectants (HR=1.35; 95% CI 1.14 to 1.59) for weekly self-reported exposure to any disinfectant)[43] (table 3).

Meta-analysis for COPD outcome

Overall, the pooled meta-analysis of these three studies[4 21 43] showed a 43% increased risk for COPD (meta-RR=1.43; 95% CI 1.31 to 1.56; I^2=0.0%; p=0.38) (figure 3). Based on the heterogeneity tests between studies, fixed methods were applied to pool the risk estimates.

No evidence of publication bias was detected (Egger's test p=0. 60) (online supplementary figure S2).

Lung function metrics

Seven studies (table 3) evaluated as outcome lung function metrics decline in occupational cleaners.[23 31 37 44–47] The majority did not find significant differences in lung function among cleaners compared with controls. For example, one large multicentre population-based study found a significant decrease of cross-shift peak expiratory flow (PEF) only,[23] and another found lower cross-shift FEV1, and PEF among cleaners with current asthma only.[45] However, a recent international population-based longitudinal study found an accelerated lung function decline among professional cleaners (FEV1: −22.4 mL/year; p=0.03, and FVC: −15.9 mL/year; p=0.002).[47] Also, a very recent workforce-based cross-sectional study in New Zealand found a significant decline in lung function metrics among cleaners compared with controls.[31]

Other health outcomes

Among other health outcomes evaluated to better clinically phenotype the specific respiratory health effects among cleaners, atopy has been the one mostly investigated, because asthma is commonly allergy-based and cleaning products often contain potent IgE-mediated sensitising agents such as chloramine-T, ortho-phthalaldehyde and enzymes. One large multinational study showed a lower prevalence of atopy in cleaners compared with office workers (38.3% vs 60.9%; p<0.05).[23] Of note, a workforce case-control study found higher atopy in cleaners with asthma than without (42% vs 10%, respectively), also associated with higher total IgE serum levels (geometric mean ratio: 2.9; 1.5–5.6).[46]

Fractionated exhaled nitric oxide (FeNO), a marker of airways inflammation and eosinophilic infiltration that has been associated with atopic asthma, has also been investigated. Three studies investigating FeNO in exhaled breath condensate after acute (preshift versus postshift) exposure to cleaning products containing chlorine did not found a significant difference between cleaners and controls.[44 46 48] Of note, in one of them, a positive association of exposure to cleaning products with biomarkers of oxidative stress and inflammation (ie, malondialdehyde (MDA), 4-hydroxynonenal (4-HNE), nitrates (NO3-), in the exhaled breath condensate was found[48] (table 3).

Grey literature

As above stated, the three studies included from searching the OpenGrey database were excluded from the final systematic review because of the low quality or missing information to assess the GRADE scoring (online supplementary table S6).

Briefly, one very small workforce surveillance study found increased asthma prevalence diagnosed via PEF diary among hospital cleaners.[49] Another workforce survey found a non-significant higher prevalence of self-reported asthma and chronic bronchitis among hospital cleaners compared with administrative controls.[50] A small population cross-sectional study showed a higher prevalence of BHR (based on histamine challenge test) and associated respiratory symptoms (eg, cough, phlegm, wheezing) compared with office workers.[51]

DISCUSSION

Our systematic review examined for the first time a broad variety of respiratory health effects in association with occupational exposure to cleaning products.

We found a clear increased risk of asthma among occupational cleaners that we quantified by performing a meta-analysis into 50%. Of note, the majority (15 out of 21) of the studies included in the meta-analysis used cleaning occupation as a *proxy* for occupational exposure to cleaning agents and therefore were not susceptible to recall bias. Most of the studies were cross-sectional by design and evaluated asthma as self-reported doctor's diagnosis or asthma symptoms; only a few managed to assess it by objective lung function tests. Also, supporting positive exposure-relationship by duration of employment or exposure (mainly self-reported) to cleaning agents was found.

Weaker positive associations were found for BHR, LRTS, URTS and rhinitis. In particular, BHR was increased among cleaners although within individual studies, this rarely reached conventional levels of statistical significance. Among the LRTS assessed, chronic cough and wheezing were reported as increased among cleaners, often when evaluated in association with an asthma diagnosis. Among the URTS, a weaker, but interesting, association with inspiratory breathing suggestive for irritant vocal cord dysfunction was found. Also, rhinitis was inconstantly found increased among cleaners, and only when associated to exposure to high molecular weight allergens in cleaning agents.

Interestingly, the majority of studies did not find an association with single lung function metrics as outcomes, namely

Table 3 Summary of epidemiological studies (chronological order) assessing the associations between cleaning occupation, tasks or agents and rhinitis, COPD, lung function and other health outcomes

Author, year	Country	Year of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% CI in parenthesis)	GRADE score
Rhinitis									
Medina-Ramón et al, 2003[19]	Spain	2000–2001	Population-based cross-sectional	4521 female domestic cleaners, 593 current, 1170 former	Questionnaire	Age, smoking	Current domestic cleaners Former domestic cleaners	Current cleaner: OR=1.08 (0.92–1.28) Former cleaner: OR=1.27 (1.12–1.47)	High
de Fátima Maçâira et al, 2007[34]	Brazil	December 2002 to May 2003	Workforce-based cross-sectional	341 cleaners	Questionnaire, skin prick test	Age, gender, smoking, atopy, number of years employment in non-domestic cleaning, inhalation accidents	Employment in non-domestic cleaning: 0.92–3 years 3–6.5 years >6.5 years	WRA/rhinitis OR=1.09 (1.00–1.18) WRA/rhinitis OR=1.28 (1.01–1.63) WRA/rhinitis OR=1.71 (1.02–2.89)	Moderate
Radon et al 2008[42]	Europe, 27 centres	1998–2003	Population-based cohort study (ECRHS II)	4994 (294 of them cleaners and caretakers)	Face-to-face interviews	Country, age at first survey, smoking, parental allergies, level of education	Occupations, asthmagens JEM	New-onset allergic rhinitis, cleaners and caretakers: OR=1.25 (0.86–1.81) Perennial rhinitis, cleaners and caretakers: OR=1.43 (0.99–2.06).	High
COPD									
Svanes et al, 2015[21]	Norway, Sweden, Denmark, Iceland, Estonia	2010–2012	Population-based cross-sectional (Respiratory Health In Northern Europe, part of ECRHS)	2138 ever cleaners (from 13 499 respondents)	Questionnaire	Age, gender, smoking, educational level, parent's educational level, BMI, centre	Occupational cleaner (ever) Duration of exposure: ≤1year 1–4 years ≥4 years	Self-reported COPD: OR=1.69(1.29–2.20) OR=1.41 (0.85–2.33) OR=1.80 (1.14–2.85) OR=1.65 (1.14–2.42)	High
De Matteis et al, 2016[4]	UK	2006–2010	Population-based cross-sectional (within the Biobank Cohort)	228 614 participants adults, 2017 cleaners	Self-administered questionnaires, face-to-face interviews and physical health measurements	Sex, age, recruitment centre, lifetime tobacco smoking	Domestic cleaners	COPD defined as FEV$_1$/FVC<LLN PR=1.43 (1.28 1.59) Never smokers: PR=1.38 (1.15 1.66) Non-asthmatics: PR=1.46 (1.29 1.65)	High
Dumas et al, 2019[43]	US	2009–2015	Workforce-based prospective cohort study (NHSII)	73 262 female registered nurses	Questionnaires	Age, smoking status and pack-years, race, ethnicity, and BMI	Highest exposure level to disinfectants, and sprays	Incident physician-diagnosed COPD Weekly use of any disinfectant: HR=1.35 (1.14–1.59) Weekly use of sprays: HR=1.27 (0.97–1.66)	High
Lung function and other health outcomes									
Zock et al, 2002[22]	11 European countries and three outside Europe	1990–1994	Population-based survey (ECRHS)	82 cleaners, 543 office workers	Spirometry, methacholine challenge test	Age, gender, smoking, study centre	Cleaning occupation	Not significantly associated with changes in FEV$_1$, FVC or FEV$_1$/FVC but was significantly associated with a decrease in PEF (p<0.05) Lower atopy in cleaners compared with office workers (38.3% vs 60.9%; p<0.05)	High
Medina-Ramón et al, 2005[37]	Spain	2000–2001	Case-control, nested within a large population-based survey	Domestic cleaning women, 40 cases (with asthma and/or chronic bronchitis symptoms, 155 controls)	Questionnaire Lung function, methacholine challenge, serum IgE testing Personal measurements of airborne chlorine and ammonia	Age, smoking, bleach, cleaning products, washing dishes, inhalation accidents, non-domestic cleaning	Female domestic cleaners	No difference between cases and controls with regards to FEV$_1$	Moderate
Corradi et al, 2012[44]	Italy	Not specified	Workforce-based cross-sectional	40 hospital cleaners, 40 controls	Spirometry	Age, gender, ethnicity, height	Hospital cleaners	Predicted FEV$_1$ %: similar in cleaners and controls. No difference in FeNO among cleaners compared with controls.	Moderate

Table 3 continued

Author, year	Country	Year of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% CI in parenthesis)	GRADE score
Vizcaya et al 2013[46]	Spain	2008–2009	Workforce-based case-control nested in a cross-sectional study among cleaning company employees	42 asthma cases, 53 controls	Spirometry during clinic visit	Age, gender, smoking	Female cleaners	Most irritant products and sprays were more often used by asthmatic cleaners. The use of multiuse products, glass cleaners and polishes at work was associated with higher FeNO, particularly in controls. No differences between cases and controls in levels of FeNO, or biomarkers of oxidative stress.	Moderate
Vizcaya et al, 2015[45]	Spain	2008–2009	Workforce-based cross-sectional panel	21 female cleaners with current asthma	Spirometry	Age, smoking, having a cold or influenza, use of respiratory medication	Cleaning agents	FEV$_1$ reduction after exposure to hydrochloric acid, solvents, and sprays among current cleaners with asthma	Low
Casimirri et al, 2016[48]	Italy	Not specified	Workforce-based cross-sectional	40 hospital cleaners, 40 non-exposed controls	Spirometry	Age, smoking, BMI	Chlorinated agents	Higher EBC biomarkers of oxidative stress and inflammation in cleaners.	Moderate
Svanes et al, 2018[47]	Many European countries	1992–1994 (ECRHS I), 1998–2002 (ECRHS II), 2010–2012 (ECRHS III)	Population-based longitudinal study	6235 subjects ECRHS I and II, 3804 subjects (ECRHS III)	Spirometry/bronchodilator test	Age, smoking pack-years, BMI, parents' education and SES	Cleaning occupation, cleaning at home, use of sprays and other agents	More rapid FEV$_1$ decline in women cleaning at home (−22.1 mL/year, p=0.01) and occupational cleaners (−22.4, p=0.03), compared with women not engaged in cleaning (−18.5) More rapid FVC decline in women cleaning at home (−13.1 mL/year, p=0.02) and occupational cleaners (−15.9, p=0.002), compared with women not engaged in cleaning (−8.8) Cleaning sprays: FEV$_1$ −22.0 mL/year, p=0.04) Other cleaning agents: FEV$_1$ −22.9 mL/year, p=0.004)	High
Brooks et al, 2020[31]	New Zealand	2008–2010	Workforce based cross-sectional	425 cleaners, 281 reference workers	Questionnaires, bronchodilator	Age, gender, ethnicity, smoking	Cleaners	Mean differences between cleaners and referents: FEV$_1$ =−0.20 L (−0.29 to −0.10) FEV$_1$ % predicted=−3.12% (−5.68 to −0.57) FVC=−0.25 L (−0.36 to −0.14) FVC % predicted=−3.25% (−5.55 to −0.96)	High

COPD, chronic obstructive pulmonary disease; EBC, exhaled breath condensate; ECRHS, European Community Respiratory Health Survey; FEV$_1$, forced expiratory volume in 1 s; FVC, forced vital capacity; GMR, geometric mean ratio; JEM, job-exposure matrix; LLN, lower-limit of normal; MEF25, maximal expiratory flow at 25% of vital capacity; MEF50, maximal expiratory flow at 50% of vital capacity; OASYS, occupational asthma expert system; PD20, administered cumulative dose of methacholine which results in a drop in FEV$_1$ by 20%; PEF, peak expiratory flow; PR, prevalence ratio.

FEV$_1$, FVC and FEV$_1$/FVC ratio. This is maybe due to well-known low sensitivity of occasional spirometry tests to detect occupational asthma or suggesting that if asthma-like symptoms arise in cleaners, it may not be due to airway obstruction but to other underlying mechanisms. Of note, a recent international population-based longitudinal study reported significant lung function decline associated with cleaning work that would support long-term respiratory health-effects.[47]

In addition, we found an increased COPD risk for cleaning occupation that we managed to quantify into 43% based on three high quality large population-based studies. It is noteworthy that the largest of the two used a spirometry-based definition of COPD and managed to confirm these findings in both never smokers and non-asthmatics, so ruling out residual confounding by both tobacco and asthma. This result is important because COPD has been largely linked to other occupational exposures such as generic VGDF (ie, vapour, gas, dust, fumes) exposure, but the evidence for cleaning agents is still scarce.

In relation to the potential associated respiratory phenotypes, no clear association with allergy or exhaled FeNO (ie, biomarker of airway inflammation in patients with asthma) was found, but an association with biomarkers of oxidative stress and inflammation (ie, MDA, 4-HNE and NO3⁻) was reported.

Among the evaluated potential causal agents, chlorine-based cleaning products, such as bleach were found associated with increased asthma risk,[37] but also ammonia, quaternary ammonium compounds, disinfectants and sterilising agents such as ethanolamide, and glutaraldehyde, especially among healthcare workers performing cleaning tasks.[27] As expected, cleaning products in spray format were associated with an higher asthma risk.[22] Nevertheless, the lack of personal quantitative exposure assessment to the above agents and their pungent odour make these findings potentially susceptible to recall bias.

Overall, our findings seem to support the still debated hypothesis that cleaning-related respiratory health effects may be caused via irritation rather than immuno-mediated underlying mechanisms. As previously suggested,[52] chronic exposure at relatively moderate doses, such as among occupational cleaners, to airborne irritative chemicals could cause inflammation and subsequent bronchoconstriction. Also, our results suggest that if exposure at work to noxious cleaning agents persists a reversible airway obstruction could become irreversible. This is confirmed by studies included in this review that found a positive exposure-response relationship by employment duration and frequency/intensity of exposure to cleaning-tasks.[21 25–27]

Our systematic review has several strengths. It evaluated a broad range of respiratory health effects and associated phenotypes, and it aimed to be very comprehensive by including also grey literature, as confirmed by the absence of publication bias. Also, we evaluated the evidence quality by applying a standard quality scoring system slightly modified to be suitable to appraise occupational epidemiology evidence. Finally, we managed to quantify a pooled risk estimate for asthma and COPD outcomes that can be used to inform public health interventions and future similar studies on the topic.

Limitations include the exclusion of articles not in English language. Also, misclassification of both exposure and outcome cannot be ruled out, and not all studies adjusted for the same potential confounders. However, both the meta-analysis for asthma and COPD outcomes among the selected studies showed a low heterogeneity that allowed us to use fixed-effect pooling methods.

In conclusion, in our systematic review, we found that occupational exposure to cleaning product is associated with several respiratory health effects, including both reversible and irreversible airway obstruction, and the suggested causal association is supported by evidence of positive exposure-response trends.

These findings have important potential public health implications: preventive measures to avoid, or at least reduce exposure to cleaning agents at workplace should be implemented, and respiratory health surveillance should be strengthened among this category of workers in order to detect early signs of respiratory health effects and so avoid any subsequent morbidity and disability. In addition, according to the precautionary principle, important downstream implications for all end-users of cleaning products during domestic housekeeping could be to suggest reducing exposures to 'as low as possible', especially to protect vulnerable subjects such as children from potentially harmful 'bystander' exposure. Our findings are particularly relevant in the current COVID-19 pandemic. Use and exposure to cleaning products in the general population has globally increased for infection control. We recommend adding to pandemic guidance documents information on cleaning-related respiratory health effects and on safe use of cleaning products to prevent the associated public health burden.

Further studies, ideally prospective cohorts using more precise quantitative exposure assessment of individual cleaning agents (eg, exact chemical composition by use of product bar codes), detailed clinical phenotyping (eg, airway inflammatory and immune biomarkers) and modern molecular methods (eg, metabolomics) would help clarify both the underlying causal agents and the relevant biological mechanisms. Filling this knowledge gap would allow implementation of effective focused preventive intervention strategies aimed to eliminate or at least control exposure to hazardous cleaning agents and identify early health effects to prevent the associated occupational respiratory health burden with important personal, medical and societal benefits.

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REFERENCES

1 Brun E. *The occupational safety and health of cleaning workers. Luxemburg: EU-OSHA – European agency for safety and health at work*, 2009.

2 Siracusa A, De Blay F, Folletti I, *et al*. Asthma and exposure to cleaning products - a European Academy of Allergy and Clinical Immunology task force consensus statement. *Allergy* 2013;68:1532–45.

3 Folletti I, Siracusa A, Paolocci G. Update on asthma and cleaning agents. *Curr Opin Allergy Clin Immunol* 2017;17:90–5.

4 De Matteis S, Jarvis D, Hutchings S, *et al*. Occupations associated with COPD risk in the large population-based UK Biobank cohort study. *Occup Environ Med* 2016;73:378–84.

5 Casas L, Nemery B. Irritants and asthma. *Eur Respir J* 2014;44:562–4.

6 Labrecque M. Irritant-Induced asthma. *Curr Opin Allergy Clin Immunol* 2012;12:140–4.

7 De Matteis S, Cullinan P. Occupational asthma in cleaners: a challenging black box. *Occup Environ Med* 2015;72:755–6.

8 Guyatt G, Oxman AD, Akl EA, *et al*. Grade guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383–94.

9 Cochran WG. The combination of estimates from different experiments. *Biometrics* 1954;10:101–29.

10 DerSimonian R, Laird N. Meta-Analysis in clinical trials. *Control Clin Trials* 1986;7:177–88.

11 Higgins JPT, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.

12 Eng A, 'T Mannetje A, Douwes J, *et al*. The New Zealand workforce survey II: occupational risk factors for asthma. *Ann Occup Hyg* 2010;54:154–64.

13 Ghosh RE, Cullinan P, Fishwick D, *et al*. Asthma and occupation in the 1958 birth cohort. *Thorax* 2013;68:365–71.

14 Jaakkola JJK, Piipari R, Jaakkola MS. Occupation and asthma: a population-based incident case-control study. *Am J Epidemiol* 2003;158:981–7.

15 Karjalainen A, Martikainen R, Karjalainen J, *et al*. Excess incidence of asthma among Finnish cleaners employed in different industries. *Eur Respir J* 2002;19:90–5.

16 Kogevinas M, Antó JM, Sunyer J, *et al*. Occupational asthma in Europe and other industrialised areas: a population-based study. *The Lancet* 1999;353:1750–4.

17 Kogevinas M, Zock J-P, Jarvis D, *et al*. Exposure to substances in the workplace and new-onset asthma: an international prospective population-based study (ECRHS-II). *Lancet* 2007;370:336–41.

18 Le Moual N, Kennedy SM, Kauffmann F. Occupational exposures and asthma in 14,000 adults from the general population. *Am J Epidemiol* 2004;160:1108–16.

19 Medina-Ramón M, Zock JP, Kogevinas M, *et al*. Asthma symptoms in women employed in domestic cleaning: a community based study. *Thorax* 2003;58:950–4.

20 Mirabelli MC, Zock J-P, Plana E, *et al*. Occupational risk factors for asthma among nurses and related healthcare professionals in an international study. *Occup Environ Med* 2007;64:474–9.

21 Svanes Øistein, Skorge TD, Johannessen A, *et al*. Respiratory health in cleaners in northern Europe: is susceptibility established in early life? *PLoS One* 2015;10:e0131959.

22 Zock JP, Kogevinas M, Sunyer J, *et al*. Asthma risk, cleaning activities and use of specific cleaning products among Spanish indoor cleaners. *Scand J Work Environ Health* 2001;27:76–81.

23 Zock JP, Kogevinas M, Sunyer J, *et al*. Asthma characteristics in cleaning workers, workers in other risk jobs and office workers. *Eur Respir J* 2002;20:679–85.

24 Abrahamsen R, Fell AKM, Svendsen MV, *et al*. Association of respiratory symptoms and asthma with occupational exposures: findings from a population-based cross-sectional survey in Telemark, Norway. *BMJ Open* 2017;7:e014018.

25 Arif AA, Delclos GL. Association between cleaning-related chemicals and work-related asthma and asthma symptoms among healthcare professionals. *Occup Environ Med* 2012;69:35–40.

26 Delclos GL, Gimeno D, Arif AA, *et al*. Occupational risk factors and asthma among health care professionals. *Am J Respir Crit Care Med* 2007;175:667–75.

27 Dumas O, Donnay C, Heederik DJJ, *et al*. Occupational exposure to cleaning products and asthma in hospital workers. *Occup Environ Med* 2012;69:883–9.

28 Gonzalez M, Jégu J, Kopferschmitt M-C, *et al*. Asthma among workers in healthcare settings: role of disinfection with quaternary ammonium compounds. *Clin Exp Allergy* 2014;44:393–406.

29 Obadia M, Liss GM, Lou W, *et al*. Relationships between asthma and work exposures among non-domestic cleaners in Ontario. *Am J Ind Med* 2009;52:716–23.

30 Vizcaya D, Mirabelli MC, Antó J-M, *et al*. A workforce-based study of occupational exposures and asthma symptoms in cleaning workers. *Occup Environ Med* 2011;68:914–9.

31 Brooks C, Slater T, Corbin M, *et al*. Respiratory health in professional cleaners: symptoms, lung function, and risk factors. *Clin Exp Allergy* 2020;50:567–76.

32 Dumas O, Boggs KM, Quinot C, *et al*. Occupational exposure to disinfectants and asthma incidence in U.S. nurses: a prospective cohort study. *Am J Ind Med* 2020;63:44–50.

33 Le Moual N, Siroux V, Pin I, *et al*. Asthma severity and exposure to occupational asthmogens. *Am J Respir Crit Care Med* 2005;172:440–5.

34 de Fátima Maçaira E, Algranti E, Medina Coeli Mendonça E, Macaira EDF, Mendonca EMC, *et al*. Rhinitis and asthma symptoms in non-domestic cleaners from the Sao Paulo metropolitan area, Brazil. *Occup Environ Med* 2007;64:446–53.

35 Karadzinska-Bislimovska J, Minov J, Risteska-Kuc S, *et al*. Bronchial hyperresponsiveness in women cooKs and cleaners. *Arh Hig Rada Toksikol* 2007;58:223–31.

36 Lee S-J, Nam B, Harrison R, *et al*. Acute symptoms associated with chemical exposures and safe work practices among hospital and campus cleaning workers: a pilot study. *Am J Ind Med* 2014;57:1216–26.

37 Medina-Ramón M, Zock JP, Kogevinas M, *et al*. Asthma, chronic bronchitis, and exposure to irritant agents in occupational domestic cleaning: a nested case-control study. *Occup Environ Med* 2005;62:598–606.

38 Wieslander G, Norbäck D. A field study on clinical signs and symptoms in cleaners at floor Polish removal and application in a Swedish Hospital. *Int Arch Occup Environ Health* 2010;83:585–91.

39 Medina-Ramón M, Zock JP, Kogevinas M, *et al*. Short-Term respiratory effects of cleaning exposures in female domestic cleaners. *Eur Respir J* 2006;27:1196–203.

40 Nielsen J, Bach E. Work-Related eye symptoms and respiratory symptoms in female cleaners. *Occup Med* 1999;49:291–7.

41 Whitworth KW, Berumen-Flucker B, Delclos GL, *et al*. Job hazards and respiratory symptoms in Hispanic female domestic cleaners. *Arch Environ Occup Health* 2020;75:70–4.

42 Radon K, Gerhardinger U, Schulze A, *et al*. Occupation and adult onset of rhinitis in the general population. *Occup Environ Med* 2008;65:38–43.

43 Dumas O, Varraso R, Boggs KM, *et al*. Association of occupational exposure to disinfectants with incidence of chronic obstructive pulmonary disease among US female nurses. *JAMA Netw Open* 2019;2:e1913563.

44 Corradi M, Gergelova P, Di Pilato E, *et al*. Effect of exposure to detergents and other chemicals on biomarkers of pulmonary response in exhaled breath from hospital cleaners: a pilot study. *Int Arch Occup Environ Health* 2012;85:389–96.

45 Vizcaya D, Mirabelli MC, Gimeno D, *et al*. Cleaning products and short-term respiratory effects among female cleaners with asthma. *Occup Environ Med* 2015;72:757–63.

46 Vizcaya D, Mirabelli MC, Orriols R, *et al*. Functional and biological characteristics of asthma in cleaning workers. *Respir Med* 2013;107:673–83.

47 Svanes Øistein, Bertelsen RJ, Lygre SHL, *et al*. Cleaning at home and at work in relation to lung function decline and airway obstruction. *Am J Respir Crit Care Med* 2018;197:1157–63.

48 Casimirri E, Stendardo M, Bonci M, *et al*. Biomarkers of oxidative-stress and inflammation in exhaled breath condensate from hospital cleaners. *Biomarkers* 2016;21:115–22.

49 Al-Fajjam SM. *Prevalence and risk factors of asthma among cleaners in the North East of England*, 2013.

50 Nasir S, Sanchez-Vazquez M, Dick F. Cross-Sectional survey of respiratory symptoms and exposures in Scottish health service cleaners. *Occup Environ Med* 2011;68:A91.

51 Mijakoski D, Karadzinska-Bislimovska J, Stoleski S. Respiratory symptoms, lung function tests, and sensitization to work-related allergens in female cleaners. European Respiratory Journal Conference: European Respiratory Society Annual Congress, 2013:42.

52 Vandenplas O, Wiszniewska M, Raulf M, *et al*. EAACI position paper: irritant-induced asthma. *Allergy* 2014;69:1141–53.