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RESEARCH ARTICLE

The Association of Current Asthma With and Without Exacerbation With Products Used and Tasks Performed by Healthcare Workers

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ABSTRACT

Background: Results from a 2014 survey of 2030 healthcare workers (76% female, mean age 48.6 years) in New York City included the association of current asthma and asthma exacerbation with the general activities of cleaning fixed surfaces and administering aerosolized medications. We extended that analysis to determine if specific products and tasks for these and other activities were associated with the same outcomes.

Methods: The survey instrument inquired about asthma-related outcomes, products used, and tasks performed. Polytomous logistic regression was used to model a three-category outcome for current asthma without and with exacerbation and no current asthma (referent). Inverse probability weights were applied in all regression models to adjust for selection and participation bias that may have resulted from a low response of 11.1% of invitees. A separate model was fit for each exposure variable and yielded adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

Results: For cleaning fixed surfaces, two products and eight tasks had increased odds of at least one adverse outcome. Enzymes had an OR = 3.01 (95% CI 1.50, 6.04) for current asthma with exacerbation, and bleach had an OR = 1.92 (95% CI 1.22, 3.01) for current asthma without exacerbation. The eight general cleaning tasks included three (cleanup blood/spills, wipe furniture, wipe equipment) associated with both adverse outcomes, and five tasks associated only with current asthma without exacerbation. For aerosolized medication tasks, the small-volume nebulizer was associated with current asthma with (OR = 1.89, 95% CI 1.06, 3.34) and without (OR = 1.66, 95% CI 1.01, 2.72) exacerbation, and two other tasks (continuous delivery system, metered dose inhaler) were associated only with current asthma without exacerbation.

Conclusions: Products and tasks in healthcare were associated with current asthma and asthma exacerbation. Future analyses will explore quantitative exposure-assessment strategies for specific chemicals and mixtures.

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1 | Introduction

Work-related asthma includes both occupational asthma (OA) that is caused by workplace conditions and work-exacerbated asthma (WEA) that is defined as "pre-existing or concurrent asthma that is worsened by workplace conditions" [1]. Statements from the American Thoracic Society (ATS) have estimated the occupational population attributable fraction for asthma at 16% [2] and that 21.5% of adults with asthma experience exacerbation due to workplace conditions [1]. Individuals with WEA that have ongoing problems with asthma symptoms related to work can experience adverse clinical [3, 4] and socioeconomic [3, 5] consequences similar to those of OA cases. Knowledge of exposures and conditions responsible for work-related asthma is important to guide prevention efforts in the workplace, as well as to assist healthcare professionals when evaluating and treating working adults with asthma.

Multiple studies have reported that healthcare workers are at an elevated risk for asthma, especially due to cleaning and disinfecting tasks and products. A recent systematic review and meta-analysis of data from numerous studies of healthcare personnel reported pooled relative risk (RR) estimates for the association of different asthma outcomes with cleaning and disinfecting [6]. These effect estimates for new-onset asthma were elevated for nurses (RR = 1.67, 95% confidence interval [CI] 1.11−2.50), and specifically for nurses who performed tasks related to cleaning/disinfecting surfaces (RR = 1.43, 95% CI 1.09−1.83) and instrument cleaning/disinfection/sterilization (RR = 1.34, 95% CI 1.09–1.65). Using data from studies that analyzed either new-onset asthma or OA, the pooled effect estimates were elevated for the chemicals bleach (RR = 2.08, 95% CI 1.24–3.49) and glutaraldehyde (RR = 1.70, 95% CI 1.14–2.53) [6].

Other studies have identified WEA as common among healthcare workers and associated with cleaning and disinfecting agents. From the multi-national population-based European Community Respiratory Health Survey (ECRHS), results suggested an association of severe exacerbation of asthma with all health occupations (RR = 1.5, 95% CI 0.95–2.4) and the healthcare-worker subgroup of nurses (RR = 1.7, 95% CI 0.99–2.9) [7]. A 2004 survey of healthcare workers in the U.S. state of Texas reported that WEA was associated with several self-reported cleaning and disinfecting exposures in any job held for at least 6 months. These included associations with bleach used in general-purpose cleaning (odds ratio [OR] = 3.13, 95% CI 1.08–9.08), any instrument cleaning/sterilization (OR = 3.40, 95% CI 1.35–8.53), and formalin/formaldehyde used to sterilize instruments (OR = 2.66, 95% CI 1.03–6.86) [8]. These investigators also reported the association of work-related asthma symptoms (OR = 3.72, 95% CI 1.70–8.12) with bleach used as a cleaner [8].

The analysis of data from a cross-sectional survey of 2030 healthcare workers in New York City yielded results for the association of current asthma and exacerbation of asthma with healthcare occupations, products, and tasks. Survey participants were employed in nine different nursing, technical, and cleaning occupations in healthcare. A study based on these data characterized work-related exposure by healthcare occupation and by self-reported performance of four general healthcare activities [9]. Both current asthma and exacerbation of asthma were associated with the two healthcare activities of cleaning fixed surfaces (OR = 1.84, 95% CI 1.26–2.68, and OR = 2.37, 95% CI 1.29–4.34, respectively) and administering aerosolized medications (OR = 1.67, 95% CI 1.15–2.43, and OR = 1.77, 95% CI 1.03–3.03, respectively) [9]. Cleaning fixed surfaces was conducted by 64% ($n = 1291$) of the participants and a substantial proportion of all nine occupations, while administering aerosolized medications was reported by 15% ($n = 301$) and dominated by respiratory therapists, licensed practical nurses, and registered nurses. Neither asthma outcome was associated with the other two general healthcare activities of disinfecting/sterilizing medical instruments and applying chemicals to patients' skin. Another study using the same data developed cluster variables for asthma symptoms and reported positive associations with different cleaning and disinfecting agents including alcohols, bleach, enzymes, and detergents, and with skin wipes used on patients and aerosolized medications [10]. Also, a health cluster variable for asthma attacks/exacerbations was associated with an exposure cluster variable for general cleaning/laboratory [10]. Neither of these studies investigated the association of asthma outcomes with specific laboratory tasks.

A better understanding of whether specific cleaning/disinfecting tasks and products, and laboratory tasks are associated with asthma outcomes could help to inform the control of harmful occupational exposures in healthcare. The questionnaire used in the study of healthcare workers in New York City collected details about cleaning/disinfecting, patient care activities, and laboratory tasks at work, making it possible to assess products used and tasks performed by each participant. The objective of the current investigation was to determine whether current asthma and exacerbation of asthma were associated with these more detailed variables, focusing on products and tasks specific to the four general activities of cleaning fixed surfaces, administering aerosolized medications, disinfecting/sterilizing medical instruments, and applying chemicals to patients' skin, and on tasks conducted in laboratories.

2 | Materials and Methods

2.1 | Study Population and Survey

Details on study methods are available in a previously published article [9]. The study protocol was reviewed and approved by the National Institute for Occupational Safety and Health (NIOSH) Institutional Review Board (IRB). All participants provided oral consent. Invitees were nurses, technicians, and cleaning staff who worked in hospitals and nursing homes in New York City and belonged to the Service Employees International Union Local 1199. With a final sample frame of 24,057 union members, we used random sampling stratified by occupation to identify 18,243 members whom we invited to participate. These individuals were contacted in 2014 and asked to complete a survey questionnaire either online or by telephone. The questionnaire inquired about demographics, work history, work tasks, indoor environmental conditions at work, and asthma-related health, with an emphasis on events and conditions in the last 12 months. The 2030 participants who completed the survey questionnaire were 11.1% of all invitees and 22.5% of the 9009 with whom telephone contact was made.

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To adjust for possible selection and participation bias, we developed inverse probability weights and applied them in all regression models, so the analysis population more closely resembled the final sample frame. Details regarding the study population and development of weights are provided in an earlier publication [9].

2.2 | Asthma Outcomes

The criteria for current asthma were self-reported history of physician-diagnosed asthma and a report of at least one of the following indications of active asthma in the last 12 months: had an attack of asthma, used asthma medication, hospitalized overnight for asthma, had urgent care or treatment for asthma, or had an asthma score of one or greater [11]. The criteria for exacerbation of asthma were having current asthma and reporting at least one of the following types of medication use or treatment in the last 12 months: increased use of inhaled steroids or fast-acting or rescue bronchodilators on a short-term basis, increased oral steroid usage as treatment for asthma, seeking of urgent treatment for asthma, or hospitalization overnight for asthma [12]. We analyzed current asthma and exacerbation of asthma in separate regression models in prior analyses, but took a different approach in the current analyses [9]. Recognizing the fact that exacerbation is a subset of current asthma, we considered the two together by creating a three-category outcome variable, in which current asthma/no exacerbation and current asthma/exacerbation were compared to no current asthma. We did not pursue exacerbation divided into moderate and severe because of concerns about small numbers that were encountered in earlier analyses [9].

2.3 | Occupational Exposures

Occupational exposures were characterized by self-reported ever/never products used and tasks performed in healthcare in the last 12 months, organized into multiple sets of dichotomous variables based on different activities. The development of these variables was driven by a comprehensive survey of five hospitals where we observed workers in 14 occupations every 5 min for the whole shift over 216 shifts to understand tasks and products [13, 14]. The 28 variables related to cleaning fixed surfaces (including the surfaces of equipment) were in five categories: 10 cleaning products, 10 general cleaning tasks, four tasks for scraping and waxing floors, three tasks for terminal cleaning of patient rooms, and one task for end-of-shift cleaning of clinical areas. Administering aerosolized medications had four task variables. The 18 variables for disinfecting or sterilizing instruments were separated into three categories: 11 products, four tasks for automated systems, and three manual tasks. The seven tasks for applying chemicals to patients' skin were separated into variables for skin wipes ($n = 5$) and other skin applications ($n = 2$). Laboratory technicians worked in clinical/medical or dental laboratories and were employed in the same institutions and belonged to the same union as other study participants. Laboratory task variables included four for clinical/medical laboratories and five for dental laboratories.

Most exposure variables were for individual products or tasks, but four were summary variables. An any-terminal-cleaning variable was based on a positive response to the survey item "Conduct terminal cleaning of patient rooms." The other two terminal-cleaning variables were based on more detailed questions about this activity. The any-skin-wipe task variable was positive if the participant had a positive response to at least one of the other four questions that addressed specific skin wipe tasks. For laboratory tasks, participants had to provide an initial positive response to an any-clinical/medical-laboratory task or any-dental-laboratory task question before they were asked about three or four specific tasks, respectively.

2.4 | Statistical Analyses

Polytomous logistic regression models of current asthma without and with exacerbation included the occupational exposures of interest and several risk factors and potential confounders: sex (female, male), race (African American, White, other, unspecified), age in four categories (19–39, 40–49, 50–59, 60 years or greater), smoking status (never, former, current), and history of allergies (no, yes). History of allergies was based on a positive response to any of the following: ever nasal or sinus allergies (including hay fever), ever eczema or any kind of skin allergy, ever allergies to animals, ever allergies to dust or dust mites, or ever allergies to latex or adhesives. The 16 participants with missing responses for potential confounders (15 for smoking status, one for sex) were deleted from regression models. For exposure and health outcome variables, missing values were typically uncommon (i.e., < 5) and assigned a "no" response. This final practice could introduce some differential misclassification (i.e., a true "yes" classified as a "no"), which would bias effect estimates to the null. A separate regression model was fit for each product or task, and each model was weighted by applying weights to adjust for selection and non-participation. We did not report results for variables with fewer than three exposed cases.

Due to concerns about potential overlap among exposure variables, we calculated the phi coefficient to characterize the extent that a pair of dichotomous product or task variables were related to each other [15]. We calculated this statistic for exposure variables that had a statistically significant association with at least one of the outcomes of interest, separately for products and for tasks related to cleaning fixed surfaces, and for aerosolized medication tasks. The phi coefficient is typically interpreted the same as a correlation coefficient. We used the Guilford descriptors for the extent of the relationship based on ranges of coefficients, whether negative or positive, these were: slight < 0.20; $0.20 \leq$ low < 0.40; $0.40 \leq$ moderate < 0.70; $0.70 \leq$ high < 0.90; very high ≥ 0.90 [16].

We conducted data management, summaries, and analyses using SAS 9.4 statistical software (SAS Institute Inc, Cary, NC).

3 | Results

3.1 | Demographics and Prevalence of Current Asthma

Characteristics of the 2030 survey participants are summarized in Table 1. They included three times as many women (76.0%) as men (24.0%), and by race, about three in five were African

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TABLE 1 | Distribution of the 2030 study participants by selected demographic and health characteristics.

Variable	N	% of total
Sex[a]		
Female	1542	76.0
Male	487	24.0
Race		
African American	1249	61.5
White	266	13.1
Other	274	13.5
Unspecified	241	11.9
Age, years[b]		
19–39	488	24.0
40–49	485	23.9
50–59	697	34.3
60 +	360	17.7
Smoking status[a]		
Never smokers	1676	83.2
Former smokers	226	11.2
Current smokers	113	5.6
History of allergies[c]		
No	997	49.1
Yes	1033	50.9
Current asthma		
Without exacerbation	99	4.9
With exacerbation	74	3.6
Total	173	8.5

[a]There was one missing value for sex and 15 missing values for smoking status.
[b]Mean age was 48.6 years, standard deviation 11.4.
[c]Defined as a positive response to any of the following: ever nasal or sinus allergies (including hay fever), ever eczema or any kind of skin allergy, ever allergies to animals, ever allergies to dust or dust mites, or ever allergies to latex or adhesives.

American (61.5%). Almost half (47.9%) were less than 50 years old, and the mean age was 48.6 years (SD 11.4). Approximately one in six participants had ever smoked (5.6% current and 11.1% former smokers), and 50.9% reported a history of allergies (Table 1). The participants worked in nine nursing, cleaning, and technical occupations. Four occupations accounted for over 80% of the group: nursing assistants ($n = 702$, 34.6%), environmental service workers ($n = 374$, 18.4%), licensed practical nurses ($n = 297$, 14.6%), and registered nurses ($n = 280$, 13.8%). Fewer worked as laboratory technicians ($n = 166$, 8.2%), respiratory therapists ($n = 75$, 3.7%), operating room technicians ($n = 63$, 3.1%), central supply workers ($n = 41$, 2.0%), and dental assistants ($n = 32$, 1.6%). The 173 participants (8.5%) with current asthma included 99 (4.9%) without exacerbation and 74 (3.6%) with exacerbation.

As presented in a prior publication, the 2030 participants had a similar sex distribution and were a little older on average relative to the 16,213 invitees who did not take part [9]. These two groups had different crude distributions by occupation. Of note, a smaller percentage of non-participants were nursing assistants (29%), and a larger percentage were environmental service workers (23%).

3.2 | Products and Tasks for Cleaning Fixed Surfaces

Table 2 includes results from regression models for the 10 cleaning products and 18 tasks related to cleaning fixed surfaces. Two cleaning products had statistically significantly elevated ORs, but with different asthma outcomes. Current asthma with exacerbation was associated with the product enzymes (reported by 155 participants), OR = 3.01 (95% CI 1.50–6.04). Current asthma without exacerbation was associated with bleach, which was used by many survey participants ($n = 721$) and had an OR = 1.92 (95% CI 1.22–3.01). Neither product had a substantially elevated OR for the other asthma outcome of interest, and were reported by different groups of workers, with a phi statistic of only 0.09. Six other cleaning products had no statistically significant results and included three that were commonly used: alcohol $n = 847$, glass cleaning products $n = 347$, and detergents $n = 253$. Two of the 10 products (i.e., acids, ammonia) had no reported OR estimates due to < 3 exposed cases for both outcomes.

The cleaning tasks were separated into four categories (Table 2). The general cleaning category had 10 tasks performed by no fewer than 143 workers. Current asthma, both with and without exacerbation, was associated with the three most common general cleaning tasks of cleanup blood/spills, wipe down furniture, and wipe down equipment, which were each performed by over 700 participants and had statistically significantly elevated ORs that ranged from 1.65 to 2.54 (Table 2). Current asthma without exacerbation was associated with five other cleaning tasks (i.e., mop floors, clean bathroom surfaces, manually mix products, polish stainless steel, spray deodorant) that were performed by 246–391 participants and had statistically significantly elevated ORs that ranged from 1.80 to 2.17. The two general cleaning tasks without statistically significant results for either outcome were polish wood and spray/clean glass surfaces. Phi coefficients were calculated for the 28 unique pairs of the eight general cleaning tasks with elevated ORs to characterize the extent to which they were associated. Over half ($n = 17$, 61%) had a moderate level of association, one-quarter low ($n = 7$, 25%), 3 (11%) slight, and only one high (Supporting Information S1: Table S1).

The four tasks for scraping and waxing floors were performed by few participants (i.e., 66–78), had low numbers of exposed cases, and had no effect estimates greater than one (Table 2). Two of the three tasks for the category of terminal cleaning of patient rooms and the one task for end-of-shift cleaning of patient care areas were relatively common (i.e., $n = 316$, 232, and 189, respectively), but none were associated with the asthma outcomes.

3.3 | Tasks for Administering Aerosolized Medications

Three of the four aerosolized medication tasks were common (i.e., reported by 238–343) and had statistically significantly elevated ORs (Table 3). The task variable for small volume nebulizer had an elevated OR for both current asthma with

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TABLE 2 | Adjusted odds ratios (95% CI) for association of asthma outcomes with using products and performing tasks to clean fixed surfaces.[a]

Product or task variable	n Exp.	Exp. cases	Current asthma without exacerbation (n = 99) Odds ratio (95% CI)	p	Exp. cases	Current asthma with exacerbation (n = 74) Odds ratio (95% CI)	p
Cleaning products							
Enzymes	155	9	1.12 (0.54, 2.31)	0.76	**13**	**3.01 (1.50, 6.04)**	**0.002**
Bleach	721	**47**	**1.92 (1.22, 3.01)**	**0.005**	30	1.24 (0.70, 2.20)	0.46
Alcohol	847	48	1.24 (0.82, 1.90)	0.31	33	1.28 (0.79, 2.09)	0.32
Detergents	253	16	1.52 (0.83, 2.80)	0.18	9	1.11 (0.51, 2.43)	0.80
Acids	37	1	NR	NR	2	NR	NR
Ammonia	59	2	NR	NR	2	NR	NR
Glass cleaning products	347	19	1.34 (0.74, 2.40)	0.33	11	1.05 (0.51, 2.14)	0.90
Phenolics	107	4	0.58 (0.21, 1.64)	0.31	7	1.90 (0.81, 4.47)	0.14
Quaternary ammonium compounds	125	5	0.82 (0.32, 2.15)	0.69	6	1.63 (0.60, 4.45)	0.34
Floor wax/strip product	123	7	1.61 (0.60, 4.35)	0.35	3	1.45 (0.40, 5.17)	0.57
Cleaning tasks							
General cleaning tasks							
Cleanup blood/spills	704	46	**2.03 (1.30, 3.18)**	**0.002**	33	**1.98 (1.16, 3.36)**	**0.012**
Mop floors	333	21	**1.86 (1.04, 3.31)**	**0.036**	12	1.31 (0.64, 2.66)	0.46
Wipe down furniture	760	52	**2.09 (1.35, 3.25)**	**0.001**	38	**2.12 (1.24, 3.62)**	**0.006**
Wipe down equipment	905	56	**1.65 (1.08, 2.54)**	**0.022**	46	**2.54 (1.52, 4.24)**	**0.0004**
Clean bathroom surfaces	332	23	**1.90 (1.10, 3.29)**	**0.021**	11	1.07 (0.50, 2.27)	0.87
Manually mix products	284	20	**2.07 (1.17, 3.65)**	**0.012**	9	0.99 (0.47, 2.09)	0.98
Polish wood	143	*11*	*1.84 (0.92, 3.68)*	*0.086*	4	0.94 (0.32, 2.79)	0.91
Polish stainless steel	246	18	**2.17 (1.18, 3.99)**	**0.012**	10	1.60 (0.77, 3.31)	0.21
Spray deodorant	391	29	**1.80 (1.10, 2.93)**	**0.020**	19	1.55 (0.89, 2.71)	0.13
Spray/clean glass surfaces	315	18	1.41 (0.78, 2.55)	0.26	11	1.21 (0.59, 2.48)	0.60
Scraping and waxing floors tasks							
Scrape floor	66	3	0.80 (0.21, 3.00)	0.74	0	NA	NA
Strip floor	70	2	NR	NR	1	NR	NR
Buff floor	78	3	0.80 (0.22, 2.88)	0.73	1	NR	NR
Wax floor	72	2	NR	NR	1	NR	NR
Terminal cleaning of patient rooms tasks							
Any terminal cleaning[b]	316	19	*1.64 (0.93, 2.89)*	*0.085*	11	1.22 (0.58, 2.55)	0.59
Clean for multidrug-resistant organisms	232	15	1.64 (0.88, 3.04)	0.12	8	1.08 (0.47, 2.48)	0.86
Fog room with hydrogen peroxide or peracetic acid	99	5	1.12 (0.44, 2.87)	0.81	1	NR	NR
Cleaning operating rooms, dialysis units, etc., at the end of shift tasks	189	12	1.4 (0.75, 2.62)	0.29	5	0.81 (0.30, 2.20)	0.68

Note: Bold indicates statistical significance, $p \leq 0.05$. *Italics* indicate borderline statistical significance, $0.05 < p \leq 0.10$.

Abbreviations: 95% CI = 95% confidence interval, Exp. = exposed, NA = not applicable because of 0 exposed cases, NR = odds ratio not reported because < 3 exposed cases.

[a]Regression models adjusted for sex, race, age by category, smoking category, and history of allergies. A separate model was fit for each product or task, and all models were weighted to adjust for selection and nonparticipation. The comparison group for exposure variables included participants who did not use the product or perform the task being studied. The comparison group for both asthma outcomes was participants without current asthma.

[b]The "Any terminal cleaning" variable was based on a positive response to the general question "Conduct terminal cleaning of patient rooms." The other two terminal cleaning variables were based on more detailed questions about this activity.

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TABLE 3 | Adjusted odds ratios (95% CI) for association of asthma outcomes with administering aerosolized medications.[a]

		Current asthma without exacerbation ($n = 98$)			Current asthma with exacerbation ($n = 74$)		
Task variable	***n* Exp.**	**Exp. cases**	**Odds ratio (95% CI)**	***p***	**Exp. cases**	**Odds ratio (95% CI)**	***p***
Small volume nebulizer	343	24	**1.66 (1.01, 2.72)**	**0.046**	19	**1.89 (1.06, 3.34)**	**0.030**
Continuous delivery system	238	18	**1.85 (1.07, 3.22)**	**0.029**	11	1.59 (0.80, 3.16)	0.19
Metered dose inhaler	279	21	**1.89 (1.11, 3.20)**	**0.019**	11	1.22 (0.61, 2.44)	0.57
Dry powder inhaler	163	12	1.65 (0.84, 3.26)	0.15	5	0.9 (0.34, 2.38)	0.83

Note: Bold indicates statistical significance, $p < 0.05$. *Italics* indicate borderline statistical significance, $0.05 < p < 0.10$.
Abbreviations: 95% CI = 95% confidence interval, Exp. = exposed.
[a]Regression models adjusted for sex, race, age by category, smoking category, and allergic status. A separate model was fit for each product or task, and all models were weighted to adjust for selection and nonparticipation. The comparison group for exposure variables included participants who did not use the product or perform the task being studied. The comparison group for both asthma outcomes was participants without current asthma.

exacerbation (OR = 1.89, 95% CI 1.06–3.34) and without exacerbation (OR = 1.66, 95% CI 1.01–2.72). The two tasks of continuous delivery system and metered dose inhaler had positive results for only current asthma without exacerbation. The phi coefficients for the pairs of these three tasks were all > 0.70 and < 0.80, indicating a high level of association (Supporting Information S1: Table S2). The fourth aerosolized medication task of using a dry powder inhaler was associated with neither outcome.

3.4 | Products and Tasks for Disinfecting or Sterilizing Instruments

Disinfecting or sterilizing instruments was conducted by fewer participants than cleaning fixed surfaces (Table 4). In fact, eight of the 11 products and six of the seven task variables were reported by fewer than 100 healthcare workers. The second most common product was bleach ($n = 168$), and it was the only variable in this group that had a statistically significantly elevated OR, specifically OR = 2.16 (95% CI 1.08–4.32) for current asthma without exacerbation (Table 4). The four tasks for automated systems had a maximum of 26 exposed participants, and all ORs were either zero or not reported due to the small number of cases. The three manual tasks had several elevated ORs, but the CIs were wide.

3.5 | Tasks for Applying Chemicals to Patients' Skin

These tasks include one summary variable for any skin wipe task, three individual skin wipe tasks, and two other skin application tasks for applying fiberglass casts and applying adhesives (Table 4). Six of these seven variables were reported by at least 224 participants, but 'apply fiberglass cast' was reported by only 28. The only statistically significant result was the association of current asthma with exacerbation with any skin wipe task, OR = 1.68 (95% CI 1.00–2.82).

3.6 | Tasks for Clinical/Medical and Dental Laboratories

Many of the laboratory tasks were performed by a few workers; six of the nine variables had fewer than three cases for one or both outcomes, and none of these variables had statistically significant results (Supporting Information S1: Table S3). The summary variable 'any clinical/medical laboratory task' had 244 exposed participants and enough exposed cases (i.e., ≥ 3) to report results, but neither OR was statistically significant. The summary 'any dental laboratory' variable included only 41 workers, the four individual dental laboratory tasks were reported by no more than 21 workers, and the ORs for these variables were either zero because of no exposed cases or not reported because of having only one or two exposed cases.

4 | Discussion

4.1 | Confirmation of Results From an Earlier Publication

A prior analysis of the current data revealed elevated ORs for current asthma and exacerbation of asthma for the general activities of cleaning fixed surfaces and administering aerosolized medications, but not for sterilizing medical instruments and applying chemicals to patients' skin [9]. The current analysis used more detailed characterizations of the same four general types of activities, and three product and 12 task variables had statistically significantly elevated ORs for at least one of the two asthma outcomes of current asthma with and without exacerbation. Consistent with the prior report, at least one of the asthma outcomes was associated with 10 of 28 variables for cleaning fixed surfaces and three of four variables for administering aerosolized medicines, but only one of 18 variables for disinfecting or sterilizing instruments and one of seven variables for applying chemicals to patients' skin.

4.2 | Results for Cleaning Fixed Surfaces and for Administering Aerosolized Medications

Efforts to prevent asthma and related symptoms associated with cleaning activities by healthcare workers often focus on the products used. However, statistically significant elevated ORs were observed for only two of 10 cleaning products but eight of 10 general cleaning tasks. This difference might reflect actual differences in the health impact of the products, or that the tasks better integrated the total effect of exposure to multiple

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TABLE 4 | Adjusted odds ratios (95% CI) for association of asthma outcomes with using products and performing tasks to disinfect or sterilize instruments or apply chemicals to patients' skin.[a]

Product or task	n Exp.	Current asthma without exacerbation ($n = 99$)			Current asthma with exacerbation ($n = 74$)		
		Exp. cases	Odds ratio (95% CI)	p	Exp. cases	Odds ratio (95% CI)	p
Products							
Enzymes	80	6	1.42 (0.56, 3.57)	0.46	2	NR	NR
Hypochlorite or hypochlorous acids	62	3	1.33 (0.38, 4.63)	0.66	2	NR	NR
Bleach	168	13	**2.16 (1.08, 4.32)**	**0.03**	5	0.89 (0.33, 2.44)	0.83
Alcohol	229	16	*1.70 (0.91, 3.18)*	*0.098*	4	0.43 (0.15, 1.24)	0.12
Ethylene oxide	43	3	1.33 (0.40, 4.41)	0.64	0	0	NA
Glutaraldehyde	76	5	1.42 (0.52, 3.86)	0.49	2	NR	NR
Ortho-phthalaldehyde	71	1	NR	NR	3	1.32 (0.37, 4.71)	0.67
Hydrogen peroxides	114	4	0.72 (0.24, 2.11)	0.54	2	NR	NR
Peracetic acid	34	3	2.25 (0.62, 8.11)	0.22	0	0	NA
Formaldehyde	38	2	NR	NR	2	NR	NR
Acetic acid	32	2	NR	NR	0	0	NA
Tasks							
Automated systems							
Operate ethylene oxide system	9	1	NR	NR	0	0	NA
Operate hydrogen peroxide system	21	0	0	NA	0	0	NA
Operate peracetic acid system	26	0	0	NA	1	NR	NR
Conduct maintenance on system	25	2	NR	NR	1	NR	NR
Manual tasks							
Manual cleaning before sterilization	111	8	1.61 (0.74, 3.51)	0.23	3	0.86 (0.25, 2.96)	0.81
Manual high−level disinfection	63	4	1.61 (0.54, 4.79)	0.39	4	1.66 (0.55, 5.05)	0.37
Handle sterilization solution	72	6	1.98 (0.82, 4.77)	0.13	2	NR	NR
Applying chemicals to patients' skin							
Skin wipes							
Any skin wipe task[b]	571	33	1.22 (0.77, 1.93)	0.39	29	**1.68 (1.00, 2.82)**	**0.048**
Disinfecting skin	515	32	1.40 (0.89, 2.22)	0.15	26	*1.62 (0.95, 2.77)*	*0.075*
Disinfect wound	282	20	*1.56 (0.92, 2.65)*	*0.10*	12	1.08 (0.55, 2.10)	0.82
Apply wound dressing	272	18	1.47 (0.84, 2.57)	0.18	8	0.76 (0.35, 1.64)	0.48
Apply adhesive removers	353	23	1.41 (0.84, 2.34)	0.19	18	1.53 (0.85, 2.76)	0.16
Other skin applications							
Apply fiberglass cast	28	2	NR	NR	2	NR	NR
Apply adhesive	224	17	1.57 (0.89, 2.77)	0.12	10	1.19 (0.57, 2.49)	0.65

Note: Bold indicates statistical significance, $p < 0.05$. *Italics* indicate borderline statistical significance, $0.05 < p < 0.10$.
Abbreviations: 95% CI = 95% confidence interval, Exp. = exposed, NA = not applicable because of 0 exposed cases, NR = odds ratio not reported because < 3 exposed cases.
[a]Regression models adjusted for sex, race, age by category, smoking category, and allergic status. A separate model was fit for each product or task, and all models were weighted to adjust for selection and nonparticipation. The comparison group for exposure variables included participants who did not use the product or perform the task being studied. The comparison group for both asthma outcomes was participants without current asthma.
[b]The "Any skin wipe task" variable was positive if the participant had a positive response to at least one of the four questions about specific skin wipe tasks.

products that are often used when cleaning. Also, the contrast in results might have been influenced by the enhanced power to detect a statistically significant difference because a greater number of participants reported cleaning tasks than products. This difference in the frequency of reports might indicate that workers more readily recalled tasks they had performed rather than the names of products. The median number of participants who reported the cleaning variables was 332.5 (143−905) for the 10 general cleaning tasks and 140 (37−847) for the 10 cleaning products. Moreover, five of the 10 products were reported by

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fewer than 143 participants, which is the number that reported the least common general cleaning task. Additionally, it is possible that the tasks for general cleaning were related to each other to such an extent that the very real adverse effects of a few tasks might have been "shared" with other tasks. Over half of the 28 unique pairs of the eight general cleaning tasks with elevated ORs had a moderate level of association, and all pairs of the three aerosolized medication tasks with elevated ORs had a high level of association.

4.3 | Disinfecting or Sterilizing Instruments

As reported in a prior publication based on the same data as used in the current investigation, cleaning fixed surfaces was much more common than disinfecting and sterilizing instruments, reported by 64% versus 15% of the survey participants respectively [9]. This difference is consistent with the staffing needs for the two activities and has been reported in other studies of healthcare workers [8, 17, 18]. For the current study, the median number of participants who reported activities related to disinfecting or sterilizing instruments was only 71 (32–229) for the 11 products and 26 (9–111) for the seven tasks. The one statistically significant result among these 18 variables was the product bleach, reported by 168 participants, for current asthma without exacerbation. It is also possible that the association with only one agent might reflect success at reducing workers' exposures while disinfecting or sterilizing instruments, perhaps in part attributable to the use of automated, enclosed systems for disinfecting endoscopes [18]. However, bleach is mostly used for manual disinfection and not used in automated systems, which further increases the chance of exposure.

4.4 | Bleach and Enzymes as Risk Factors for Current Asthma

Many participants in the current study reported using bleach, and it was the second most common product for both cleaning fixed surfaces and disinfecting and sterilizing instruments. It was identified as a risk factor for current asthma without exacerbation in both settings. In neither setting was bleach associated with exacerbation of current asthma. Investigation using the same data reported associations between three cluster variables based on asthma symptoms and the use of bleach for cleaning surfaces and disinfecting instruments [10]. The three cluster variables were mild asthma symptoms, undiagnosed/untreated asthma, and asthma attacks/exacerbation. Other studies have also reported that healthcare workers commonly use bleach and that it is a risk factor for asthma outcomes. For example, in a 2004 study of 3650 healthcare workers in Texas, 55.5% reported using bleach for general-purpose cleaning and it was a risk factor for both work-related asthma symptoms and WEA [8]. A subsequent 2016 study used similar methods to investigate asthma among 2421 healthcare workers in Texas [18]. Using bleach for cleaning building surfaces was reported by 75.6% of the participants, and it was associated with new-onset asthma [18]. From the ECRHS, only 18% of nurses reported using ammonia and/or bleach cleaning products more than once per week, but it was a risk factor for new-onset asthma [19]. As noted in the Introduction, a recent systematic review and meta-analysis yielded an elevated pooled RR for the association of either new-onset asthma or OA with bleach [6]. The results for bleach were less clear from another recent systematic review of evidence for cleaning product exposure and respiratory and skin symptoms in healthcare workers [20]. The review authors reported an elevated and statistically significant meta risk ratio for the association of asthma with cleaning or disinfecting tasks or agents, and the summary effect estimate for bleach was elevated but with a wide CI [20].

Enzymes for cleaning fixed surfaces was the only product variable associated with current asthma with exacerbation, with the largest statistically significant OR of 3.01. As with bleach, the association of this product with asthma outcomes has been reported by other studies. The previous analysis of the current data that used cluster variables based on asthma symptoms reported that the use of enzymes in either cleaning or disinfecting was associated with the outcomes of undiagnosed/untreated asthma and asthma attacks/exacerbation [10]. From an analysis of data from the Nurses' Health Study II, exposure to enzymatic cleaners was associated with poor asthma control [21].

Regarding underlying mechanisms, chlorine bleach is one of many cleaning and disinfecting products that are irritants, thought to cause inflammation through direct tissue damage. Detailed pathologic mechanisms of irritant-induced asthma are not fully understood, but inhalation of chemical irritants can damage the airway epithelium, resulting in airway inflammation, increased lung permeability, neurogenic inflammation, and airway epithelium remodeling [22–24]. These chemicals can also directly activate sensory nerves by stimulating either chemosensory cells or chemoreceptors. The analysis of bronchoalveolar lavage fluid from patients with irritant-induced asthma revealed that increased neutrophil counts were twice as common as increased eosinophil counts [25]. The European Academy of Allergy and Clinical Immunology position paper on irritant-induced asthma summarized the pathologic changes as characteristic of a toxic mechanism in the acute phase, and resembling those of patients with allergic asthma in the long-term [24]. Some cleaning and disinfecting products contain agents such as enzymes with the potential to induce immune sensitization, generally via a type 2 immune response. Type 2 immunity involves the differentiation, proliferation, and activation of antigen-specific TH2 cells which, together with group 2 innate lymphoid cells, produce type 2 cytokines such as IL-4, IL-5, IL-9, and IL-13. This leads to activation of effector myeloid cells, including eosinophils, mast cells, and basophils, and supports production of antigen-specific IgE [26].

4.5 | Tasks Conducted in Laboratories

The small number of participants who performed laboratory tasks limited our ability to investigate most of the specific tasks. The only variable with more robust numbers was for any clinical/medical laboratory task, which had the only suggestive positive finding for current asthma without exacerbation and a null finding for the exacerbation outcome. A recent study of French healthcare workers investigated asthma and exposures to cleaning and disinfecting products [27]. The researchers constructed exposure clusters, including one with 393 participants that was

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75% laboratory staff. While the emphasis was on exposure to cleaning and disinfecting products, the laboratory cluster members would have also experienced exposures from non-cleaning duties that accounted for most of their time. This cluster had unremarkable results for current asthma, but an association with asthma symptom score for women [27]. These findings suggest that the asthma symptom status might be a more sensitive indicator of the impact of laboratory-related exposures than asthma status.

4.6 | Limitations and Strengths

The limitations of the current investigation include aspects of the study design. In particular, the cross-sectional nature of the study means that we cannot be entirely certain about the temporal sequence of occupational exposures related to product use or tasks performed and subsequent asthma. Consequently, the effect estimates are probably inflated because, in some instances, the outcome preceded the exposure.

Also, the self-reported nature of both the occupational exposures and health outcomes likely introduced non-differential misclassification of both, leading to effect estimates possibly biased toward or away from the null [28, 29], as well as differential misclassification that would likely push effect estimates away from the null [30]. Pilot studies suggest that smartphone applications might allow study participants to scan barcodes on cleaning product containers at work to generate a more accurate account of exposures than self-reports, including in healthcare settings [31, 32]. Also, we did not account for unmeasured factors such as other occupational irritants and allergens, which may have confounded effect estimates. These limitations suggest the current results should be interpreted with some caution.

We have already noted that small sample sizes can limit a study's ability to detect risk factors. Examining Tables 2 through 4, the presence of < 3 exposed cases meant 11 exposures had no effect estimates for the two outcomes and another 11 exposures had only one effect estimate. A small number of exposed cases is certainly consistent with an actual low risk for an exposure metric, but these same 22 exposures also had very few exposed participants overall. In particular, the statistics for the number of exposed participants were a median of 32 and a mean of 38 for exposures with no effect estimates, and a median of 72 and a mean of 72 for exposures with an estimate for only one of the two asthma outcomes. The 20 exposures with effect estimates for both outcomes, but no statistically significant results, had a median of 230.5 and a mean of 260 exposed participants. Finally, the 15 exposures with effect estimates for both outcomes and at least one that was statistically significant had a median of 333 and a mean of 429 exposed participants. The last two groups shared the characteristic of having effect estimates for both asthma outcomes, but there was still a statistically significant difference ($p = 0.013$, Mann–Whitney U test) when comparing the number of exposed participants. The overall positive relationship between the number of exposed participants and statistically significant results suggests that small sample sizes likely limited our ability to identify risk factors for current asthma with and without exacerbation.

The current study was conducted in New York City, which differs from most communities in the United States, and the results might not be relevant in other locations, especially for prevalence estimates. However, the assessment focused on job tasks that are thought to be more consistent, have similar exposure profiles, and thus similar health risk across hospitals. Similar tasks have been reported for occupations in different regions of the United States and the world [14, 33, 34].

Examples of similarities and differences between the current study and other studies are evident in the prevalence of current asthma and any allergies. The prevalence of 8.5% for current asthma is close to national estimates from the 2011 to 2016 National Health Interview Survey (NHIS) of 8.8% for the healthcare and social assistance industry, and by occupation group of 8.6% for healthcare practitioners and technical, and 8.8% for healthcare support [35]. However, a study of several hundred healthcare workers during 2012–2014 at a medical center in Milwaukee, Wisconsin, reported a much higher 17.6% prevalence for current asthma, suggesting that prevalence estimates may vary considerably by study location [36]. About half (50.9%) of the current participants were positive for a history of allergies, which was defined very broadly to include any nasal or sinus allergy, any skin allergy, or ever an allergic reaction to animals, dust or dust mites, or latex or adhesives. From the 2021 NHIS, 31.8% of adults reported a diagnosed seasonal allergy, eczema, or food allergy [37]. From a general population survey conducted in the United States in 2018–2019, 41.7% of adult participants reported allergies [38]. The higher 50.9% with reported allergies for participants in the current study might in part reflect healthcare workers' greater awareness of, and willingness to report, their own allergic conditions than members of the general public.

Another concern is that the current study was conducted in 2014, and some results may not be relevant today. For example, the use of cleaners and disinfectants in healthcare settings accelerated during the COVID-19 pandemic [39]. The CEO of a US company that matches users with cleaning services listed five ways that cleaning medical settings has changed after the pandemic: increased frequency of disinfection, increased attention to aerosol transmission, using more advanced disinfectants, changes to cleaning services, and greater investment in cleaning [40]. With this in mind, post-pandemic healthcare workers might be at greater risk of exposure to cleaners and disinfectants and related health effects than when the current study took place. Additional studies and surveillance are needed to confirm or challenge the generalizability of results from this study to other locations and time periods.

The current study has several strengths. For example, it enlisted healthcare workers from a variety of occupations including those that require less formal education such as nursing assistants ($n = 702$) and environmental service workers ($n = 374$) that together accounted for over half the participants. This study is unusual among healthcare worker studies because the participant sample is majority African American (61.5%). However, race was unlikely to have confounded effect estimates because regression models were adjusted for race. The survey instrument used for the current analyses inquired about a

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relatively large number of products and tasks in healthcare, providing a level of detail not seen in all studies of these workers. While several products and tasks were reported by a few participants, the numbers were sufficient for many other variables to conduct meaningful analyses.

4.7 | Prevention

Preventive interventions that could potentially reduce the frequency or intensity of work-related symptoms for current asthma cases include changing the cleaning products and improving protection for workers during the administration of aerosolized medications. Cleaning in healthcare settings would ideally prevent infections while not causing adverse health effects due to the irritant or allergic qualities of cleaning products [41]. While frameworks for achieving these goals have been proposed, more research is needed to better understand the specific causes and their mechanisms [41]. In considering alternative cleaning products, the potential advantage of using "green" versus conventional products to minimize adverse respiratory outcomes has yet to be fully demonstrated [42, 43]. Results from a focus group study in six healthcare facilities in Texas suggested that healthcare workers typically had been trained in using exposure controls, including personal protective equipment (PPE) like respiratory protection and gloves, when performing cleaning tasks or administrating aerosolized medications [44]. Sometimes, workers not directly involved in these activities experience "bystander" exposures despite attempts to minimize such events. The investigators emphasized the need for better communication of work-related health risks and more consistent implementation of PPE protocols [44].

5 | Conclusions

The current study identified that at least one of two asthma outcomes (i.e., current asthma without and with exacerbation) was associated with 10 of 28 variables for cleaning fixed surfaces and three of four variables for administering aerosolized medicines. These results provide more details about earlier findings that the same adverse outcomes were associated with more general variables for the two types of activities. Additional work is needed to develop more effective strategies to prevent adverse health effects associated with cleaning and administering aerosolized medications. With this in mind, the current research team plans to investigate strategies for characterizing quantitative occupational exposures for specific chemicals and mixtures of chemicals in healthcare with the goal of providing additional guidance for the prevention of work-related respiratory symptoms and diseases.

Author Contributions

P.K.H. and M.A.V. conceptualized and designed the study with input from X.L., M.J.H., P.K.H., and M.A.V. planned and managed the data collection. P.K.H., M.A.V., X.L., and C.P.G. planned the data analysis, and S.M.R. and X.L. implemented the analysis. P.K.H. and M.A.V. interpreted the results. P.K.H. drafted the original manuscript, and all authors contributed to multiple revisions to yield the final manuscript.

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Disclosure

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Ethics Statement

This study was reviewed and approved by the NIOSH IRB under 45 C.F.R. part 46.110; 45 C.F.R. part 46.117(c)(2). All participants provided oral consent.

Conflicts of Interest

The authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.
Table S1: Phi statistics for general cleaning tasks. **Table S2:** Phi statistics for selected aerosolized medication tasks. **Table S3:** Adjusted odds ratios (95% CI) for association of asthma outcomes with tasks related to activities in clinical or medical laboratories and dental laboratories.

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