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ORIGINAL RESEARCH

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The relationship between cleaning product exposure and respiratory and skin symptoms among healthcare workers in a hospital setting: A systematic review and meta-analysis

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Abstract

Background and Aims: Several studies from multiple work settings have reported an increase in asthma and asthma-like respiratory symptoms in workers exposed to cleaning or disinfecting agents. Hospital workers perform many cleaning and disinfecting activities and may be vulnerable to respiratory and skin symptoms caused by these agents. This systematic review and meta-analysis aim to quantify the risk of asthma and asthma-like symptoms in hospital workers exposed to cleaning/disinfecting agents. A secondary aim is to assess associated risks of skin symptoms in those studies.

Methods: MEDLINE, EMBASE, CDSR, CENTRAL, CINAHL databases, and references of relevant review articles were searched. NHLBI quality assessment tools were used to assess the quality of the included studies. A total of 2550 articles were retrieved and 34 studies met criteria to be included. The software R version 4.0.5 was used to perform the meta-analysis. The random-effects model was used to pool the results due to within-studies heterogeneity.

Results: Meta-analysis of 10 studies evaluating the association between occupational cleaning exposures and asthma demonstrated a 35% increased risk in exposed hospital workers (meta-RR = 1.35, 95% CI: 1.09–1.68). The risk of asthma increased when workers were exposed to bleach compared with nonexposed workers (meta-RR = 1.51, 95% CI: 0.54–4.18), but was not statistically significant. Two studies investigated the relationship between respiratory and skin symptoms and produced mixed results.

Conclusions: The results suggest a need for preventive practices to reduce the risk of asthma and asthma-like symptoms in hospital workers exposed to occupational cleaning/disinfecting agents. Trial registration number: CRD42020137804.

KEYWORDS

asthma, cleaning, disinfecting agents, hospital workers, respiratory symptoms

1 | INTRODUCTION

Cleaning and disinfecting tasks make up a significant portion of the duties of healthcare professionals and other workers in-hospital settings, especially to reduce risks of infection. These tasks can range from common housekeeping practices performed by cleaning staff, to surface and equipment cleaning and disinfection by healthcare workers such as nurses, respiratory therapists, physiotherapists, and radiographers. Multiple agents may be used for these tasks including quaternary ammonium compounds, bleach, and hydrogen peroxide. Cleaning and disinfection of endoscopes and surgical equipment may include use of potential respiratory sensitizers such as enzymes, and aldehydes such as glutaraldehyde or ortho-phthaldehyde. Many of these tasks and agents have been associated with respiratory sensitization or irritation.[1,2] Previous studies have reported an increased risk of asthma, asthma-like respiratory symptoms, as well as skin symptoms among healthcare workers exposed to cleaning or disinfecting agents.[3–5] Specifically, bleach has been associated with asthma-like respiratory symptoms and hand dermatitis[6]; however, few studies have evaluated the relationship between respiratory and skin symptoms. Additionally, previous evidence of increased respiratory and skin symptoms among this population was derived from self-reported measures of exposures. Therefore, there is a potential for bias toward reporting cleaning agents with stronger odors, causing uncertainty regarding the specific agents that may cause both respiratory and skin symptoms among hospital workers.[7]

A recent systematic review conducted by Romero Starke et al. addressed a similar research question, the risk of obstructive respiratory diseases among healthcare workers exposed to cleaning or disinfecting agents compared with a nonexposed group[8]; however, the review did not focus on all hospital workers and did not aim to evaluate skin symptoms among exposed healthcare workers with respiratory symptoms, nor to identify specific agents in the search strategy.

The aim of our study was to perform a comprehensive systematic review and meta-analysis of the available literature to quantify the risk of asthma and asthma-like symptoms in hospital workers exposed to cleaning or disinfecting agents. Furthermore, we aimed to identify risks of associated skin symptoms among the included studies, and the potential underlying causal agents.

2 | METHODS

2.1 | Literature search strategy and eligibility criteria

The systematic review was conducted following the PRISMA guidelines and the protocol was registered in PROSPERO (CRD42020137804) on April 28, 2020. The following electronic bibliographic databases were searched on October 5, 2017 and updated on August 9, 2021: Ovid MEDLINE, Ovid MEDLINE(R) ePub Ahead of Print and In-Process & Other Non-Indexed Citations, EBM Reviews—Cochrane Database of Systematic Reviews (Ovid), EBM Reviews—Cochrane Central Register of Controlled Trials (Ovid), Embase (Ovid), and CINAHL (EBSCOhost). The search strategy consisted of using a combination of subject headings and free text terms for asthma, occupational exposures, healthcare personnel, and specific cleaning and disinfecting agents Terms for asthma included such terms as asthma, wheeze, bronchial hyperreactivity, respiratory hypersensitivity, and airflow obstruction among others. Terms for workplace exposure included such terms as occupational disease, occupational exposure, work, occupation, job-site, and occupational air pollutants among others. Terms for healthcare workers included varied types of healthcare personnel and health facilities among others, Terms for cleaning products included terms for disinfectants, detergents, surface-active agents, ammonium compounds, anti-infective agents, acetic acid, 2-propanol, chloramines, phenols, and decontamination procedures among others (full search strategies are included in the Table S1). The search strategy was adapted for each database. Additional studies were found by examining the references of relevant reviews. All studies that evaluated respiratory outcomes, symptoms, diseases, or lung function measures in relation to occupational cleaning or disinfecting tasks or products in any hospital workers were included. Among the included studies, data regarding skin outcomes were also sought. Inclusion criteria were grouped according to the population-exposure-comparator-outcome (PECO) framework:

- Population—populations in which individuals worked in a hospital setting;
- Exposures—studies of individuals with exposure at work to cleaning and/or disinfecting agents;
- Comparators—studies reporting comparative effect estimates, specifically case-control or cohort studies reporting risk, rate, or odds across groups exposed to different levels of cleaning and/or disinfecting agents (including binary comparisons of exposed/unexposed), and across groups with and without asthma or asthma-like symptoms;
- Outcome—studies reporting incident asthma or asthma-like symptoms;
- Among subjects with asthma or asthma-like symptoms, the presence of reported skin symptoms was an additional outcome;
- English-language full-text available;
- Publication up to 6th August 2021.

We excluded studies that did not meet the inclusion criteria above. Randomized controlled trials, nonrandomized trials, cohort studies, and case control studies available in English were included. No restrictions regarding country, patient age, race, gender, and date were made. Case series, research in progress, conference proceedings, dissertations, books, editorials, letters, and review articles were excluded. Studies including occupational settings located outside of a medical centre or hospital were also excluded. A full list of inclusion and exclusion criteria is available in Table S2.

2.2 | Selection process, data collection process, and quality assessment

Two reviewers independently screened the study titles and abstracts to exclude studies that did not meet the eligibility criteria. The full texts of the included studies were also screened independently by two reviewers. A consensus decision was made for disagreements regarding the inclusion of articles. If a disagreement was not resolved, a third reviewer was consulted for a final decision. Data extraction was completed independently by two reviewers using a modified form of the Cochrane Public Health Group Data Extraction and Assessment Template, adapted for this study according to the study aims and inclusion/exclusion criteria (Table S3). Two reviewers independently assessed the risk of bias in the included studies using the NHLBI quality assessment tools, suitable for the type of study, for example, observational cohort and cross-sectional studies (Table S4). A third reviewer was consulted for a final, deciding rating when there were quality assessment differences. The final scoring classification was ranked as poor, fair, or good.

2.3 | Statistical methods for meta-analysis

Meta-analyses were considered to quantify the risk of respiratory and skin symptoms that are associated with cleaning and disinfecting agents. Studies included in the systematic review that received a "fair" or "good" quality score according to the NHLBI quality assessment tools were considered for the meta-analyses. The main reported effect measures between occupational exposure to cleaning or disinfecting products and asthma or asthma-like symptoms were pooled using the random-effects model. The random-effects model was chosen in consideration of the heterogeneity within the studies in terms of populations, age, and exposures. The Mantel-Haenszel method was used to calculate the weights of the studies. Higgins I^2 statistic was used to determine within-studies heterogeneity. A threshold of $I^2 \geq 50\%$ was used to determine substantial within-studies heterogeneity.[9] Subgroup analysis by study design was performed. Pooled risk ratio estimates were presented as meta-relative risks (RRs) and 95% CIs. Statistical significance was determined by a *p*-value of less than 0.05. The package "meta" in the software R version 4.0.5 was used to perform the meta-analysis.[10] Funnel plots and Egger's test results were used to assess potential publication bias. Subgroup analyses were performed post-hoc to determine associations with different study classifications of asthma and asthma-like symptoms, and with specific reported exposures when comparable studies were available for meta-analyses.

3 | RESULTS

A total of 2549 articles were retrieved from all databases, with one additional article identified through manual searching. There were 158 duplicate articles removed and 2315 articles excluded from title and abstract screening. The full texts of 77 articles were screened. A total of 34 articles met the study inclusion criteria. Reasons for the exclusion of studies are listed in the PRISMA flow diagram (Figure 1). Based on risk of bias assessments, most of the included studies received a "fair" quality score. Notably, one study received "poor" quality scores,[4] and four studies received "good" quality scores.[11–14] One study received a "good/fair" quality assessment score because it met 10 of 14 criteria, however, the participation rate and sample size was low, resulting in a "good/fair" quality assessment rating.[15] Overall, the quality of the studies was fair. There were no randomized controlled studies and most studies were cross-sectional. A quantitative meta-analysis was performed among ten "fair" or "good" quality studies evaluating the association between exposure to cleaning or disinfecting tasks or agents and asthma risk. A quantitative meta-analysis was also performed among three "fair" or "good" quality studies that evaluated the association between bleach exposure and asthma risk. Results of other studies could not be pooled due to important differences in how the exposures and outcomes were defined, or differences in the comparison groups used.

3.1 | Asthma

Of the 34 studies meeting inclusion criteria, 23 studies investigated associations between occupational cleaning exposures and asthma. Tables 1 and 2 include the tasks and exposures reported in these studies. Only studies that investigated asthma as an outcome were included in this portion of the systematic review and Table 1. Twelve studies that investigated only asthma-like symptoms were summarized separately in Table 2. When studies investigated multiple outcomes, such as asthma, asthma-like symptoms, and skin symptoms, then they were included in each of the respective tables (Tables 1–3).

Five of the 23 studies were prospective and the remainder were cross-sectional or retrospective in design. Thirteen studies were performed in the United States of America,[12,13,15,16,18–20,23,26,27,29–31] and one study was performed in the United Kingdom[24] among healthcare and other hospital workers. Three studies were performed in Canada,[5,17,21] two studies were performed in France,[1,25] one study was performed in Sweden,[22] and one study collected data from participants located in ten European countries.[11] One study was performed in Australia[28] and one study was performed in the United States of America and Canada.[14] Occupational exposures to cleaning or disinfecting tasks or agents were assessed by self-report with the exception of five studies. Four studies used a job-exposure matrix (JEM) or a job task exposure matrix (JTEM) to estimate occupational exposure to cleaning agents[12,13,19,20] and one study used three methods to estimate exposure to cleaning agents: self-report, expert assessment, and an asthma-specific JEM.[1] With regard to outcome definitions for asthma, six studies used *current asthma*, described as presently having asthma.[1,16,23,26–28] Twelve studies used the definition of *new-onset asthma*, *reported asthma*, or *post-hire asthma*, that were defined as asthma onset diagnosed after entry into a healthcare profession.[5,11,12,17–21,24,25,29,35] One study used the definition of

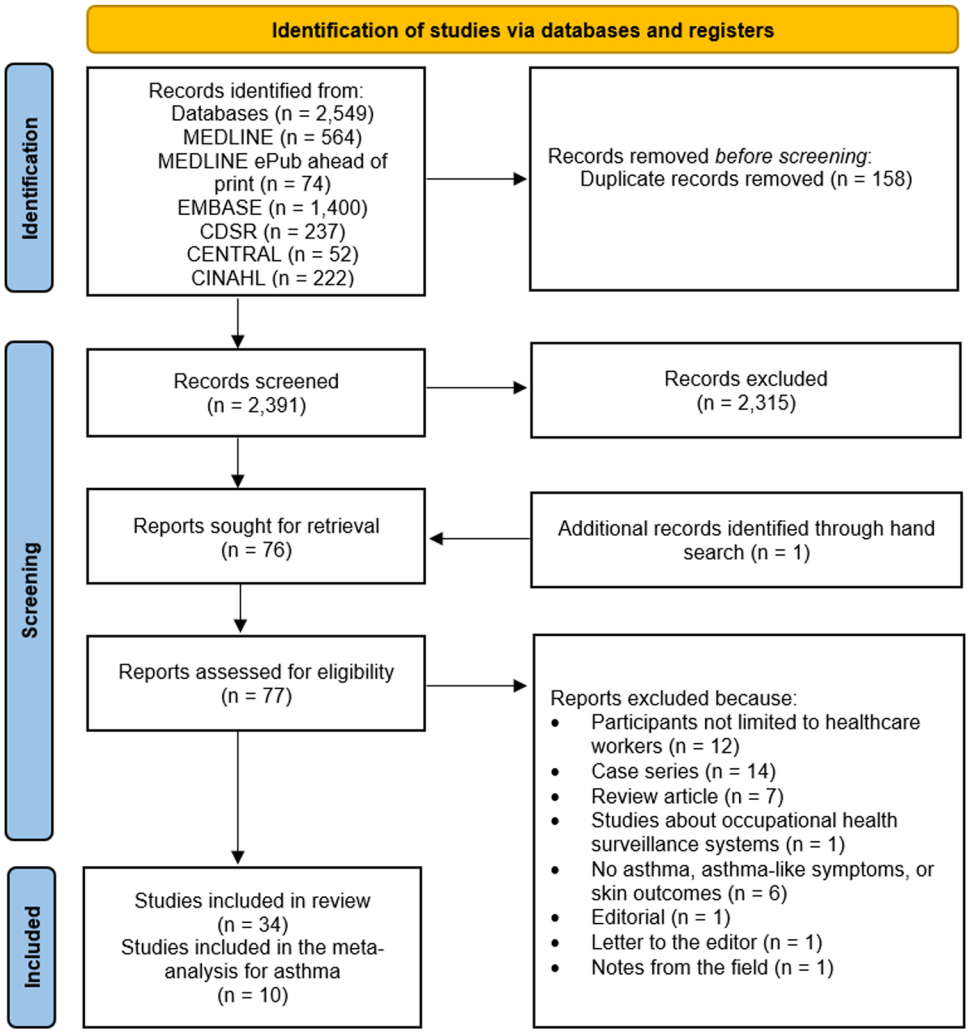

FIGURE 1 PRISMA flow diagram illustrating the process of screening and selecting articles related to occupational cleaning exposures and respiratory symptoms from a search of electronic bibliographic databases.

adult-onset asthma, defined as asthma reported at 16 years of age or older.[22] Two studies investigated asthma incidence in prospective cohort studies of female registered nurses.[14,30] Last, one study assessed asthma control using the Asthma Control Test.[13] All studies received a risk bias assessment score of "fair" or "good."

Exposure to cleaning and disinfecting tasks or cleaning and disinfecting products was associated with increased asthma risk in most studies.[1,5,11,12,14,17,19,20,22,23,25,27,29,31] Of note, two studies conducted different analyses using the same data set.[29,31] An increase in the frequency of performed disinfection tasks from never or monthly to weekly or daily was associated with increased odds of new-onset asthma (odds ratio [OR] = 3.13, 95% CI: 1.05–9.35).[25] The use of disinfectants to clean medical instruments was associated with poorly controlled asthma (OR = 1.37, 95% CI: 1.05–1.79) and very poorly controlled asthma (OR = 1.88, 95% CI: 1.38–2.56).[13] Among asthmatic hospital workers, the most frequently reported exposure agents were glutaraldehyde (38%), latex (26%), and various cleaning products (15%).[24] Latex is not a cleaning product; however, it may be used during cleaning tasks and can be a confounding factor when assessing the effects of cleaning and disinfecting agents on asthma risk. When considered separately, exposure to latex was associated with an increased risk of new-onset asthma and current asthma.[11,20] Three studies reported that exposure to bleach significantly increased the risk of current, new-onset, or undiagnosed asthma among hospital workers.[1,11,31] Similarly, one study also found that both latex and bleach exposures were associated with increased odds of new-onset asthma; however, these results were not statistically significant.[25] Exposure to quaternary ammonium compounds was found to result in an increased risk of new-onset asthma among hospital workers.[1,25] One study found that exposure to formaldehyde, glutaraldehyde, hypochlorite bleach, hydrogen peroxide, and enzymatic cleaners was associated with poor asthma control ($p < 0.05$ for all exposures), but exposure to alcohol and quaternary ammonium compounds was not associated with poor asthma control.[13]

Several studies investigated glutaraldehyde as an occupational cleaning exposure. Dimich-Ward et al. found that hospital healthcare workers exposed to glutaraldehyde had an increased risk of new-onset asthma compared to unexposed healthcare workers.[17]

TABLE 1 Summary of epidemiological studies (chronological order) assessing the associations between cleaning tasks or agents and asthma

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
Ellett et al.[16]	United States of America	1995	Cross sectional	3988 members of SGNA members exposed, 929 ASPAN members exposed, 830 ASPAN members nonexposed	Glutaraldehyde	Questionnaire	Age, gender, smoking status, prior health problems	No statistically significant differences in the number of respondents reporting asthma ($p < 0.592$).	Fair
Liss et al.[5]	Canada	2000–2001	Cross sectional	1719 medical radiation technologists and a control group of 1848 physiotherapists	Cleaning tasks conducted by radiation technologists	Questionnaire, methacholine challenge test	Age, gender, smoking status	Prevalence of new-onset asthma upon starting work in the profession was greater among medical radiation technologists: OR = 1.7 with a significant gender interaction ($p = 0.016$) Among females: age-adjusted OR = 1.3 (95% CI: 0.9–1.9) Among males: age-adjusted OR = 5.3 (95% CI: 1.4–20.2)	Fair
Dimich-Ward et al.[17]	Canada	1999–2000	Cross sectional	275 respiratory therapists and a control group of 628 physiotherapists	Occupation, work exposures (glutaraldehyde)	Questionnaire	Nasal allergies, time in profession, living with a smoker	Respiratory therapists tended to have a higher risk of having asthma attacks: OR = 2.6 (95% CI: 1.4–4.7) and asthma diagnosed after entering the profession: OR = 2.4 (95% CI: 1.2–4.7) Sterilizing instruments with glutaraldehyde-based instruments was associated with reported asthma: OR = 3.2 (95% CI: 11.1–9.3)	Fair
Pechter et al.[18]	United States of America	1993–1997	Cross sectional	305 healthcare workers	Cleaning products (glutaraldehyde, formaldehydes, ammonia, bleach,	Interview	Age, gender, smoking status, occupation	Healthcare workers accounted for 16% of the confirmed cases of work-related asthma. Cases	Fair

(Continues)

TABLE 1 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
					disinfectants, carpet cleaners, floor strippers, quaternary ammonium compounds)			were primarily among hospital workers and nurses. The most commonly reported exposures include cleaning products (24%), latex (20%), and poor air quality (12%).	
Delclos et al.[12]	United States of America	2003	Cross sectional	3650 health professionals	Cleaning products using an asthma risk factor JEM specifically for healthcare worker populations	Questionnaire, JEM, methacholine challenge test	Age, BMI, smoking status, occupation, race/ethnicity, atopy	Reported asthma medical instrument cleaning: OR = 2.22 (95% CI: 1.34–3.67) Surface cleaners: OR = 2.02 (95% CI: 1.20–3.40)	Good
Mirabelli et al.[11]	10 European countries	1991–1999	Population-based prospective cohort study (ECRHS-II)	332 nurses and a reference population of 2481 administrative staff	Cleaning products (ammonia, bleach, liquid multiuse products, washing products, spray cleaning products)	Questionnaire	BMI, race/ethnicity	Compared with the reference group, an increased risk for new-onset asthma was observed among those using ammonia and/or bleach at work: RR = 2.16 (95% CI: 1.03–4.53); among those using liquid multi-use products at work: RR = 1.16 (95% CI: 0.61–2.19); among those using washing powders: RR = 1.65 (95% CI: 0.77–3.53); among any products in spray form: RR = 2.36 (95% CI: 0.99–5.64)	Good
Arif et al.[19]	United States of America	Not specified	Cross sectional	3650 healthcare professionals	Cleaning tasks, use of powdered latex gloves, administration of aerosolised medications, use of adhesives/removers	Questionnaire	Age, gender, race/ethnicity, atopy, smoking status, BMI, seniority	Reported asthma Cleaning medical instruments: OR = 1.67 (95% CI: 1.06–2.62) General disinfectants and cleaning products:	Fair

TABLE 1 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								OR = 1.72 (95% CI: 1.00–2.94) Use of powdered latex gloves: OR = 1.6 (95% CI: 1.01–2.50)	
Delclos et al.[20]	United States of America	2004	Cross sectional	3650 healthcare workers	Occupational exposures (cleaning products, disinfectants)	Questionnaire	Age, seniority, gender, race/ethnicity, ever smoking, profession	As assessed by a JEM, current asthma was associated with cleaning products involved with instrument cleaning: PR = 1.19 (95% CI: 1.02–1.39) and powdered latex gloves: PR = 1.11 (95% CI: 0.95–1.32).	Fair
Liss et al.[21]	Canada	1998–2002	Retrospective database study	120 claimants from the healthcare industry	Work-related exposure that occurred in a healthcare setting including cleaning agents, bleach, fresheners, ammonia products, and glutaraldehyde	WSIB database	Age, gender, BMI	Five claims were allowed for occupational asthma. Rate of allowed claims for work-exacerbated asthma was significantly greater in healthcare than in the rest of the workforce: RR = 2.1 (95% CI: 1.7–2.6, $p < 0.0001$) Rate of work-exacerbated asthma claims was 2.1 times greater than that in the rest of the workforce ($p < 0.0001$)	Fair
Dumas et al.[1]	France	2003–2007	Case control	179 hospital workers, 545 controls selected from a previous case-control study	Cleaning tasks and cleaning products	Questionnaire, expert assessment, and the asthma JEM	Gender, BMI	From expert assessment, female hospital workers exposed >1 day/week to cleaning/disinfecting tasks: OR = 1.04 (95% CI: 0.64–1.70); moderate/high intensity exposure: OR = 1.45 (95% CI: 0.81–2.62). From expert assessment + asthma	Fair

(Continues)

TABLE 1 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								JEM, female hospital workers exposed to moderate/high exposure to cleaning/disinfecting tasks: OR = 2.32 (95% CI: 1.11–4.86); moderate/high exposure to bleach: OR = 2.11 (95% CI: 0.88–5.03); moderate/high exposure to quaternary ammonium: OR = 1.93 (95% CI: 0.85–4.40); moderate/high exposure to sprays: OR = 2.87 (95% CI: 1.02–8.11).	
Kim et al.[22]	Sweden	2008	Cross sectional	429 healthcare workers exposed to cleaning tasks, 1727 healthcare workers not exposed to cleaning tasks, 10,030 nonhealthcare workers	Cleaning tasks	Questionnaire	Age	Prevalence of adult-onset asthma was significantly higher among healthcare workers compared with nonhealthcare workers ($p = 0.003$)	Fair
Le Moual et al.[23]	United States of America	1992–2000	Prospective cohort study	1054 female operating room nurses and 7661 administrative nurses	Cleaning/disinfecting tasks	Questionnaire	Age, race/ethnicity, smoking status, BMI, physician examinations	A significant association between operating room nursing and severe persistent asthma compared with administrative nursing: adjusted OR = 2.48 (95% CI: 1.06–5.77).	Fair
Walters et al.[24]	United Kingdom	1991–2011	Retrospective case series	182 healthcare workers	Glutaraldehyde, cleaning products, acrylates, formaldehyde, antimicrobial drugs	Specific allergen IgE, inhalation test, serial peak flow	Age, gender, BMI, occupation	There were 182 SHIELD notifications of occupational asthma in healthcare workers, representing 5%–19% of the annual notifications.	Fair

TABLE 1 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								Most frequently encountered agents: glutaraldehyde (38%), latex (26%), and cleaning products (15%).	
Gonzalez et al.[25]	France	2006–2007	Cross sectional	543 healthcare workers	Cleaning and disinfection tasks (quaternary ammonium compounds, chlorinated products/bleach, glutaraldehyde)	Questionnaire	Age, gender, BMI, total number of years working in healthcare, smoking status	Healthcare workers had a higher risk of developing new-onset asthma when exposed to general disinfecting tasks: OR = 4.68 (95% CI: 1.08–20.22)	Fair
Casey et al.[26]	United States of America	Not specified	Cross sectional	78 disinfectant product users and 85 disinfectant product nonusers	Surface disinfectant product containing hydrogen peroxide, peracetic acid, and acetic acid	Questionnaire	Age, gender, race/ethnicity, smoking	No significant difference between current asthma diagnoses among product users and nonusers ($p = 0.66$). Highly exposed workers had a >3-fold excess of current asthma compared with the US population: SMR = 3.47 (95% CI: 1.48–8.13).	Fair
Dumas et al.[13]	United States of America	2014	Prospective cohort study	4102 female registered nurses	Exposure to disinfectants (formaldehyde, glutaraldehyde, hypochlorite, bleach, hydrogen peroxide, alcohol, quats, enzymatic cleaners).	Questionnaires, Asthma Control Test, nurse-specific JTEM	Age, race, BMI, smoking status	Disinfectant use to clean medical instruments was associated with poorly controlled asthma: OR = 1.37 (95% CI: 1.05–1.79) and very poorly controlled asthma: OR = 1.88 (95% CI: 1.38–2.56) ($p_{trend} = 0.004$ after adjustment for potential confounders). Exposure to formaldehyde, glutaraldehyde, hypochlorite bleach, hydrogen peroxide, and enzymatic cleaners was	Good

(Continues)

TABLE 1 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								associated with poor asthma control (all $p_{trend} < 0.05$). Exposure to quaternary ammonium compounds and alcohol was not associated with poor asthma control.	
Kurth et al.[27]	United States of America	2012–2014	Cross sectional	105 clinical nurses, 95 hospital office and administrative support workers, 51 patient care occupations	Sterilization/disinfection of medical instruments, cleaning equipment or surfaces, using chemicals in lab (alcohol, bleach, glass cleaner, detergent, quaternary ammonium compounds)	Questionnaire	Age, race/ethnicity, gender, smoking status, seniority, days per week working	Participants exposed to cleaning equipment and environmental surfaces had a significantly higher prevalence of current asthma compared to nonexposed participants: PR = 1.83 (95% CI: 1.16–2.90). Patient care workers disinfecting or sterilizing medical instruments had a higher PR for current asthma compared with nonexposed workers: PR = 2.81 (95% CI: 1.38–5.72).	Fair
Barnes et al.[28]	Australia	December 2016–June 2017	Cross sectional	1112 healthcare workers	Chlorhexidine-based hand hygiene solutions	Questionnaire	Age, gender, race, work environment, occupation	128/1050 (12.2%) had current asthma during the previous year. Nurses and midwives reported asthma most frequently (13.7%).	Fair
Caridi et al.[29]	United States of America	2014	Cross sectional	2030 healthcare workers	Common healthcare tasks including cleaning fixed surfaces and sterilizing medical instruments	Questionnaire and telephone interviews	Age, gender, race/ethnicity, occupation, place of work, smoking	Cleaning fixed surfaces had statistically significant associations with post-hire asthma: OR = 1.76 (95% CI 1.09 to 2.85) and current asthma: OR = 1.84 (95% CI: 1.26–2.68).	Fair

TABLE 1 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
Dumas et al.[30]	United States of America	2009–2013	Prospective cohort study	61,539 female nurses	Exposure to disinfectants (formaldehyde, glutaraldehyde, bleach, hydrogen peroxide, alcohol quats, or enzymatic cleaners)	Questionnaire	Age, race, smoking habits, BMI	No significant association was observed between incident asthma and weekly use of disinfectants to clean surfaces: HR = 1.12 (95% CI: 0.87–1.43) or weekly use of disinfectants to clean medical instruments: HR = 1.13 (95% CI: 0.87–1.48). No association was observed between high-level exposure to specific disinfectants evaluated by the JTEM (formaldehyde, glutaraldehyde, bleach, hydrogen peroxide, alcohol quats, or enzymatic cleaners) and incident asthma.	Good
Su et al.[31]	United States of America	2014	Cross sectional	2030 healthcare workers	Cleaning and disinfecting activities	Questionnaire, telephone interviews, hierarchical clustering	Age, gender, race/ethnicity, occupation, place of work, smoking	Undiagnosed/untreated asthma was associated with chlorine bleach: OR = 3.07 (95% CI: 1.75–5.39); enzymes: OR = 2.57 (95% CI: 1.18–5.58); detergents: OR = 3.04 (95% CI: 1.56–5.90). Disinfection products were associated with mild asthma symptoms: OR = 1.81 (95% CI: 1.09–2.99) and undiagnosed/untreated asthma: OR = 3.42 (95% CI: 1.24–9.39).	Fair

(Continues)

TABLE 1 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								Mild asthma symptoms were associated with alcohols: OR = 1.34 (95% CI: 1.01–1.76) and chlorine bleach: OR = 1.44 (95% CI: 1.09–1.91).	
Patel et al.[15]	United States of America	2016–2017	Cross sectional	413 certified nurse aids	Exposure to cleaning tasks and compounds	Questionnaire	Age, race, atopy, obesity, smoking, years at job	The prevalence of new-onset asthma was 3.6%. No regression analysis was performed because there were too few new-onset asthma cases.	Good/fair
Dumas et al.[14]	United States of America and Canada	2010–present	Prospective cohort study	17280 female nurses	Occupational use of high-level disinfectants (glutaraldehyde, ortho-phthalaldehyde, peracetic acid, hydrogen peroxide)	Questionnaire	Age, race, ethnicity, smoking habits, BMI	Nurses with >5 years of HLD use had an increased risk of incident asthma: adjusted HR = 1.39 (95% CI: 1.04–1.86). Asthma risk was significantly increased among women with >5 years of HLD use but no current use: adjusted HR = 1.46 (95% CI: 1.00–2.12). No significant associations were observed between specific types of HLDs and incident asthma due to low numbers.	Fair

Abbreviations: ASPAN, American Society of PeriAnaesthesia Nurses; BMI, body mass index; ECRHS, European Community Respiratory Health Survey; HLD, high-level disinfectant; HR, hazard ratio; JEM, job exposure matrix; JTEM, job task exposure matrix; OASYS, occupational asthma expert system; PEFR, peak expiratory flow rate; PR, prevalence ratio; RR, relative risk; SBPT, specific bronchial provocation test; SGNA, Society of Gastroenterology Nurses and Associates, SMR, standardized morbidity ratio; WSIB, Workplace Safety & Insurance Board.

TABLE 2 Summary of epidemiological studies (chronological order) assessing the associations between cleaning tasks or agents and asthma-like symptoms

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
Kern[32]	United States of America	1988	Cross sectional	51 clinical laboratory, phlebotomy, and radiology department employees	Acetic acid	Questionnaire, methacholine challenge test	Age, gender, smoking status, history of atopy or asthma	Risk of RADS was higher in subjects with high exposure to 100% acetic acid: OR = 9.8 (95% CI: 0.902–264.6).	Fair
Ellett et al.[16]	United States of America	1995	Cross sectional	3988 members of SGNA members exposed, 929 ASPAN members exposed, 830 ASPAN members nonexposed	Glutaraldehyde	Questionnaire	Age, gender, smoking status, prior health problems	More exposed SGNA respondents reported a worsening of nose/throat problems ($x^2 = 26.77$, $p < 0.002$) and breathing problems ($x^2 = 16.54$, $p < 0.011$) compared with either ASPAN group. No statistically significant differences in the number of respondents reporting rhinitis and chest pain.	Fair
Vyas et al.[33]	United Kingdom	Not specified	Cross sectional	348 endoscopy nurses and 18 former employees who had left their jobs for health reasons	Airborne exposures of glutaraldehyde, succinaldehyde, and formaldehyde from cleaning tasks	Questionnaire, spirometry, pulmonary function tests, skin prick test, total serum IgE and IgE RAST	Age, gender, smoking status	Irritation of nose ($p < 0.01$) and eyes ($p < 0.05$) in current workers exposed to glutaraldehyde. No association between glutaraldehyde exposure to LRTS were found.	Fair
Liss et al.[5]	Canada	2000–2001	Cross sectional	1719 medical radiation technologists and a control group of 1,848 physiotherapists	Cleaning tasks conducted by radiation technologists	Questionnaire, methacholine challenge test	Age, gender, smoking status	Medical radiation technologists had increased odds of reporting 2 or more work-related respiratory symptoms (cough, wheeze, chest tightness): adjusted OR = 3.9 (95% CI: 2.6–5.5).	Fair
Dimich-Ward et al.[17]	Canada	1999–2000	Cross sectional	275 respiratory therapists and a control group of 628 physiotherapists	Glutaraldehyde	Questionnaire	Nasal allergies, time in profession, living with a smoker	Wheeze: OR = 2.1 (95% CI: 1.1–3.8) Woken by cough: OR = 2.3 (95% CI: 1.3–3.9)	Fair

(Continues)

TABLE 2 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
Delclos et al.[12]	United States of America	2003	Cross sectional	3650 health professionals	Cleaning products using an asthma risk factor JEM specifically for healthcare worker populations	Questionnaire, JEM, methacholine challenge test	Age, BMI, smoking status, occupation, race/ethnicity, atopy	Bronchial hyperresponsiveness-related symptoms were associated with general cleaning: OR = 1.63 (95% CI: 1.21–2.19) and exposure to a chemical spill: OR = 2.02 (95% CI: 1.28–2.31)	Good
Nayebzadeh[34]	Canada	Not specified	Cross sectional	53 healthcare workers	Glutaraldehyde	Interview	Age, gender, race/ethnicity, BMI	3.7% of participants reported coughing as a symptom, and 53% reported itchy nose. 41% reported headache, 68% reported burning eyes, and 73% reported itchy eyes. A higher prevalence of these symptoms was observed where unsafe work practices were taking place.	Fair
Arif et al.[19]	United States of America	Not specified	Cross sectional	3650 healthcare professionals	Cleaning tasks, use of powdered latex gloves, administration of aerosolised medications, use of adhesives/removers	Questionnaire	Age, gender, race/ethnicity, atopy, smoking status, BMI, seniority	Nurses exposed to disinfectants and cleaning products were at significantly increased odds of having BHR-related symptoms: OR = 1.57 (95% CI: 1.11–2.21).	Fair
Arif and Delclos[35]	United States of America	2004–2005	Cross sectional	3650 healthcare professionals	Exposures in the longest held job (cleaning agents, disinfectants, sterilants, general purpose cleaning, instrument cleaning/sterilization)	Questionnaire	Age, gender, race/ethnicity, BMI, seniority, atopy, smoking status	Odds of work-related asthma symptoms (wheeze, shortness of breath) increased in a dose-dependent manner from OR = 2.64 (95% CI: 0.57–12.14) for once a week exposure to OR = 5.37 (95% CI: 1.43–20.16) for more than once a day exposure to cleaning agents. Work-related asthma symptoms	Fair

TABLE 2 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								General purpose cleaning: OR = 3.93 (95% CI: 1.66–9.32) Instrument cleaning: OR = 2.14 (95% CI: 1.06–4.32) Bleach: OR = 3.72 (95% CI: 1.70–8.12) Detergents: OR = 2.84 (95% CI: 1.33–6.08) Disinfectants: OR = 2.50 (95% CI: 0.78–8.09) Ammonia: OR = 2.45 (95% CI: 1.28–4.69)	
Kim et al.[22]	Sweden	2008	Cross sectional	429 healthcare workers exposed to cleaning tasks, 1727 healthcare workers not exposed to cleaning tasks, 10,030 nonhealthcare workers	Cleaning tasks	Questionnaire	Age	Healthcare workers exposed to cleaning products had significantly increased odds of having asthmatic symptoms (breathlessness, shortness of breath, cough, wheeze) in the past 12 months compared with nonhealthcare workers: OR = 1.9 (95% CI: 1.4–2.5).	Fair
Lee et al.[3]	United States of America	Not specified	Cross sectional	183 cleaning workers employed at a university medical centre and affiliated health sciences campuses	Exposures during cleaning tasks (liquid multi-use cleaning products, polishes, waxes, disinfectants, bleach, solvents, glass cleaning, etc.)	Questionnaire	Age, gender, race/ethnicity, education level, job title	Significant associations were found between respiratory symptoms and medium exposure to tasks using spray products: OR = 3.16 (95% CI: 1.24–8.04); high exposure to liquid multi-use cleaners: OR = 2.35 (95% CI: 1.02–5.43); carpet cleaners: OR = 2.33 (95% CI: 1.00–5.43).	Fair
Lipińska-Ojrzanowska et al.[4]	Poland	Not specified	Cross sectional	142 cleaning workers in health centres	Cleaning tasks (chloramine T, chlorhexidine, formaldehyde, glutaraldehyde,	Questionnaire, IgE serum, skin prick test, pulmonary function test	Age, gender, smoking status, presence of a pet at home	47.2% of cleaners (67/142) developed at least one work-related respiratory symptom. Airway ailments were observed most	Poor

(Continues)

TABLE 2 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
					benzalkonium chloride)			frequently among cleaners (45%).	
El-Helaly et al.[36]	Saudi Arabia	2012–2014	Prospective cohort study	56 nurses responsible for disinfection and sterilization of medical instruments and equipment	Exposure to splashes, spills, mists, vapors, gases during use of cleaning chemicals (quaternary ammonium compounds, chlorhexidine, ortho-phthalaldehyde, glutaraldehyde, formaldehyde, bleach, endozyme1, ethylene oxide)	Questionnaire, spirometry	Age, gender, smoking, BMI, education level	Prevalence of work-related cough increased from 5.4% in 2012 to 17.9% in 2014 ($p = 0.06$). All participants who had worked with cleaning chemicals for more than 10 years (60.7%) had significant decreases in spirometry parameters FEV_1 and FVC from 2012 to 2014.	Fair
Casey et al.[26]	United States of America	Not specified	Cross sectional	78 disinfectant product users and 85 disinfectant product nonusers	Surface disinfectant product containing hydrogen peroxide, peracetic acid, and acetic acid	Questionnaire	Age, gender, race/ethnicity, smoking	Product users had a higher prevalence of work-related wheeze than nonusers ($p < 0.05$). Disinfectant users also reported a higher prevalence of work-related asthma-like symptoms, shortness of breath, cough, chest tightness, and asthma attack, although these were not statistically significant.	Fair
Kurth et al.[27]	United States of America	2012–2014	Cross sectional	105 clinical nurses, 95 hospital office and administrative support workers, 51 patient care occupations	Sterilization/disinfection of medical instruments, cleaning equipment or surfaces, using chemicals in lab (alcohol, bleach, glass cleaner, detergent, quaternary ammonium compounds)	Questionnaire	Age, race/ethnicity, gender, smoking status, seniority, days per week working	Participants cleaning/disinfecting surfaces had a significantly higher PR of wheeze compared with nonexposed participants: PR = 1.50 (95% CI: 1.12–2.02) Participants exposed to cleaning and disinfecting products had significantly higher PRs for wheeze compared to nonexposed participants.	Fair

TABLE 2 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								Bleach: PR = 1.57 (95% CI: 1.18–2.09); glass cleaner: PR = 1.64 (95% CI: 1.14–2.36); detergent: PR = 1.56 (95% CI: 1.14–2.13)	
Hawley et al.[37]	United States of America	2015	Cross sectional	50 hospital cleaning staff	Hydrogen peroxide, peracetic acid, and acetic acid	Questionnaires, time-weighted average air samples	Age, gender, tenure, smoking status	28.6% reported asthma-like symptoms in the previous 12 months. Shortness of breath was significantly associated with increased exposure to a total mixture of hydrogen peroxide, peracetic acid, and acetic acid ($p = 0.022$) and oxidant mixture of hydrogen peroxide and peracetic acid exposure ($p = 0.017$). Prevalence of wheeze in the previous 12 months was 2.5–2.8-fold higher in the highest exposure groups compared to the lowest exposure group.	Fair
Rangkooy et al.[38]	Iran	Not specified	Cross sectional	30 persons of operation room with exposure to formaldehyde and 30 persons not usually exposed to formaldehyde in an educational hospital	Formaldehyde	NIOSH procedure No. 3500, respiratory symptoms, pulmonary function tests	Age, weight, gender, work experience	The prevalence of coughing, shortness of breath, and nasal irritation were significantly higher in the exposed group than the control ($p < 0.05$). Prevalence of wheezing was not significantly higher in the exposed group.	Fair
Barnes et al.[28]	Australia	December 2016–June 2017	Cross sectional	1112 healthcare workers	Chlorhexidine-based hand hygiene solutions	Questionnaire	Age, gender, race, work environment, occupation	37/1050 (3.5%) experienced wheeze/cough in the previous year.	Fair

(Continues)

TABLE 2 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
Caridi et al.[29]	United States of America	2014	Cross sectional	2030 healthcare workers	Common healthcare tasks including cleaning fixed surfaces and sterilizing medical instruments	Questionnaire and telephone interviews	Age, gender, race/ethnicity, occupation, place of work, smoking	Cleaning fixed surfaces was significantly associated with BHR-related symptoms: OR = 1.38 (95% CI: 1.08–1.77); wheeze: OR = 1.45 (95% CI: 1.08–1.94).	Fair
Patel et al.[15]	United States of America	2016–2017	Cross sectional	413 certified nurse aids	Exposure to cleaning tasks and compounds	Questionnaire	Age, race, atopy, obesity, smoking, years at job	The prevalence of BHR symptoms was 26.9%. Increased odds for BHR symptoms were associated with patient care cleaning: OR = 1.71 (95% CI: 0.45–6.51); instrument cleaning: OR = 1.33 (95% CI: 0.66–2.68); glutaraldehyde or orthophthalaldehyde: OR = 1.33 (95% CI: 0.66–2.68); latex glove use during 1992–2000: OR = 1.62 (95% CI: 0.84–3.12).	Good/fair
Garrido et al.[6]	Canada	2018–2019	Cross sectional	307 administrative staff, and nursing and cleaning staff	Exposure to disinfectants (bleach, hydrogen peroxide, isopropanol, quaternary ammonium compounds).	Questionnaire	Age, gender	Exposed healthcare workers had an increased risk of respiratory symptoms: adjusted OR = 2.17 (95% CI: 1.18–4.14). Washing instruments manually, cleaning operating rooms, cleaning sanitary rooms, using aerosol products, preparing disinfectants, and filling devices with cleaning products were cleaning tasks associated with respiratory symptoms such as wheeze, shortness or breath, chest tightness, or cough.	Fair

TABLE 2 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								No specific cleaning agents had a statistically significant association with respiratory symptoms.	
Jalali et al.[39]	Iran	2019	Cross sectional	60 pathology laboratory staff	Formaldehyde	Questionnaire, face-to-face interviews, NIOSH procedure No. 3500	Age, weight, gender, work experience, type of work, daily working hours, exposure patterns	Wheezing (24%) and cough (21.7%) were the most prevalent respiratory problems in exposed workers. Occupational exposure in 28.3% (n = 17) of employees was above the range recommended by the OSHA.	Fair

Abbreviations: ASPAN, American Society of PeriAnesthesia Nurses; BHR, bronchial hyperresponsiveness; ECRHS, European Community Respiratory Health Survey; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; JEM, job exposure matrix; LTRS, lower tract respiratory symptom; NIOSH, National Institute for Occupational Safety and Health; OASYS, occupational asthma expert system; OSHA, Occupational Safety and Health Administration; PR, prevalence ratio; RADS, reactive airways dysfunction syndrome; RAST, radio allergosorbent test; RR, relative risk; SGNA, Society of Gastroenterology Nurses and Associates; UTRS, upper tract respiratory symptoms.

TABLE 3 Summary of epidemiological studies (chronological order) assessing the associations between cleaning tasks or agents and skin symptoms

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
Ellett et al.[16]	United States of America	1995	Cross sectional	3988 members of SGNA members exposed, 929 ASPAN members exposed, 830 ASPAN members nonexposed	Glutaraldehyde	Questionnaire	Age, gender, smoking status, prior health problems	No statistically significant differences in the number of respondents reporting dermatitis ($p < 0.222$). Fewer exposed respondents showed an improvement in skin symptoms ($x^2 = 2.65$, $p < 0.002$).	Fair
Vyas et al.[33]	United Kingdom	Not specified	Cross sectional	348 endoscopy nurses and 18 former employees who had left their jobs for health reasons	Airborne exposures of glutaraldehyde, succinaldehyde, and formaldehyde from cleaning tasks	Questionnaire, spirometry, pulmonary function tests, skin prick test, total serum IgE and IgE RAST	Age, gender, smoking status	Work-related contact dermatitis was reported by 44% of endoscopy nurses exposed to glutaraldehyde and 56.7% of those exposed to a composite of succinaldehyde and formaldehyde.	Fair
Liss et al.[5]	Canada	2000–2001	Cross sectional	1719 medical radiation technologists and a control group of 1848 physiotherapists	Cleaning tasks conducted by radiation technologists	Questionnaire, methacholine challenge test	Age, gender, smoking status	Skin symptoms associated with latex: OR = 2.5 (95% CI: 1.9–3.4)	Fair
Lipińska-Ojrzanowska et al.[4]	Poland	Not specified	Cross sectional	142 cleaning workers in health centres	Cleaning tasks (chloramine T, chlorhexidine, formaldehyde, glutaraldehyde, benzalkonium chloride)	Questionnaire, IgE serum, skin prick test, pulmonary function test	Age, gender, smoking status, presence of a pet at home	24% of cleaners (34/142) had work-related skin symptoms. Cleaners with respiratory symptoms had significantly greater odds of having skin symptoms compared with cleaners without respiratory symptoms: OR = 2.62 (95% CI: 1.11–6.21).	Poor
Lee et al.[3]	United States of America	Not specified	Cross sectional	183 cleaning workers employed at a University Medical Centre and affiliated	Exposures during cleaning tasks (liquid multi-use cleaning products, polishes, waxes, disinfectants, bleach,	Questionnaire	Age, gender, race/ethnicity, education level, job title	Chemical-related symptoms (respiratory, eye, nervous, skin, and gastrointestinal systems) were more common among hospital	Fair

TABLE 3 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
				health sciences campuses	solvents, glass cleaning, etc.)			cleaning workers than campus cleaning workers: OR = 1.29 (95% CI: 0.57–2.91). 13.1% of participants (24/183) experienced dermal symptoms related to chemical exposure (itchy or burning skin, or rash) several times yearly. 2.7% of participants (5/183) experienced dermal symptoms related to chemical exposure daily. Contact dermatitis was significantly more frequent in workers with chemical-related symptoms than workers without ($p = 0.012$).	
Casey et al.[26]	United States of America	Not specified	Cross sectional	78 disinfectant product users and 85 disinfectant product nonusers	Surface disinfectant product containing hydrogen peroxide, peracetic acid, and acetic acid	Questionnaire	Age, gender, race/ethnicity, smoking	Skin symptoms were reported by 19% of all participants (31/163), and 61% of skin problems (19/31) were described to be work-related. No statistically significant differences in the number of disinfectant product users and nonusers reporting skin problems in the last 12 months ($p = 0.32$).	Fair
Barnes et al.[28]	Australia	December 2016–June 2017	Cross sectional	1112 healthcare workers	Chlorhexidine-based hand hygiene solutions	Questionnaire	Age, gender, race, work environment, occupation	Of those with self-reported hay fever or asthma, 40.1% reported localized rash in the past 12 months, including 33.3% who experienced	Fair

(Continues)

TABLE 3 (Continued)

Author	Country	Period of data collection	Study design	Study population	Type of exposure	Method of data collection	Covariates	Findings	Quality assessment score
								localized rash every day; 79.5% reported dry skin and 36.6% reported eczema in response to chlorhexidine. No significant association between widespread rash and cough or wheeze was found among those with eczema or contact dermatitis.	
Garrido et al.[6]	Canada	2018–2019	Cross sectional	307 administrative staff, and nursing and cleaning staff	Exposure to disinfectants (bleach, hydrogen peroxide, isopropanol, quaternary ammonium compounds).	Questionnaire	Age, gender	Exposed healthcare workers had an increased risk of skin symptoms: adjusted OR = 1.77 (95% CI: 1.00–3.17). Actual disinfecting tasks were associated with hand dermatitis: adjusted OR = 2.19 (95% CI: 1.10–4.66). Bleach was the only specific cleaning agent that was significantly associated with hand dermatitis: adjusted OR = 2.54 (95% CI: 1.32–5.13).	Fair

Abbreviations: ASPAN, American Society of PeriAnesthesia Nurses; RAST, radio allergosorbent test; SGNA, Society of Gastroenterology Nurses and Associates

Ellett et al. and Gonzalez et al. found similar results; however, the risks reported in these studies were not statistically significant.[16,25]

Two studies found contrasting results. Casey et al. evaluated the association between a surface disinfectant product containing hydrogen peroxide, peracetic acid, and acetic acid. No significant differences between current asthma diagnoses were found among product users and nonusers ($p = 0.66$).[26] Last, Dumas et al. found no significant association between weekly use of disinfectants and incident asthma, and no significant association between high-level exposure to specific disinfectants and incident asthma.[30]

3.2 | Meta-analyses for asthma

Ten studies evaluating asthma with fair or good quality scores were selected for a meta-analysis.[1,5,6,11,16,17,22,25,26,29] When studies presented multiple risk estimates for asthma, the quantitative summary that defined occupational asthma the best was selected. For instance, quantitative summaries for new-onset asthma were selected over quantitative summaries for ever asthma diagnoses. The outcome definitions for the studies included in the meta-analysis included *current asthma* (ever asthma and report of asthma attacks, respiratory symptoms, or treatment of asthma in the past 12 months, or physician-diagnosed asthma that was still present),[1,6,16,26] *new-onset asthma*, *reported asthma*, or *post-hire asthma* (reported onset of physician-diagnosed asthma after entering a healthcare profession),[5,11,17,25,29] and *adult-onset asthma* (asthma reported at the age of 16 years old or later).[22]

The pooled meta-analysis of the 10 studies demonstrated a significant 35% increased risk for asthma among hospital healthcare workers exposed to cleaning or disinfecting tasks or agents (meta-RR = 1.35, 95% CI: 1.09–1.68, $p = 0.01$, $I^2 = 30\%$) (Figure 2). The pooled risk estimate was higher among cross-sectional studies (meta-RR = 1.45; 95% CI: 1.10–1.90, $p = 0.01$, $I^2 = 25\%$) (Figure 2). No evidence of publication bias was observed (Egger's test $p = 0.66$) (Figure S1).

Before 2000, powdered latex gloves were used as personal protective equipment by most hospital staff, including cleaners.[12] After 2000, there was a reduction in usage of powdered latex gloves due to increasing reports of latex allergy reactions.[12] Therefore, latex may have been a confounding factor in estimating the risk from cleaning agents. A meta-analysis on studies conducted after 2000 was performed to identify any change in risks over time that may have been associated with decreased use of powdered latex gloves or other preventive exposure measures in hospitals since that time. The risk of asthma attributed to cleaning or disinfecting tasks or agents decreased from a 35% increased risk to a 28% increased risk after 2000 (meta-RR = 1.28, 95% CI: 1.04–1.57, $p = 0.03$, $I^2 = 14\%$)

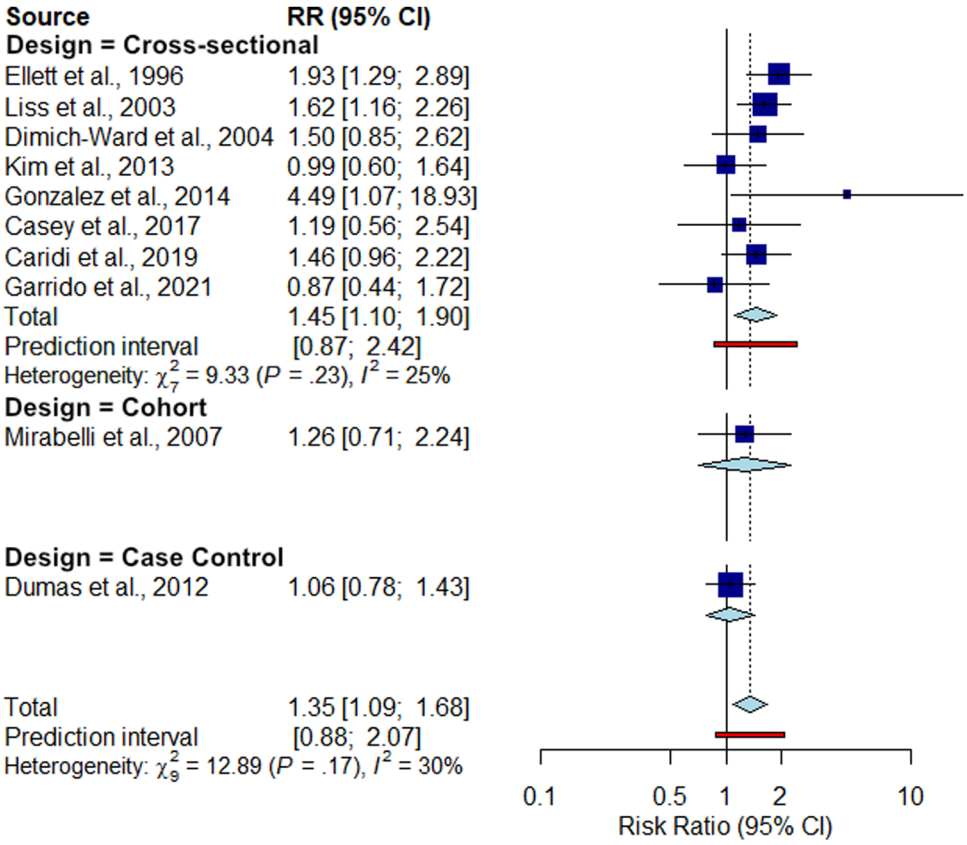

FIGURE 2 Forest plot illustrating a meta-analysis of 10 studies evaluating the association between exposure to cleaning or disinfecting tasks or agents and asthma risk; RR, relative risk.

(Figure 3). No evidence of publication bias was observed (Egger's test $p = 0.54$) (Figure S2).

Among cross-sectional studies, an additional subgroup analysis by study definition of asthma was performed. The results of five of the eight cross-sectional studies that evaluated new-onset asthma, reported asthma, or adult-onset asthma were pooled,[5,17,22,25,29] excluding studies that evaluated current asthma.[6,16,26] An additional subgroup analysis was performed to focus on new-onset asthma, adult-onset asthma, posthire asthma and post-hire reported asthma, since asthma caused by occupational cleaning exposures is more expected to occur within these subgroups. When focusing on new-onset asthma, adult-onset asthma, post-hire asthma, or reported asthma outcomes, a nonsignificant 46% increased risk was determined among healthcare workers exposed to cleaning or disinfecting agents or tasks (meta-RR = 1.46, 95% CI: 0.99–2.14, $p > 0.05$, $I^2 = 20\%$) (Figure 4). No evidence of publication bias was observed (Egger's test $p = 0.52$) (Figure S3).

3.3 | Bleach

The pooled meta-analysis of three studies evaluating asthma in relation to bleach exposure demonstrated a nonsignificant 51% increased risk among exposed healthcare workers (meta-RR = 1.51, 95% CI: 0.54–4.18, $p = 0.23$; $I^2 = 48\%$) (Figure 5).[1,11,25] No evidence of publication bias was observed (Egger's test $p = 0.19$) (Figure S4).

3.4 | Asthma-like respiratory symptoms

Twenty-two studies assessed the associations between cleaning tasks or agents and lower and upper respiratory tract symptoms (LRTS and URTS respectively) (Table 2). All but one of the studies used a cross-sectional study design. All studies received a quality assessment score of "fair" or "good: except for 1 study, which received a "poor" quality score.[4]

Nineteen of the 21 "fair" or "good" quality studies evaluated only LRTS or asthma-like symptoms, such as wheeze, cough, shortness of breath, and breathlessness.[3–6,12,15,17,19,22,26–29,32,35–39] Most reported increased risks of LTRS associated with cleaning tasks and disinfectants.[3,5,6,17,22,26,27,29,35–38] One study reported that the odds of work-related asthma symptoms such as shortness of breath and wheeze increased in a dose-dependent manner (OR = 2.64, 95% CI: 0.57–12.14 for once a week exposure to OR = 5.37, 95% CI: 1.43–20.16 for more than once daily exposure).[35] One study found a nearly 10-fold risk of reactive airways dysfunction syndrome (RADS) in hospital workers exposed to 100% acetic acid (OR = 9.8, 95% CI: 0.902–264.6).[32] Four studies reported increased odds of bronchial hyperresponsiveness (BHR)-related symptoms, such as trouble breathing, wheezing, shortness of breath, and chest tightness, associated with general cleaning tasks and cleaning and disinfectant products.[12,15,19,29] In particular, Patel et al. found that BHR symptoms were associated with glutaraldehyde/orthophthalaldehyde (OR = 1.33, 95% CI: 0.66–2.68) and latex glove use during 1992–2000 (OR = 1.62, 95% CI: 0.84–3.12).[15]

Four studies evaluated URTS in addition to LRTS.[33,34,38,40] One study demonstrated a significant increase in worsening nose and

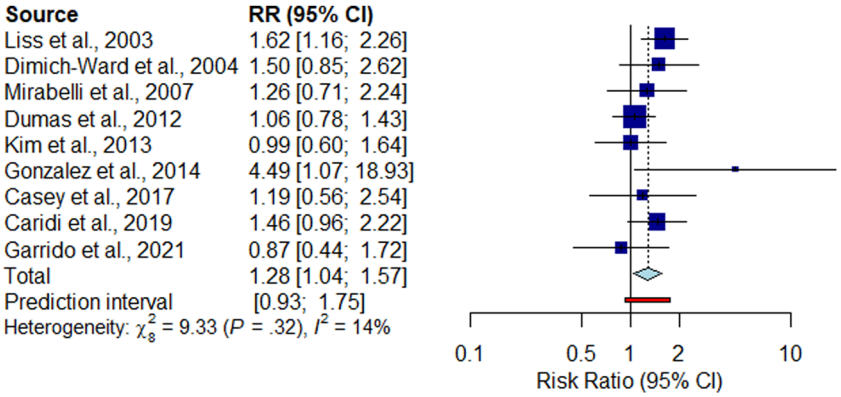

FIGURE 3 Forest plot illustrating a meta-analysis of nine studies conducted after the year 2000 evaluating the association between exposure to cleaning or disinfecting tasks or agents and asthma risk; RR, relative risk.

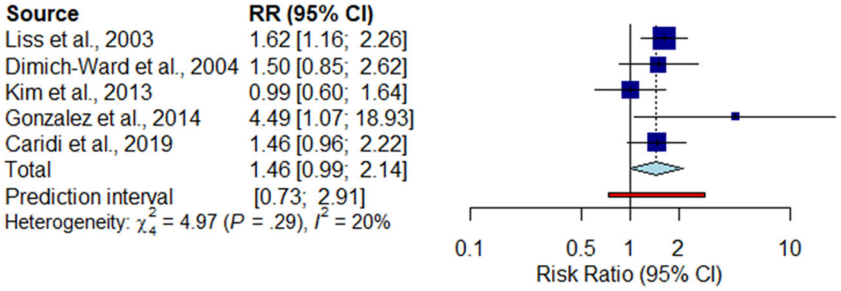

FIGURE 4 Forest plot illustrating a meta-analysis of five cross-sectional studies evaluating the association between exposure to cleaning or disinfecting tasks or agents and risk of new-onset, adult-onset, post-hire, and reported asthma; RR, relative risk.

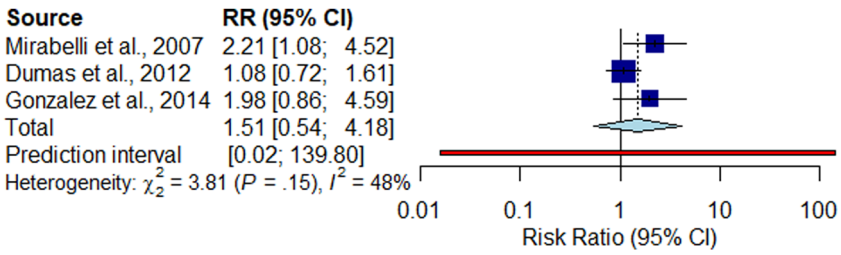

FIGURE 5 Forest plot illustrating a meta-analysis of three studies evaluating the association between bleach exposure and asthma risk; RR, relative risk.

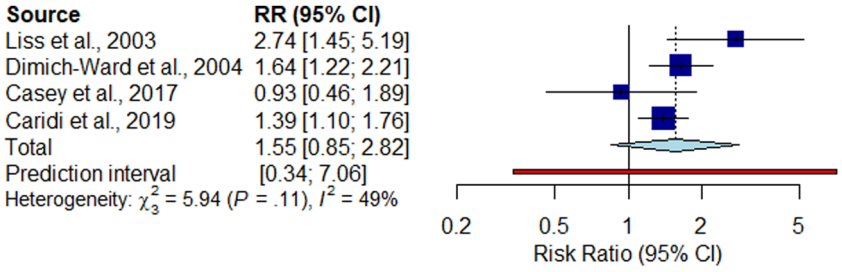

FIGURE 6 Forest plot illustrating a meta-analysis of four studies evaluating the association between exposure to cleaning or disinfecting tasks or agents and risk of wheeze; RR, relative risk.

throat problems among nurses exposed to glutaraldehyde ($p < 0.002$).[16] Similarly, a second study showed a significant increase in nose ($p < 0.01$) and eye irritation ($p < 0.05$) in nurses exposed to glutaraldehyde.[33] Rankooy et al. found that the prevalence of nasal irritation was significantly higher in a group exposed to formaldehyde compared with a control group ($p < 0.05$).[38] Last, Nayebzadeh et al. reported an increased prevalence of LRTS and URTS when unsafe work practices were occurring.[34] Examples of unsafe work practices included leaving unused containers uncovered, the inappropriate storing or disposing contaminated linen and paper towels, and causing spills or leakages of solution from containers.[34]

3.5 | Meta-analysis for wheeze

The pooled meta-analysis of four studies evaluating the risk of wheeze among healthcare workers exposed to cleaning or disinfecting tasks or agents demonstrated a nonsignificant 55% increased risk among exposed healthcare workers (meta-RR = 1.55, 95% CI: 0.85–2.82, $p = 0.10$; $I^2 = 49\%$) (Figure 6).[5,17,26,29] No evidence of publication bias was observed (Egger's test $p = 0.80$) (Figure S5).

3.6 | Skin symptoms associated with respiratory symptoms

Only two studies directly investigated the risk of skin symptoms in relation to respiratory symptoms.[4,28] Lipińska-Ojrzanowska et al. found that healthcentre cleaners with respiratory symptoms had significantly increased odds of having skin symptoms compared with healthcentre cleaners without respiratory symptoms (OR = 2.62, 95% CI: 1.11–6.21); however, this study received a poor quality assessment score, indicating a high risk of bias.[4] Barnes et al. found that 40.1% of exposed healthcare workers with hay fever or asthma reported localized rash, 79.5% reported dry skin, and 36.6% reported eczema in response to chlorhexidine.[28] No significant association was found between the respiratory symptoms and skin symptoms experienced among exposed healthcare workers with eczema or contact dermatitis.[28] Last, Lee et al. evaluated the risk of skin symptoms in relation to more general chemical-related symptoms, which may include the respiratory, eye, nervous, skin, or gastrointestinal symptoms.[3] This study reported that contact dermatitis was significantly more frequent in workers with chemical-related symptoms compared with workers without chemical-related symptoms ($p = 0.012$).[3]

4 | DISCUSSION

This systematic review and meta-analysis found a 35% increased asthma risk among healthcare and other hospital workers exposed to cleaning and disinfecting tasks or cleaning and disinfecting agents, compared with other workers ($p = 0.01$). After 2000 the excess risk of asthma attributed to cleaning or disinfecting tasks or agents decreased to 28%, suggesting a possible earlier confounding effect of natural rubber latex exposure and/or other exposure changes. The risk of asthma attributed to cleaning and disinfecting tasks or agents increased (to 45%) when subgroup analysis was performed to focus on new-onset asthma and adult-onset asthma diagnoses; however, this increased risk was not statistically significant. Assessment of specific agents showed a nonsignificant 51% increased asthma risk associated with bleach exposure, and most studies also reported an increased asthma risk associated with exposure to glutaraldehyde, bleach, and quaternary ammonium compounds. No exposure-response relationships between potential causal agents and reported asthma could be determined due to the lack of quantitative exposure analysis. Four studies reported no statistically significant differences between current asthma diagnoses among disinfectant product users

and nonusers.[16,25,26,30] These contrasting results may be due to the possibility that workers without direct use of disinfectants were exposed to the vapors of the disinfectant products, which can also induce asthma.[26] Also, the study population of one of the studies that found contrasting results was restricted to nurses who had no asthma after over 20 years of occupational exposure.[30] The authors then investigated the development of asthma among these nurses in the following 6 years, and found incident asthma to be unrelated to disinfectants.[30] Therefore, the unique characteristics of this limited study population and a "healthy worker" effect may have contributed to the unexpected results found.

Cleaning and disinfecting tasks or agents were also found to be associated with an increased risk of LRTS and URTS in studies that investigated asthma-like symptoms and URTS, such as nasal irritation. The meta-analysis for wheezing symptoms found a nonsignificant 55% increased risk among exposed healthcare workers.

Among the studies included in the systematic review, there were very limited results regarding the relationship between respiratory and skin symptoms. One study evaluated the relationship between respiratory and skin symptoms and found increased odds of skin symptoms in healthcare workers with respiratory symptoms[4]; however, this study was given a "poor" quality assessment score, with a high risk of bias potentially affecting the reliability of the results. A second study found that exposed healthcare workers with hay fever or asthma also reported skin symptoms such as localized rash, dry skin, and eczema in response to chlorhexidine, suggesting a potential relationship between respiratory and skin symptoms; however, no significant association was found between the respiratory symptoms and skin symptoms experienced among exposed healthcare workers with eczema or contact dermatitis.[28] Lee et al. reported that contact dermatitis was significantly more frequent in workers with chemical-related symptoms compared with workers without chemical-related symptoms[3]; however, the outcome definition for chemical-related symptoms in this study included symptoms associated with respiratory, skin, gastrointestinal, eye, or nervous systems, making it difficult to discern the relationship between respiratory symptoms and contact dermatitis specifically. Due to the limited available data, no conclusions can be drawn about possible associations between respiratory and skin symptoms related to cleaning and disinfecting agents in hospital workers.

A strength of this systematic review was its comprehensiveness, as indicated by a lack of observed publication bias. Also, the systematic review included independent assessment from a minimum of two reviewers for the title and abstract screening, full-text screening, and risk of bias assessment stages of the methods. Another strength is that most of the included studies have a low risk of bias assessment, as deemed by a "fair" or "good" quality assessment score. Only one study received a "poor" quality assessment score, and the risk of bias in this study was considered in the interpretation of the results. Last, pooled risk estimates were obtained that quantify the risk of asthma among healthcare workers exposed to cleaning or disinfecting agents or tasks. The pooled risk estimates can be used to inform future public health interventions and research studies regarding similar topics.

One of the limitations of this systematic review is the exclusion of articles written in languages other than English. Additionally, almost all of the included studies used self-report measures to collect data, which is subject to recall bias. For instance, cleaning products and disinfectants that have a more pungent and noxious smell might be more memorable.[7] In a study conducted in Arizona, participants with asthma were more likely to report feeling sick in the presence of compounds with a strong odor, such as cleaning agents.[7] Studies using objective or quantitative assessments of occupational exposures and outcomes would be less susceptible to recall bias. In addition, this review did not include an assessment of preventive measures in each study setting. Potentially there may be significant differences in occupational hygiene measures in different settings that may have affected the extent of exposures and rates of respiratory symptoms in different studies (as was reported by Nayebzadeh).[34]

Another weakness of this review involves the heterogeneity of the studies included in the meta-analyses. Although none of the meta-analyses had substantial heterogeneity ($I^2 \geq 50\%$), there was moderate heterogeneity within the included studies of each meta-analysis. Possible causes of within-studies heterogeneity could include the misclassification of outcomes and exposures, and how different studies may not have adjusted for the same potential confounders. Consequently, a fixed effect model could not be used to pool the studies. Also, several included papers assessed only one exposure without considering potential concurrent exposures.[16,28,32,34,38,39] The results may be confounded by other unknown concurrent exposures, causing the results to be unreflective of any true relationships. Last, the possibility of the healthy worker effect was a limitation of our review.[41] Many of the studies included in our review were cross-sectional in design and could have missed those who had left the healthcare workforce due to respiratory and/or skin symptoms. This could have resulted in an underestimation of the respiratory and skin symptoms in the study population. An association between asthma history and subsequent job changes in nurses was previously found, supporting the possibility of the healthy worker effect bias in cross-sectional studies regarding disinfectant exposures.[42] More prospective cohort studies that follow healthcare workers from early stages of their career and examine the influence of exposure duration, similar to the study conducted by Dumas et al., would limit the healthy worker bias effect.[14]

5 | CONCLUSIONS

In conclusion, this review found a higher risk of asthma among healthcare workers exposed to cleaning or disinfecting tasks or agents. These findings are consistent with the results of previously conducted systematic reviews.[8,43] Compared with this review, both previous reviews determined a greater increase in asthma risk associated with cleaning or disinfecting tasks.[8,43] The limitations found in this review may contribute to a potential underestimation of

the risk. The findings highlight the importance of implementing safe work practices and control measures that protect healthcare workers from potentially harmful occupational cleaning and disinfecting exposures. The results of this review are especially relevant during the COVID-19 pandemic, when the use of cleaning and disinfecting agents has increased to prevent the transmission of the virus. Future studies using a prospective cohort design and quantitative exposure assessments of specific cleaning or disinfecting agents are recommended because they will decrease the potential of healthy worker effect bias and allow for the determination of an exposure-response relationship. Measuring exposure to specific cleaning or disinfecting agents in future studies will also help to further elucidate underlying causal agents. Also, further research regarding skin symptoms among healthcare workers with asthma-like respiratory symptoms is suggested. The studies that were included in this review evaluated asthma-like respiratory symptoms but have not fully explored the skin symptoms that may be concurrently occurring among healthcare workers with respiratory symptoms. Preventive measures that have been advised for those working with cleaning/disinfecting agents have included use of safe products when possible, safety education of workers, appropriate use of protective equipment, and good ventilation.[44]

Filling these gaps in knowledge could help with earlier prevention and treatment interventions to take place for these workers.

AUTHOR CONTRIBUTIONS

Kelly T.L. Dang: paper reviews; formal Analysis; writingReviewEditing. Kelly Dang performed formal analyses, wrote the original draft and contributed to review and editing of the final manuscript. Ameth Garrido contributed to the formal analyses, investigation, writing, and review of the manuscript. Shivonne Prasad contributed investigation, writing, and review of the manuscript. Marina Afanasyeva contributed to the project administration, review, and editing of the manuscript. Joshua Lipszyc contributed to the project conceptualization, investigation and review, and editing of the manuscript. Ani Orchanian-Cheff contributed to the data curation, methodology, and writing, review, and editing of the manuscript. Susan M. Tarlo contributed to the project conceptualization, methodology, investigation, project administration, supervision, validation, and review and editing of the manuscript.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Additional data are available in the online supplement.

TRANSPARENCY STATEMENT

The lead author (manuscript guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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