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Occupational Exposure Patterns to Disinfectants and Cleaning Products and Its Association With Asthma Among French Healthcare Workers

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ABSTRACT

Background: Disinfectants and cleaning products (DCPs) are important asthma risk factors among healthcare workers. However, healthcare work involves heterogenous cleaning tasks and co-exposure to many chemicals. These multidimensional aspects have rarely been considered. We aimed to identify patterns of occupational exposure to DCPs and study their associations with asthma.

Methods: CONSTANCES is a French population-based cohort of ≈220,000 adults. Current asthma and asthma symptom score were defined by questionnaire at inclusion (2012–2021). Healthcare workers completed a supplementary questionnaire on their current/last held occupation, workplace, and cleaning activities that were used in unsupervised learning algorithms to identify occupational exposure patterns. Logistic and negative binomial regression models, adjusted for potential confounders, were used to assess associations with asthma outcomes.

Results: In 5512 healthcare workers, four occupational exposure clusters were identified: Cluster1 (C1, 42%, reference), mainly characterized by low exposed nurses and physicians; C2 (7%), medical laboratory staff moderately exposed to common DCPs (chlorine/bleach, alcohol); C3 (41%), nursing assistants and nurses highly exposed to a few DCPs (mainly quaternary ammonium compounds); and C4 (10%), nurses and nursing assistants highly exposed to multiple DCPs (e.g., glutaraldehyde, hydrogen peroxide, and acids). Among women ($n = 3734$), C2 (mean score ratio [95% CI]: 1.31 [1.02; 1.68]) and C3 (1.18 [1.03; 1.36]) were associated with higher asthma symptom score, and an association was suggested between C3 and current asthma (odds ratio 1.22 [0.99; 1.51]).

Conclusion: In a large population of healthcare workers, four DCP exposure patterns were identified, reflecting the heterogeneity of healthcare jobs. Two patterns, including one characterized by laboratory workers, were associated with greater asthma symptoms in women.

Laurent Orsi and Orianne Dumas Contributed equally to this study.

1 | Introduction

Asthma is a common chronic non-communicable disease, with around 300 million individuals affected globally [1]. In France, the prevalence of current asthma varies from 6% to 9.5% in adults depending on the definition used [2, 3]. Clinically, asthma is characterized by variable symptoms of bronchospasm and airway inflammation including dyspnea, chest tightness, wheezing, cough, and phlegm, which can occur spontaneously or in response to external triggers (i.e., smoke, viruses, air pollution, allergens, and microbes) [4].

Workplace environments notably contribute to the prevalence of adult asthma [5, 6]. Occupational exposures can cause or exacerbate asthma [5, 7]. Approximately 15% of adult asthma cases are linked to occupational exposures, and 20% of adults with asthma experience exacerbations at the workplace [8, 9]. Occupational asthma can be attributed to exposure to sensitizers such as flours, latex or diisocyanates [10], and to irritants [5]. In contrast with work-related asthma due to other agents, incidence of work-related asthma attributed to disinfectants and cleaning products (DCPs) has increased in the past decades, particularly among women [11]. The use of DCPs involves exposures to various chemicals which may have important adverse respiratory effects.

Although studies report associations between workplace use of DCPs and asthma [7, 12–14], limited data are available on specific products/compounds [15, 16] or specific tasks [17]. In a few cross-sectional studies, exposure to DCPs, in particular glutaraldehyde, bleach, alcohol, ammonia, or quaternary ammonium compounds (QACs), were associated with asthma outcomes [17–21]. The literature is nonetheless heterogeneous about products in general, as results for products/compounds are not systematically replicated across studies [12, 19, 20, 22–25].

Healthcare workers, frequently exposed to DCPs, are known to present an increased risk of developing asthma [25, 26]. In France, there were around 1.2 million healthcare workers in 2022, a group composed of 53% nurses, 19% physicians, and 4% laboratory staff [27]. Cleaning habits involve the use of various substances and performing various tasks. Previous studies mainly focused on a few substances, not necessarily reflecting the reality of multiple exposures in the working environment. Clustering methods appear to be useful to better characterize the multidimensional aspect of exposure [17, 28] by identifying groups of participants sharing common characteristics, and using a large amount of data with multiple co-occurring exposures. To the best of our knowledge, only one study [17] used clustering methods to investigate cleaning and disinfecting activities and assessed their associations with asthma outcomes in a population of 2030 New York healthcare workers.

In the present study, we aimed to identify occupational exposure patterns to DCPs among a large population of French healthcare workers with unsupervised clustering methods and to investigate the associations between those patterns with current asthma and asthma symptom score.

2 | Materials and Methods

2.1 | Study Population

CONSTANCES (https://www.constances.fr/en/home/) is a French general population-based cohort [29] that includes around 220,000 participants aged 18–69 years from 24 Health Prevention Centres ("Centres d'examens de santé") located in 21 cities across France between 2012 and 2021. CONSTANCES included people affiliated with the main national health insurance (about 85% of the French population) [29]. At inclusion, participants had a complete health examination and completed a self-administrated questionnaire to collect data on lifestyle and respiratory health, as well as full job history. Occupations were coded according to French classifications of occupations ("Profession et Catégories Socio-professionnelles," PCS 2003, https://www.insee.fr/fr/information/2400059) and of activities ("Nomenclature d'Activités Française," NAF, https://www.insee.fr/fr/information/2406147), and subsequently transcoded into International Standard Classification of Occupation (ISCO)-88 codes [30].

In 2022, participants potentially exposed to DCPs either in their last or longest-held job were identified based on a list of jobs classified as exposed (either "medium" or "high" exposure) to DCPs according to the occupational asthma-specific job-exposure matrix (OAsJEM) [7, 31]. All identified participants were invited to self-complete a specific additional questionnaire on occupational exposure to DCPs. Three versions of the questionnaire were used according to job category: healthcare or medical laboratory workers, cleaning workers, and food industry workers. Participants received either paper questionnaires or web questionnaires based on their preference. Paper questionnaires were sent in January 2022 with a reminder in March 2022, and returned up to end of 2023, at the latest. Web questionnaires were sent in January 2022, with recalls in February and April 2022, then closed at the end of April 2022. The present study focuses on healthcare workers ($n = 11{,}050$ invited).

2.2 | Asthma

Asthma was defined based on questionnaires at inclusion in the CONSTANCES cohort (2012–2021), using standardized definitions (dichotomous and semi-quantitative) similar to those previously used in the European Community Respiratory Health Survey (ECHRS) and Epidemiological Study on the Genetics and Environments of Asthma (EGEA) [32, 33].

2.2.1 | Current Asthma

Ever asthma was defined by a positive answer to the question "*have you ever had asthma?*". Current asthma was defined among participants with ever asthma by the report in the last 12 months of asthma attacks or symptoms (wheezing, awakening with chest tightness, attack of shortness of breath at rest, attack of shortness of breath after exercise, and awakening by an attack of shortness of breath), or use of an asthma treatment. Age at asthma onset was used to distinguish adult-onset asthma (> 16 years) from childhood-onset asthma (≤ 16 years).

2.2.2 | Asthma Symptom Score

The asthma symptom score, a semi-quantitative score ranging from 0 to 5 previously described and validated [34, 35], was defined as the sum of five asthma symptoms reported in the past 12 months: breathlessness while wheezing, awakening with chest tightness, attack of shortness of breath at rest, attack of shortness of breath after exercise, and awakening by attack of shortness of breath.

2.3 | Occupational Exposure

The DCP-specific questionnaire for healthcare workers was adapted from similar questionnaires used in ECRHS [23], EGEA [19, 36], and the Nurses' Health Study II [37]. Questions were asked for the current or last held job and for the longest held job, if different from the current or last held job. It included questions on occupations (12 items including physicians, nurses, midwives, and laboratory workers), workplaces (15 items including liberal (private or office) practice, hospitals, retirement homes, medical analysis laboratories), the frequency of seven cleaning tasks for different surfaces or material, the frequency of use of 14 specific DCPs (formaldehyde, glutaraldehyde, ortho-phthalaldehyde, bleach/chlorine, hydrogen peroxide, peracetic acid, acetic acid, alcohol, ammonia, QACs, ethylene oxide, phenolic disinfectant, enzymatic cleaner, and organic/green products), the daily duration and the type (sprays, wipes) of DCPs use, and the frequency (daily or weekly) of 11 various tasks (e.g., hand washing with disinfectants), habits (e.g., use of respiratory protection), or other inhalation exposure (e.g., chemical spill cleaning, and exposure to surgical fumes). These DCPs were selected either because of their frequency of use in the healthcare environment, their known respiratory risk, or their irritant or sensitizing potential [11]. Sprays and wipes were selected because of their variable inhalation risks (via projection or evaporation) and organic or green products because their use is increasing and their respiratory health impact remains poorly documented [38, 39]. All these questionnaire items are listed in Tables 2, 3 and 4.

For specific DCPs, the examples of main brand names used in French healthcare settings were provided for each agent. In addition, participants could fill in the brand name of the products they used if they did not know the active compound. The safety data sheets of provided brand names was searched to determine the products' main active compounds.

2.4 | Statistical Analysis

The main analysis concerned exposure patterns based on current or last held job and a supplementary analysis concerned those based on longest held job (see Section 3.3.1).

2.4.1 | Cluster Identification

A total of 52 variables and 134 characteristics were collected for both the current and last held job. Variables were mainly dichotomous variables ("no" vs. "yes") and ordinal frequency (< 1 day/week, 1–3 days/week, 4–7 days/week; or < 1 time/day, 1–3 times/day, 4–10 times/day, > 10 times/day) of tasks and products used, or daily duration (1 h/day, 1-4 h/day, > 4 h/day) of use of DCPs. All these categories of variables were used in unsupervised learning algorithms to identify clusters.

Missing data were handled with two steps of imputations, simple imputations followed by multiple imputations. First, for questions relating to occupation, workplace, cleaning tasks, and products used (which each included 7–14 items), when participants had answered at least one item of the specific question, missing data for items of the same question were considered as "no" (occupation/workplace) or "never" (tasks, product), in accordance with methods used to deal with missing data in food frequency questionnaires [40], which have similar structures. For other questions, any missing data were then handled by multiple imputations during the multiple correspondence analysis steps.

Clusters were identified based on current or most recent work, using multiple correspondence analysis in hierarchical agglomerative clustering (HAC) [41] followed by k-means algorithms. As HAC method is a classification method initially designed for quantitative variables, we used multiple correspondence analysis to transform qualitative variables to quantitative ones. We followed the majority rules to determine the optimal number of clusters. We used 30 validation indices (see details in Table S1) by combining the number of classes, Euclidian distances, and the complete agglomerative method implemented in the NbClust R package [42].

Unsupervised learning algorithms were conducted using R version 4.3.2 (Copyright 2023, The R Foundation) for statistical computing with "FactoMineR" [43] and "NbClust" [42] packages.

2.4.2 | Associations Between Clusters and Asthma Outcomes

Cross-sectional analysis of the associations between occupational exposure patterns and current asthma and the asthma symptom score were evaluated by logistic regression and negative binomial regression, respectively, adjusted for age, sex, body mass index (BMI), and smoking status. Associations were also assessed separately in women and men, as job tasks and asthma phenotypes may vary according to sex, and interaction with sex was tested by including the interaction term in the models.

Sensitivity analyses were performed: (1) by excluding participants with childhood onset asthma to focus on adult asthma, which may have been triggered by occupational exposures; (2) using occupational exposure clusters identified using the longest held job to take into account long-term exposure; (3) when using occupational exposure clusters identified based on the current or most recent held job, by excluding participants who were included more than 5 years before 2022, the year in which the questionnaire on occupational exposure to DCPs was completed, as these participants are more likely to have a potential change in exposure since inclusion, or (4) using clusters identified on the basis of complete population data without any missing data handling to assess potential bias due to missing data in the results.

Statistical analyses were conducted using SAS version 9.4 software (SAS Institute Inc., Cary, NC). All p values were two-sided and considered significant at the 0.05 level.

3 | Results

3.1 | Population Characteristics

Among 11,050 healthcare workers who received the specific additional questionnaire on their occupational exposure, 5833 returned the questionnaire (response rate 52.8%; Figure 1). Compared to non-respondents ($n = 5176$), participants who did return this questionnaire were older (47.6 vs. 45.1 years; Table S2), less often have current asthma (8.86% vs. 10.33%), with a lower asthma symptom score (27.74% vs. 31.33% with at least one symptom), and less often non-smokers (54.30% vs. 50.59%).

Cluster-analysis based on current or most recent job concerned 5512 healthcare workers (Figure 1) whose answers confirmed that their current or most recent job corresponded to the selection criteria. Among these, 44.6% were nurses, 54.6% were working in a hospital, and 84% used at least one DCP per week. Some were excluded from the analyses of associations between exposure patterns and asthma outcomes because they started the job after the inclusion ($n = 583$) or had missing data on their asthma status ($n = 138$) (Figure 1). Therefore, we included in the association study 4791 participants with a mean age of 48.85 ± 12.46 years. Among them, 83.39% were women, 26.75% had 4 years postsecondary education, and 7.99% had current asthma (Table 1). Excluded participants mainly differed from included participants in age, smoking, and respiratory outcomes (Table S3). For current asthma analysis, we included 4382 participants, excluding those with noncurrent asthma ($n = 230$) and missing data for BMI or smoking status, and for asthma symptom score, 4478 participants excluding only those with missing data for covariates (Table S3).

3.2 | Occupational Exposures Clusters

Four clusters of occupational exposure patterns to DCPs based on current or most recent held healthcare job were identified according to the majority rules (proposed by six indices).

The first cluster, C1 ($n = 2337$), represented 42.4% of participants and was mainly characterized by nurses (44.6%) and physicians (27.6%) working in a hospital (52.9%) or in private practice (24.6%) (Table 2). Most of them used DCPs less than 1 h a day (85.5%). About a third of them performed cleaning tasks on medical instruments (32.6%) or surfaces (35.6%) and other medical devices (33.0%) 1–3 days per week, and few (10%–12%) of them performed these tasks more frequently (4–7 days per week) (Table 3). Most of them used specific DCPs less than 1 day per week except for alcohol (17.8%) and QACs (33.5%), used between 1 and 3 days per week. They moderately used both sprays (28.4%) and wipes (29.4%). More than half disinfected their hands at work (56.5%) more than 10 times a day (Table 4).

C2 ($n = 393$, 7.13%) was mainly characterized by work as laboratory staff (74.8%). Their workplace was medical analysis laboratories (65.4%). Almost all laboratory staff were present in this cluster (together, the other clusters accumulated less than 1% of laboratory staff). C2 was also characterized by medical technicians (27.5%) and work in hospital (46.1%) (Table 2). Their cleaning tasks were performed on laboratory tools (62.1%), surfaces (43.8%), and medical instruments (21.9%) between 4 and 7 days per week. Most of them used DCPs less than 1 h a day (82.7%). They had the highest frequency of use of alcohol (47.6%) 4–7 days per week, and the second-highest frequency of the use of chlorine or bleach 4–7 days per week (20.9%), after C4 (Table 3). They used QACs (44.8%) 4–7 days per week. They also used sprays (30.5%) and wipes (13.2%) 4–7 days per week. They also used respiratory protections (23.6%) 4–7 days per week. They washed their hands at work with disinfectants between 4 and 10 times a day (32.8%). Notably, 30.0% had ever cleaned a chemical spill (Table 4).

C3 ($n = 2237$, 40.5%) was mainly characterized by nurses (47.7%) and nursing assistants (29.7%) who worked in a hospital (54.8%) and in retirement homes (18.6%). They performed cleaning tasks on medical instruments (56.6%), surfaces (75.2%), toilets (31.0%), other medical instruments (54.98%), and other locations and equipment (17.1%) 4–7 days per week. More than half used DCPs in the workplace less than 1 h per day (57.8%). Between 4 and 7 days per week, they used QACs (63.2%), alcohol (28.3%), glutaraldehyde (13.4%), and enzymatic cleaners (8.90%). They had the highest frequency of use of sprays 4–7 days per week (58.9%). They also used wipes 4–7 days per week (43.3%). They used respiratory protections (44.1%) 4–7 days per week.

C4 ($n = 545$, 9.88%) was mainly characterized by nurses (58.7%), nursing assistants (14.7%), and dentists (10.1%) who worked in a hospital (67.3%), followed by private practice (23.9%), clinic (23.5%), and maternity clinic (10.1%). They had the highest frequency of cleaning medical instruments (86.8%), operating rooms (49.9%), and endoscopes (20.7%) between 4 and 7 days per week. Compared to other clusters, they had the highest duration per day of use of DCPs, as 40.6% used DCPs 1–4 h a day (40.6%) and 25.7% for more than 4 h a day. They also had the most frequent use (4–7 days a week) of many DCPs: QACs (73.4%), glutaraldehyde (43.9%), alcohol (40.4%), hydrogen peroxide (29.7%), enzymatic cleaner (26.4%), formaldehyde (21.8%), bleach or chlorine (21.1%) (comparable to C2 [20.9%]), peracetic acid (14.3%), and ortho-phthalaldehyde (8.81%). They also used both sprays (52.3%) and wipes (47.3%), respiratory protections (60.2%), and were exposed to surgical fumes (28.3%) and administrated anesthetic (59.1%) 4–7 days per week. They washed hands with disinfectants at work (77.3%) and during surgical disinfection more than 10 times a day more frequently than other clusters. They had the highest frequency of cleaning chemicals spill (34.3%) close to those in C2 (30.0%).

3.3 | Associations Between Occupational Exposure Patterns and Asthma

C1 was used as the reference, as it was the least-exposed cluster in frequency and quantity of products. It was also the cluster with the highest number of participants. Results of the

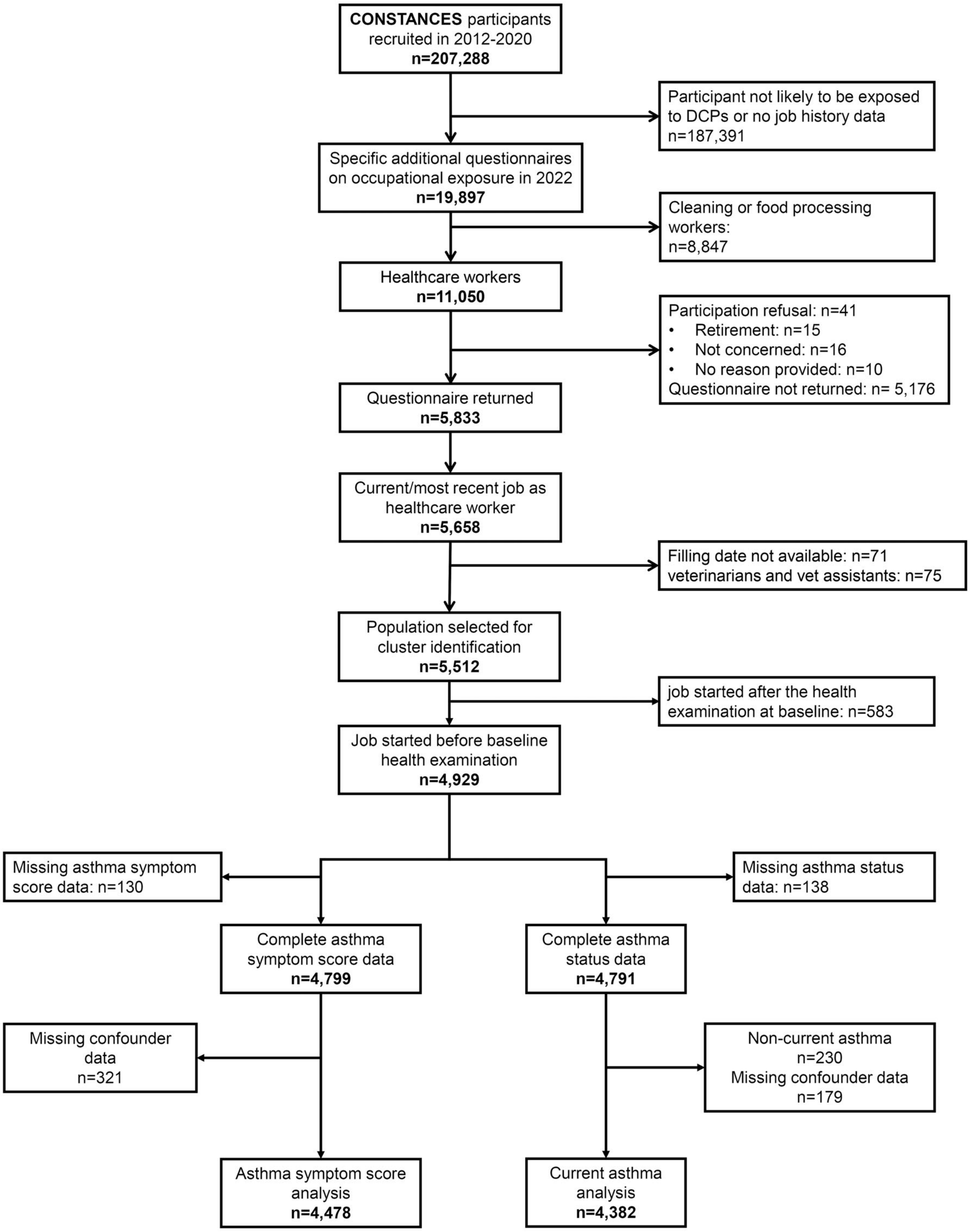

FIGURE 1 | Selection of the study population.

associations of clusters, with current asthma and asthma symptom score are presented in Table 5.

No significant association was found between any cluster and current asthma, neither in all participants nor after stratification by sex (Table 5). However, an association was suggested between C3 and current asthma (adjusted odds ratio (OR) [95% confidence interval] = 1.22 [0.99; 1.51]) among women).

C2 was associated with a higher asthma symptom score (adjusted mean score ratio (aMSR) [95% confidence interval] = 1.22 [0.98; 1.53]) at borderline significance. Among women, C2 and C3 were associated with higher asthma symptom score (MSR = 1.31 [1.02; 1.68] and MSR = 1.18 [1.03; 1.36], respectively). Among men, C3 was associated with a lower asthma symptom score (MSR = 0.61 [0.40; 0.92]) than C1. The interaction with sex was significant ($p = < 0.0001$).

TABLE 1 | Characteristics of occupational exposure patterns to disinfectants and cleaning products among healthcare workers.

Characteristics of participants	Included participants	C1	C2	C3	C4	*p* value
Participants, *n*	4791	1970	366	1953	502	
Age (years), mean ± SD	48.85 ± 12.46	48.99 ± 12.73	50.02 ± 13.11	47.98 ± 11.99	50.77 ± 12.42	**< 0.0001**
Sex, women, %	83.39	78.93	78.69	89.30	81.27	**< 0.0001**
Smoking status, %						**0.01**
Non-smokers	54.10	53.15	57.78	55.92	47.90	
Smokers	12.35	12.23	10.28	12.80	12.61	
Ex-smokers	33.55	34.62	31.94	31.28	39.50	
Body mass index, kg/m^2, %						**0.0047**
≤ 25	63.29	65.69	65.93	60.62	62.27	
[25–30]	25.97	25.44	22.25	27.32	25.56	
≥ 30	10.74	8.87	11.81	12.05	12.17	
Education level, %						**< 0.0001**
< High school	9.75	3.59	24.09	10.83	15.23	
High school	10.66	7.45	11.60	13.36	12.02	
2-3 years postsecondary	46.93	43.44	62.71	47.01	48.90	
≥ 4 years postsecondary	26.75	39.05	22.1	14.91	27.85	
Other	0.42	0.31	0.0	0.62	0.40	
Asthma symptom score, %						0.19
0	73.50	75.01	70.03	72.46	74.18	
1	17.57	16.95	19.89	18.22	15.78	
2	5.62	5.32	7.00	5.58	5.94	
3	1.85	1.67	1.40	1.84	2.87	
4	0.92	0.57	1.40	1.11	1.23	
5	0.54	0.47	0.28	0.79	0.0	
Current asthma	7.99	7.36	9.02	8.55	7.57	0.56

p values were calculated using Chi-2 test for categorical variables and the student's t-test for quantitative variables. Bold values indicate statistical significance.

3.3.1 | Sensitivity Analyses

After excluding participants with childhood onset asthma, among women, membership in cluster C3 was associated with current asthma (OR = 1.38 [1.04; 1.83]) (Table S4). In addition, C3 was still associated with a higher asthma symptom score (MSR = 1.18 [1.02; 1.37]), and C2 was of borderline significance with slightly lower MSR. No association was found among men. The interaction with sex was significant.

After identifying occupational exposure clusters to DCPs based on participants' longest held job, in all participants, C2 was associated with a higher asthma symptom score score (MSR = 1.20 [0.96; 1.53]) with borderline significance. Among women, both C2 and C3 were associated with a higher asthma symptom score (aMSR= 1.30 [1.02; 1.65] and 1.11[0.98; 1.26], respectively), the latest being at borderline significance. Among men, C3 was significantly associated with a lower symptom score (0.67 [0.46; 0.96]). The interaction with sex was significant (Table S5).

After excluding participants who were included more than 5 years before 2022, C3 was associated with current asthma among women (OR = 1.48 [1.10; 2.00]). For asthma symptom score, results were similar to those in the main analysis. Among women, C3 was associated with higher score (MSR = 1.28 [1.05; 1.56]). Among men, C3 was associated with a lower score (MSR = 0.52 [0.30; 0.91]) than C1. The interaction with sex was significant (Table S 6).

Using clusters based on complete current or most recent job data (without missing data imputation), similar results to these main results were found (data not shown).

4 | Discussion

In a large population of more than 5000 French healthcare workers, we identified four clusters of occupational exposures to DCPs: C1 mainly characterized by physicians and nurses, with the lowest exposure in terms of frequency and quantity of

TABLE 2 | Participant's occupations, workplaces, surfaces, and material cleaned according to clusters.

Characteristics of participants	Participants	C1	C2	C3	C4
Participants, *n*	5512	2337	393	2237	545
Nurse	44.6	44.6	7.38	47.7	58.7
Nursing assistant	17.7	9.58	1.53	29.7	14.9
Physicians	15.6	27.6	8.14	7.24	3.85
Medical technician	3.52	1.50	27.5	1.70	2.39
Midwife	3.36	5.91	0.76	1.70	1.10
Anesthetic assistant	1.31	1.03	0.00	0.09	8.44
Dentist	2.21	1.07	0.00	1.88	10.1
Dental assistant	1.49	0.21	0.51	1.34	8.26
Pediatric nurse	3.14	3.68	0.25	3.40	1.83
Assistant pediatric nurse	2.92	1.93	0.00	4.96	0.92
Laboratory staff	5.53	0.34	74.8	0.09	0.18
Other medical or healthcare staff	6.91	8.39	3.82	6.71	3.67
Workplaces					
Liberal practice	20.1	24.6	4.33	17.2	23.9
Hospital	54.6	52.9	46.1	54.8	67.3
Clinic	12.5	13.1	7.63	10.2	23.5
Maternity clinic	5.77	8.64	1.02	2.55	10.1
Patient's homes	12.4	14.0	3.05	14.2	4.77
Retirement homes	13.2	11.6	1.78	18.6	6.61
Daycare Centers	2.99	1.84	0.00	5.14	1.28
Medical analysis laboratory	5.32	0.77	65.4	0.45	1.47
Surfaces and material cleaned					
Medical instruments					
< 1 day/week	44.0	55.4	74.6	35.9	5.87
1–3 days/week	17.8	32.6	3.56	7.47	7.34
4–7 days/week	38.2	12.1	21.9	56.6	86.8
Surfaces					
< 1 day/week	35.2	53.7	47.8	18.3	16.2
1–3 days/week	19.2	35.6	8.40	6.48	8.99
4–7 days/week	45.6	10.7	43.8	75.2	74.9
Toilets					
< 1 day/week	74.1	87.1	94.2	59.3	68.0
1–3 days/week	10.1	11.4	0.76	9.70	12.7
4–7 days/week	15.8	1.45	5.09	31.0	22.4
Laboratory tools					
< 1 day/week	89.1	96.9	22.9	95.4	77.8
1–3 days/week	3.01	2.65	15.1	0.94	4.40
4–7 days/week	7.87	0.43	62.1	3.71	17.8
Operating rooms					
< 1 day/week	92.3	97.4	99.2	98.2	41.1
1–3 days/week	1.85	1.93	0.25	0.31	8.99
4–7 days/week	5.86	0.68	0.51	1.48	49.9

(Continues)

TABLE 2 | (Continued)

Characteristics of participants	Participants	C1	C2	C3	C4
Endoscopes					
< 1 day/week	95.7	98.6	99.2	99.0	66.8
1–3 days/week	1.98	1.33	0.51	0.36	12.5
4–7 days/week	2.38	0.13	0.25	0.63	20.7
Other medical devices					
< 1 day/week	48.7	57.3	96.2	35.9	30.3
1–3 days/week	18.7	33.0	1.02	9.12	9.54
4–7 days/week	32.6	9.80	2.80	55.0	60.2
Other locations or equipment					
< 1 day/week	85.3	90.3	91.4	80.8	78.2
1–3 days/week	4.35	7.45	1.78	2.06	2.39
4–7 days/week	10.3	2.23	6.87	17.1	19.5

Note: Results are presented as %, unless otherwise specified.

products used; C2 characterized by laboratory staff highly exposed to main DCPs such as alcohol, chlorine, bleach, or QACs with a daily use of DCPs of less than 1 h; C3 mainly characterized by nurses and nursing assistants highly exposed to few DCPs and mainly QACs, also with less than 1 h of daily use; and C4 characterized by nurses and nursing assistants highly exposed to multiple DCPs, some with over 4 h of daily use. Using C1 as reference, we found associations between clusters C2 and C3 and higher asthma symptoms score among women, and between C3 and lower symptom scores in men. Although overall we found no significant association with current asthma, an association was suggested between C3 and current asthma in women.

To our knowledge, this study is one of the two large studies to identify exposures clusters to DCPs among healthcare workers. The previous one [17] used similar methods, namely hierarchical agglomerative classifications (HAC) using scree plots and dendrograms to determine a number of clusters of cleaning and disinfecting activities. HAC methods have proved robust for assessing occupational exposure by grouping jobs with similar responses to questionnaires increasing the homogeneity of exposure estimates within clusters [44]. In the present study, we used, in addition to examining scree plots and dendrograms, 30 indices [42] to determine the optimal number of clusters in a partitioning of data set during the clustering process and to select the number proposed by the majority of them to be more robust. HAC was followed by k-means algorithm steps to consolidate the classification. Finally, our study covered a wider spectrum of products used including glutaraldehyde, hydrogen peroxide, peracetic acid, acetic acid, or ammonia and cleaning/disinfection tasks.

We acknowledge that using self-reported exposure data potentially leads to information and misclassification bias. Researchers have noted a discrepancy between self-reported exposure levels and expert exposure assessments for DCPs [19, 36]. Exposure to specific DCPs is frequently underestimated by healthcare workers, potentially due to a lack of awareness regarding the composition [37]. In addition, two studies [36, 45] reported differences in self-reported occupational exposure estimates according to asthma status, suggesting a differential bias. In our study, exposures patterns were estimated using unsupervised clustering methods based on various characteristics. This could attenuate the influence of subjective perceptions and differences in awareness between participants related to asthma status on estimates for specific exposures but would not completely eliminate them as the data were collected by self-administered questionnaire. In addition, exposure was assessed retrospectively in 2022 after the respiratory health assessment performed at inclusion. As a result, we excluded participants who started their jobs after inclusion, and in a sensitivity analysis, we also excluded participants included more than 5 years before 2022, thereby strengthening our results.

Missing data were between 1% and 30% depending on the variables. We first performed simple imputations as commonly done with comparable questionnaires with numerous items [40], assuming that the reason why participants did not answer a question is because they did not perform this task or used this product. Then, we performed multiple imputations on the missing data remaining in the data set. We also performed occupational exposures cluster identification using only participants with complete data and found similar clusters with similar characteristics. The response rate to the questionnaire was 53%, which is relatively low and could induce systematic bias. There were differences in participation rate according to asthma status, and few differences in the professions represented, and therefore probably few in exposures, which probably had no major influence on the results. The response rate may have been impacted by the COVID-19 pandemic, which was still ongoing in 2022 when the questionnaire was sent, a period during which healthcare workers were highly consulted. Nonetheless it was consistent with that previously reported [46]: investigating response rate of 350 studies in healthcare workers including physicians and nurses, the authors reported average response rate of 57% with 50% among nurses. In specific studies on occupational respiratory health among healthcare workers, reported response rates ranged between 22% and 66% [17, 25, 47, 48]. In addition, as differences between included and excluded

TABLE 3 | Product used according to occupational exposure patterns to DCPs.

Characteristics of participants	Participants	C1	C2	C3	C4
Participants	5512	2337	393	2237	545
Formaldehyde					
< 1 day/week	92.8	97.2	89.3	96.2	62.2
1–3 days/week	3.27	2.31	4.58	0.94	16.0
4–7 days/week	3.96	0.47	6.11	2.86	21.8
Glutaraldehyde					
< 1 day/week	82.3	89.0	90.1	83.4	43.5
1–3 days/week	6.91	9.88	2.29	3.22	12.6
4–7 days/week	10.8	1.11	7.63	13.4	43.8
Ortho-phthalaldehyde					
< 1 day/week	97.7	99.2	99.2	99.2	84.0
1–3 days/week	1.18	0.77	0.25	0.31	7.16
4–7 days/week	1.14	0.04	0.51	0.54	8.81
Bleach, chlorine					
< 1 day/week	80.7	90.5	61.1	78.1	64.2
1–3 days/week	10.9	8.90	18.1	10.9	14.7
4–7 days/week	8.33	0.64	20.9	11.0	21.1
Hydrogen peroxide					
< 1 day/week	88.4	94.4	90.3	90.2	54.1
1–3 days/week	4.90	5.31	4.58	1.79	16.2
4–7 days/week	6.71	0.34	5.09	8.05	29.7
Peracetic acid					
< 1 day/week	96.2	98.9	98.2	98.4	74.1
1–3 days/week	1.94	1.07	1.02	0.67	11.6
4–7 days/week	1.83	0.00	0.76	0.89	14.3
Acetic acid					
< 1 day/week	97.3	99.1	92.4	99.2	85.0
1–3 days/week	1.63	0.73	4.83	0.49	7.89
4–7 days/week	1.09	0.13	2.80	0.31	7.16
Alcohol					
< 1 day/week	64.6	72.7	31.6	66.2	47.3
1–3 days/week	12.5	17.8	20.9	5.45	12.3
4–7 days/week	22.9	9.50	47.6	28.3	40.4
Ammonia					
< 1 day/week	98.3	99.3	96.4	98.8	93.4
1–3 days/week	0.96	0.64	3.05	0.40	3.12
4–7 days/week	0.73	0.04	0.51	0.80	3.49
Quaternary ammonium compounds (QACs)					
< 1 day/week	41.4	54.1	44.0	33.4	17.4
1–3 days/week	17.3	33.5	11.2	3.35	9.17
4–7 days/week	41.4	12.4	44.8	63.2	73.4
Ethylene oxide					
< 1 day/week	99.1	99.7	99.8	99.7	93.8

(Continues)

TABLE 3 | (Continued)

Characteristics of participants	Participants	C1	C2	C3	C4
1-3 days/week	0.51	0.30	0.00	0.18	3.12
4-7 days/week	0.36	0.00	0.25	0.09	3.12
Phenolic disinfectant					
< 1 day/week	98.8	99.6	99.0	99.5	92.1
1–3 days/week	0.67	0.39	0.51	0.04	4.59
4–7 days/week	0.56	0.04	0.51	0.45	3.30
Enzymatic cleaner					
< 1 day/week	88.3	93.7	86.8	88.9	64.2
1–3 days/week	4.68	5.95	4.83	2.19	9.36
4–7 days/week	6.98	0.39	8.40	8.90	26.4
sprays					
< 1 day/week	50.4	65.2	63.4	36.0	37.1
1–3 days/week	15.6	28.4	6.11	5.14	10.6
4–7 days/week	34.0	6.42	30.5	58.9	52.3
wipes					
< 1 day/week	55.4	61.5	78.6	48.2	42.2
1–3 days/week	17.5	29.4	8.14	8.49	10.5
4–7 days/week	27.1	9.16	13.2	43.3	47.3
Organic or green products					
< 1 day/week	91.7	93.6	98.0	89.5	88.8
1–3 days/week	4.08	5.43	1.27	3.26	3.67
4–7 days/week	4.15	0.94	0.76	7.29	7.52

Note: Results are presented as %, unless otherwise specified.

participants were observed in the present study, a potential selection bias cannot be dismissed.

We identified four clusters consistent with the literature in occupations and main products used. Even if the previous study [17] identified five clusters, four of them were similar across both studies: a cluster with the lowest exposure in terms of frequency and quantity of products that is like C1; a cluster characterized by laboratory staff exposed to alcohol, chlorine or bleach that is like C2; and two clusters, both characterized by nurses and nurses' assistants. The latter differ in tasks and products used. As in our study, one of them was characterized by moderate use of cleaning alcohols; the other, by the highest and most diversified exposures (alcohols, high-level disinfectants, bleach, enzymes, etc.). These clusters are similar to C3 and C4. However, in our work, the use of QACs was higher in each of the clusters identified than in the previous study, consistent with a higher rate of QACs use overall in our population (41%, 4–7 days/week). In our questionnaire, we included brand names of major products containing each type of substance, which likely led to a more accurate assessment of QACs exposure. Furthermore, since the COVID-19 pandemic, the use of QACs containing disinfectants increased in homes, workplaces, and industries [49–51].

Various studies in the literature have found associations of exposure to DCPs in general, and of specific DCPs, with asthma characteristics including current asthma [18–20, 22, 23, 25, 47, 52–54]. The literature is more heterogeneous regarding specific tasks and products/compounds associated with asthma. Clustering methods provide the benefit of considering the multidimensional aspect of exposure [17, 28] compared to studies focused on one or few substances. We found associations with higher asthma symptom score, but fewer associations with current asthma. A previous analysis in the same CONSTANCES cohort [7] found associations between occupational exposures to irritants (including DCPs) and higher asthma symptom score but no associations with current asthma. Similarly, a previous study, with comparable methodology, reported mild symptoms and undiagnosed or untreated asthma associated with DCPs exposure clusters [17]. Overall, these results suggest that DCPs, which often involve irritant exposures, may be associated with a specific asthma phenotype less documented and possibly underdiagnosed. Furthermore, using symptom score makes analysis more powerful than the dichotomous analysis of asthma. A lower power to detect modest associations is therefore a possible explanation for the nonsignificant associations with current asthma.

We observed an association between C2 characterized by medical laboratory staff and higher asthma symptom score. This was consistent with the literature on laboratory staff and asthma characteristics, even if it is limited. Using unsupervised methods to assess occupational exposures among healthcare

TABLE 4 | Cleaning habits according to occupational exposure patterns to DCPs.

Characteristics of participants	Participants	C1	C2	C3	C4
Participants	5512	2337	393	2237	545
Diluting products before use	51.9	31.1	55.2	63.0	75.2
Duration of use of cleaning/disinfecting products in the workplace					
< 1 h/day	68.9	85.5	82.7	57.8	33.8
1–4 h/day	22.2	11.1	12.5	31.0	40.6
> 4 h/day	8.87	3.38	4.83	11.2	25.7
Use of respiratory protection					
< 1 day/week	56.2	63.6	71.8	52.5	28.4
1–3 days/week	10.4	17.8	4.58	3.40	11.4
4–7 days/week	33.4	18.6	23.7	44.1	60.2
hand washing with disinfectants at work					
< 1 times/day	9.23	11.6	19.9	6.03	4.77
1–3 times/day	6.57	8.64	15.5	3.80	2.57
4–10 times/day	19.6	23.3	32.8	14.5	15.4
> 10 times/day	64.6	56.5	31.8	75.6	77.3
hand washing with disinfectants during surgical disinfection					
< 1 times/day	72.5	76.8	87.0	76.5	26.8
1–3 times/day	8.73	10.4	4.33	5.68	17.1
4–10 times/day	8.49	7.19	5.09	6.57	24.4
> 10 times/day	10.3	5.56	3.56	11.2	31.7
Exposure to surgical fumes					
< 1 day/week	93.4	95.3	99.2	99.2	57.4
1–3 days/week	3.07	3.34	0.00	0.58	14.3
4–7 days/week	3.50	1.37	0.76	0.18	28.3
Anesthetic administration					
< 1 day/week	83.4	85.5	97.2	91.9	28.8
1–3 days/week	7.26	10.1	1.78	4.07	12.1
4–7 days/week	9.40	4.36	1.02	4.02	59.1
Chemical spill clean-up	11.2	6.20	30.0	7.55	34.3

Note: Results are presented as %, unless otherwise specified.

workers, the US study [17] found associations between a cluster similar to our C2 with asthma attacks and exacerbations. This cluster was characterized by laboratory staff alongside nurses' assistants working in hospitals and laboratories. They frequently used alcohol and bleach linked to laboratory work or material preparation.

We observed frequent use of sprays and wipes, but daily use of sprays was slightly more common than use of wipes. This was the case for all participants, as well as for clusters C2, C3, and C4. Previous studies have reported associations between the use of both sprays and wipes and asthma [38, 39] This underlines the diversity of products and the importance of exposure routes. Sprays have long been studied and their respiratory health risks are well documented, with consistent associations with asthma in multiple reports [22, 23, 55]. They are notable for their ability to disperse airborne particles for inhalation. Interest in wipes is more recent [38, 39]. Ready-to-use wipes can lead to the use of large quantities of compounds on small surfaces. Even if less aerosols are emitted, there have been reports of relationships between wipe use and an increase in asthma symptoms [39]. Lastly, use of green/organic products was less common (< 10% of daily use in all clusters, with the highest use in C3 and C4). Although green products may seem less harmful, their frequent use has been reported to be associated with asthma symptoms, although the association may be weaker than with conventional products [39].

We also observed that 30% of participants in C2 had ever carried out chemical spill cleaning in line with the increased risk of asthma reported in cleaning chemical spills [56] and the acute irritant-induced asthma caused by accidental exposure to high chemical concentrations [57]. We also observed sex differences in associations with asthma symptoms score: C3 was associated with a higher score only in women, with a significant sex interaction. This may reflect previously reported gender

TABLE 5 | Associations of occupational exposure patterns to DCPs with current asthma and asthma symptoms score.

Current asthma		OR [95% CI]	
	***n* total/*n* with current asthma**		***p* value**
All	4382/383		
C1	1877/145	1 [Ref]	
C2	353/33	1.27 [0.85;1.90]	0.24
C3	1851/167	1.15 [0.91;1.47]	0.25
C4	480/38	1.03 [0.70;1.52]	0.88
Women	3835/312		
C1	1555/106	1 [Ref]	
C2	288/24	1.06 [0.71;1.58]	0.79
C3	1744/155	1.22 [0.99;1.51]	0.07
C4	408/27	0.93 [0.64;1.35]	0.71
Men	764/71		
C1	415/39	1 [Ref]	
C2	78/9	1.19 [0.63;2.25]	0.60
C3	209/12	0.85 [0.52;1.38]	0.51
C4	94/11	1.13 [0.61;2.08]	0.70
Interaction test			0.12
Asthma symptom score	***n***	**MSR [95% CI]**	
All	4478		
C1	1970	1 [Ref]	
C2	366	1.22 [0.98; 1.53]	0.08
C3	1953	1.10 [0.96; 1.25]	0.17
C4	502	1.05 [0.85; 1.30]	0.64
Women	3734		
C1	1555	1 [Ref]	
C2	288	**1.31 [1.02; 1.68]**	**0.03**
C3	1744	**1.18 [1.03; 1.36]**	**0.02**
C4	408	1.04 [0.82; 1.30]	0.77
Men	744		
C1	415	1 [Ref]	
C2	78	0.87 [0.50;1.52]	0.64
C3	209	**0.61 [0.40; 0.92]**	**0.02**
C4	94	1.13 [0.69; 1.83]	0.64
Interaction test			**< 0.0001**

Note: Odds ratios (OR) were estimated by logistic regression adjusted on age, sex, smoking habits, and body mass index, whereas mean score ratios (MSR) were estimated by negative binomial regressions adjusted on age, sex, smoking habits, and body mass index. Bold values indicate statistical significance.

differences [7] in terms of exposure and effect of using DCPs that could be partly explained by disparities in jobs and tasks between genders, even in the same job [58]. In addition, C3 was the cluster with the highest proportion of women. C3 was associated with a lower symptom score in men. This was not an expected result. However, excluding participants with childhood onset asthma, the inverse association between C3 and asthma symptom score in men was no longer observed, suggesting a potential healthy worker hire effect in men. In contrast, the association between C3 and asthma symptom score in women remained unchanged. A stronger healthy worker effect has been suggested in men as it can be easier to switch jobs following a deterioration in health status [59].

Moreover, we did not find any associations with C4, which was the most exposed cluster in terms of frequency, duration and quantity of products. The finding of no associations with the most exposed cluster also suggests a healthy worker bias, as already discussed in previous studies [59–62]. As these occupations are highly exposed to DCPs, it is possible that participants suffering from asthma or respiratory symptoms stopped working or did not choose this job. Our clusters were identified based on current jobs; considering exposure in a previous job could potentially limit the healthy worker effect bias by identifying people who have changed jobs following asthma onset. However, we identified similar clusters based on the longest occupied job and we found comparable associations between asthma outcomes. These results should be interpreted carefully, because 86% of current held job were also the longest held job. Both populations may not be dissimilar enough to observe different results.

Our results emphasize the need to prevent and limit exposure to DCPs among healthcare workers. It may be recommended [11, 63], first, to reduce the use of substances with well-characterized respiratory toxic effects favoring nonchemical alternative (e.g., microfiber cleaning technologies, ultraviolet, ozonated water) that may maintain antimicrobial efficacy while minimizing chemical toxicity. Second, targeted education for healthcare workers should be provided to ensure awareness of specific risks associated with various DCPs, promote adherence to proper usage guidelines, and improve the labeling of products that may cause irritation or sensitization. Third, implementing ventilation measures and reducing spray application by, for instance, wetting cleaning cloths before surface disinfection, can limit aerosolization and consequent inhalation risks. Finally, establishing clearer protocols to prevent overexposure or inadvertent mixing of cleaning products, combined with the proper use of personal protective equipment (e.g., gloves and appropriate respiratory protection), may further protect healthcare worker by minimizing direct contact and inhalation of potentially harmful agents.

In conclusion, we identified four distinct clusters of occupational exposures to DCPs among healthcare workers, reflecting the diversity of healthcare jobs, in particular nursing, and highlighting various exposure patterns. Two of these clusters, including laboratory staff who are a poorly documented population, were positively associated with asthma symptoms in women. Overall, our study underscores the importance of detailed exposure assessment, given the multidimensional aspect of exposures, in understanding occupational respiratory health risks for workplace safety.

Author Contributions

Bakari Ibrahim contributed to the analysis and interpretation of the data, and primary manuscript preparation. Nicole Le Moual and Rachel Nadif contributed to the study conception, data interpretation, and critical revision of the manuscript. Bénédicte Leynaert, Nicolas Roche, and Raphaëlle Varraso were involved in the data interpretation and critical revision of the manuscript. Guillaume Sit and Céline Ribet contributed to the acquisition, curation, and interpretation of the data and critical revision of the manuscript. Marcel Goldberg and Marie Zins contributed to funding acquisition, the acquisition, curation, and interpretation of the data, and critical revision of the manuscript. Laurent Orsi contributed to the methodology, data interpretation, and critical revision of the manuscript. Orianne Dumas participated in the funding acquisition, study conception, acquisition of the data, data interpretation, and critical revision of the manuscript. All authors approved the final version of the manuscript.

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Ethics Statement

The CONSTANCES cohort received legal authorization from the French National Data Protection Authority (no. 910486) and the ethical approval from the Institutional Review Board of the National Institute for Medical Research (no. 01-011). The specific project "Occupational exposure to cleaning products and disinfectants and respiratory health in the Constances cohort" received approval from the ethics evaluation committee, Institutional Review Board of the National Institute for Medical Research (no. 21-781bis).

Consent

All participants gave informed consent to participate.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data are available on reasonable request. Data can be provided on reasonable request after approval by the CONSTANCES scientific committee.

References

1. J. Stern, J. Pier, and A. A. Litonjua, "Asthma Epidemiology and Risk Factors," *Seminars in Immunopathology* 42, no. 1 (2020): 5–15, https://doi.org/10.1007/s00281-020-00785-1.

2. M. C. Delmas, L. Bénézet, C. Ribet, et al., "Prévalence De L'asthme Chez L'adulte en France, Données de la Cohorte Constances," *Revue des Maladies Respiratoires* 38, no. 8 (2021): 797–806, https://doi.org/10.1016/j.rmr.2021.05.007.

3. C. Raherison-Semjen, A. Izadifar, M. Russier, et al., "Self-Reported Asthma Prevalence and Management in Adults in France in 2018: Asthmapop Survey," *Respiratory Medicine and Research* 80 (2021): 100864, https://doi.org/10.1016/j.resmer.2021.100864.

4. C. Porsbjerg, E. Melén, L. Lehtimäki, and D. Shaw, "Asthma," *Lancet* 401, no. 10379 (2023): 858–873, https://doi.org/10.1016/S0140-6736(22)02125-0.

5. S. M. Tarlo and C. Lemiere, "Occupational Asthma," *New England Journal of Medicine* 370, no. 7 (2014): 640–649, https://doi.org/10.1056/NEJMra1301758.

6. GBD 2016 Occupational Chronic Respiratory Risk Factors Collaborators, "Global and Regional Burden of Chronic Respiratory Disease in

2016 Arising From Non-Infectious Airborne Occupational Exposures: A Systematic Analysis for the Global Burden of Disease Study 2016," *Occupational and Environmental Medicine* 77, no. 3 (2020): 142–150, https://doi.org/10.1136/oemed-2019-106013.

7. G. Sit, L. Orsi, Y. Iwatsubo, et al., "Chronic Occupational Exposures to Irritants and Asthma in the Constances Cohort," *Occupational and Environmental Medicine* 81, no. 3 (2024): 129–135, https://doi.org/10.1136/oemed-2023-109100.

8. P. D. Blanc, I. Annesi-Maesano, J. R. Balmes, et al., "The Occupational Burden of Nonmalignant Respiratory Diseases. An Official American Thoracic Society and European Respiratory Society Statement," *American Journal of Respiratory and Critical Care Medicine* 199, no. 11 (2019): 1312–1334, https://doi.org/10.1164/rccm.201904-0717ST.

9. P. K. Henneberger, C. A. Redlich, D. B. Callahan, et al., "An Official American Thoracic Society Statement: Work-Exacerbated Asthma," *American Journal of Respiratory and Critical Care Medicine* 184, no. 3 (2011): 368–378, https://doi.org/10.1164/rccm.812011ST.

10. P. Maestrelli, P. K. Henneberger, S. Tarlo, P. Mason, and P. Boschetto, "Causes and Phenotypes of Work-Related Asthma," *International Journal of Environmental Research and Public Health* 17, no. 13 (2020): 4713, https://doi.org/10.3390/ijerph17134713.

11. H. H. Mwanga, O. Dumas, N. Migueres, N. Le Moual, and M. F. Jeebhay, "Airway Diseases Related to the Use of Cleaning Agents in Occupational Settings," *Journal of Allergy and Clinical Immunology: In Practice* 12, no. 8 (2024): 1974–1986, https://doi.org/10.1016/j.jaip.2024.02.036.

12. O. Dumas, A. J. Gaskins, K. M. Boggs, et al., "Occupational Use of High-Level Disinfectants and Asthma Incidence in Early- to Mid-Career Female Nurses: A Prospective Cohort Study," *Occupational and Environmental Medicine* 78, no. 4 (2021): 244–247, https://doi.org/10.1136/oemed-2020-106793.

13. M. V. Andrianjafimasy, M. Febrissy, F. Zerimech, et al., "Association Between Occupational Exposure to Irritant Agents and a Distinct Asthma Endotype in Adults," *Occupational and Environmental Medicine* 79, no. 3 (2022): 155–161, https://doi.org/10.1136/oemed-2020-107065.

14. G. Sit, R. Varraso, L. K. Fezeu, et al., "Occupational Exposures to Irritants and Sensitizers, Asthma and Asthma Control in the Nutrinet-Santé Cohort," *Journal of Allergy and Clinical Immunology: In Practice* 10, no. 12 (2022): 3220–3227.e7, https://doi.org/10.1016/j.jaip.2022.08.047.

15. R. W. H. Li, J. C. Lipszyc, S. Prasad, and S. M. Tarlo, "Work-Related Asthma From Cleaning Agents Versus Other Agents," *Occupational Medicine* 68, no. 9 (2018): 587–592, https://doi.org/10.1093/occmed/kqy137.

16. H. H. Mwanga, R. Baatjies, T. Singh, and M. F. Jeebhay, "Work-Related Allergy and Asthma Associated With Cleaning Agents in Health Workers in Southern African Tertiary Hospitals," *American Journal of Industrial Medicine* 65, no. 5 (2022): 382–395, https://doi.org/10.1002/ajim.23344.

17. F. C. Su, M. C. Friesen, M. Humann, et al., "Clustering Asthma Symptoms and Cleaning and Disinfecting Activities and Evaluating Their Associations Among Healthcare Workers," *International Journal of Hygiene and Environmental Health* 222, no. 5 (2019): 873–883, https://doi.org/10.1016/j.ijheh.2019.04.001.

18. A. A. Arif and G. L. Delclos, "Association Between Cleaning-Related Chemicals and Work-Related Asthma and Asthma Symptoms Among Healthcare Professionals," *Occupational and Environmental Medicine* 69, no. 1 (2012): 35–40, https://doi.org/10.1136/oem.2011.064865.

19. O. Dumas, C. Donnay, D. J. J. Heederik, et al., "Occupational Exposure to Cleaning Products and Asthma in Hospital Workers," *Occupational and Environmental Medicine* 69, no. 12 (2012): 883–889, https://doi.org/10.1136/oemed-2012-100826.

20. M. Gonzalez, J. Jégu, M. C. Kopferschmitt, et al., "Asthma Among Workers in Healthcare Settings: Role of Disinfection With Quaternary Ammonium Compounds," *Clinical & Experimental Allergy* 44, no. 3 (2014): 393–406, https://doi.org/10.1111/cea.12215.

21. D. Vizcaya, M. C. Mirabelli, J. M. Antó, et al., "A Workforce-Based Study of Occupational Exposures and Asthma Symptoms in Cleaning Workers," *Occupational and Environmental Medicine* 68, no. 12 (2011): 914–919, https://doi.org/10.1136/oem.2010.063271.

22. O. Dumas, A. S. Wiley, C. Quinot, et al., "Occupational Exposure to Disinfectants and Asthma Control in Us Nurses," *European Respiratory Journal* 50, no. 4 (2017): 1700237, https://doi.org/10.1183/13993003.00237-2017.

23. M. C. Mirabelli, J. P. Zock, E. Plana, et al., "Occupational Risk Factors for Asthma Among Nurses and Related Healthcare Professionals in an International Study," *Occupational and Environmental Medicine* 64, no. 7 (2007): 474–479, https://doi.org/10.1136/oem.2006.031203.

24. H. H. Mwanga, R. Baatjies, and M. F. Jeebhay, "Occupational Risk Factors and Exposure-Response Relationships for Airway Disease Among Health Workers Exposed to Cleaning Agents in Tertiary Hospitals," *Occupational and Environmental Medicine* 80, no. 7 (2023): 361–371, https://doi.org/10.1136/oemed-2022-108763.

25. J. Patel, D. Gimeno Ruiz de Porras, L. E. Mitchell, et al., "Cleaning Tasks and Products and Asthma Among Health Care Professionals," *Journal of Occupational & Environmental Medicine* 66, no. 1 (2024): 28–34, https://doi.org/10.1097/JOM.0000000000002990.

26. O. Archangelidi, S. Sathiyajit, D. Consonni, D. Jarvis, and S. De Matteis, "Cleaning Products and Respiratory Health Outcomes in Occupational Cleaners: A Systematic Review and Meta-Analysis," *Occupational and Environmental Medicine* 78, no. 8 (2021): 604–617, https://doi.org/10.1136/oemed-2020-106776.

27. Démographie des professionnels de santé au 1er janvier 2022: révision à la baisse sur les professions paramédicales pour privilégier la qualité des données | Direction de la recherche, des études, de l'évaluation et des statistiques, accessed March 6, 2025. https://drees.solidarites-sante.gouv.fr/communique-de-presse/demographie-des-professionnels-de-sante-au-1er-janvier-2022-revision-la-baisse.

28. M. Marbac, M. Sedki, M. C. Boutron-Ruault, and O. Dumas, "Patterns of Cleaning Product Exposures Using a Novel Clustering Approach for Data With Correlated Variables," *Annals of Epidemiology* 28, no. 8 (2018): 563–569.e6, https://doi.org/10.1016/j.annepidem.2018.05.004.

29. M. Goldberg, M. Carton, A. Descatha, et al., "Constances: A General Prospective Population-Based Cohort for Occupational and Environmental Epidemiology: Cohort Profile," *Occupational and Environmental Medicine* 74, no. 1 (2017): 66–71, https://doi.org/10.1136/oemed-2016-103678.

30. C. Pilorget, B. Dananché, L. Garras, et al., "Development of a Crosswalk to Convert French PCS2003 Into International ISCO88 Occupational Classifications. Application to the Occupational Asthma-Specific Job-Exposure Matrix (OAsJEM)," *Annals of Work Exposures and Health* 68, no. 7 (2024): 688–701, https://doi.org/10.1093/annweh/wxae049.

31. N. Le Moual, J. P. Zock, O. Dumas, et al., "Update of an Occupational Asthma-Specific Job Exposure Matrix to Assess Exposure to 30 Specific Agents," *Occupational and Environmental Medicine* 75, no. 7 (2018): 507–514, https://doi.org/10.1136/oemed-2017-104866.

32. L. Cazzoletti, A. Marcon, C. Janson, et al., "Asthma Control in Europe: A Real-World Evaluation Based on an International Population-Based Study," *Journal of Allergy and Clinical Immunology* 120, no. 6 (2007): 1360–1367, https://doi.org/10.1016/j.jaci.2007.09.019.

33. F. Kauffmann and M. H. Dizier, "EGEA (Epidemiological Study on the Genetics and Environment of Asthma, Bronchial Hyperresponsiveness and Atopy)—Design Issues," *Clinical & Experimental Allergy* 25, no. Suppl 2 (1995): 19–22, https://doi.org/10.1111/j.1365-2222.1995.tb00413.x.

34. J. Pekkanen, J. Sunyer, J. M. Anto, and P. Burney, "Operational Definitions of Asthma in Studies on Its Aetiology," *European Respiratory*

Journal 26, no. 1 (2005): 28–35, https://doi.org/10.1183/09031936.05.00120104.

35. J. Sunyer, J. Pekkanen, R. Garcia-Esteban, et al., "Asthma Score: Predictive Ability and Risk Factors," *Allergy* 62, no. 2 (2007): 142–148, https://doi.org/10.1111/j.1398-9995.2006.01184.x.

36. C. Donnay, M. A. Denis, R. Magis, et al., "Under-Estimation of Self-Reported Occupational Exposure by Questionnaire in Hospital Workers," *Occupational and Environmental Medicine* 68, no. 8 (2011): 611–617, https://doi.org/10.1136/oem.2010.061671.

37. C. Quinot, O. Dumas, P. Henneberger, et al., "Development of a Job-Task-Exposure Matrix to Assess Occupational Exposure to Disinfectants Among U.S. Nurses," *Occupational and Environmental Medicine* 74, no. 2 (2017): 130–137, https://doi.org/10.1136/oemed-2016-103606.

38. E. Pacheco Da Silva, G. Sit, M. Goldberg, et al., "Household Use of Green and Homemade Cleaning Products, Wipe Application Mode, and Asthma Among French Adults From the Constances Cohort," *Indoor Air* 32, no. 7 (2022): e13078, https://doi.org/10.1111/ina.13078.

39. E. Pacheco Da Silva, R. Varraso, A. M. Lenzotti, et al., "Household Use of Green Cleaning Products, Disinfecting Wipes, and Asthma Control Among Adults," *Journal of Allergy and Clinical Immunology: In Practice* 12, no. 4 (2024): 919–926.e7, https://doi.org/10.1016/j.jaip.2023.12.029.

40. W. Willett, *Nutritional Epidemiology* (Oxford University Press, 2012).

41. J. H. Ward, Jr., "Hierarchical Grouping to Optimize an Objective Function," *Journal of the American Statistical Association* 58, no. 301 (1963): 236–244, https://doi.org/10.1080/01621459.1963.10500845.

42. M. Charrad, N. Ghazzali, V. Boiteau, and A. Niknafs, "NbClust: An R Package for Determining the Relevant Number of Clusters in a Data Set," *Journal of Statistical Software* 61 (2014): 1–36, https://doi.org/10.18637/jss.v061.i06.

43. F. Husson, J. Josse, S. Le, and J. Mazet, FactoMineR: Multivariate Exploratory Data Analysis and Data Mining. Published Online February 29, 2024, https://cran.r-project.org/web/packages/FactoMineR/index.html.

44. M. C. Friesen, S. M. Shortreed, D. C. Wheeler, et al., "Using Hierarchical Cluster Models to Systematically Identify Groups of Jobs With Similar Occupational Questionnaire Response Patterns to Assist Rule-Based Expert Exposure Assessment in Population-Based Studies," *Annals of Occupational Hygiene* 59, no. 4 (2015): 455–466, https://doi.org/10.1093/annhyg/meu101.

45. G. L. Delclos, D. Gimeno, A. A. Arif, F. G. Benavides, and J. P. Zock, "Occupational Exposures and Asthma in Health-Care Workers: Comparison of Self-Reports With a Workplace-Specific Job Exposure Matrix," *American Journal of Epidemiology* 169, no. 5 (2008): 581–587, https://doi.org/10.1093/aje/kwn387.

46. J. V. Cook, H. O. Dickinson, and M. P. Eccles, "Response Rates in Postal Surveys of Healthcare Professionals Between 1996 and 2005: An Observational Study," *BMC Health Services Research* 9 (2009): 160, https://doi.org/10.1186/1472-6963-9-160.

47. G. L. Delclos, D. Gimeno, A. A. Arif, et al., "Occupational Risk Factors and Asthma Among Health Care Professionals," *American Journal of Respiratory and Critical Care Medicine* 175, no. 7 (2007): 667–675, https://doi.org/10.1164/rccm.200609-1331OC.

48. A. A. Arif, G. L. Delclos, and C. Serra, "Occupational Exposures and Asthma Among Nursing Professionals," *Occupational and Environmental Medicine* 66, no. 4 (2009): 274–278, https://doi.org/10.1136/oem.2008.042382.

49. P. I. Hora, S. G. Pati, P. J. McNamara, and W. A. Arnold, "Increased Use of Quaternary Ammonium Compounds During the SARS-CoV-2 Pandemic and Beyond: Consideration of Environmental Implications," *Environmental Science & Technology Letters* 7, no. 9 (2020): 622–631, https://doi.org/10.1021/acs.estlett.0c00437.

50. R. Nguyen, R. P. Seguin, D. H. Ross, et al., "Development and Application of a Multidimensional Database for the Detection of Quaternary Ammonium Compounds and Their Phase I Hepatic Metabolites in Humans," *Environmental Science & Technology* 58, no. 14 (2024): 6236–6249, https://doi.org/10.1021/acs.est.3c10845.

51. A. K. Mahony, P. J. McNamara, and W. A. Arnold, "Quaternary Ammonium Compounds (QACs) in Wastewater Influent and Effluent Throughout the COVID-19 Pandemic," *Environmental Science & Technology* 57, no. 48 (2023): 20148–20158, https://doi.org/10.1021/acs.est.3c04413.

52. P. A. Clausen, M. Frederiksen, C. S. Sejbæk, et al., "Chemicals Inhaled From Spray Cleaning and Disinfection Products and Their Respiratory Effects. A Comprehensive Review," *International Journal of Hygiene and Environmental Health* 229 (2020): 113592, https://doi.org/10.1016/j.ijheh.2020.113592.

53. B. Hawley, M. Casey, M. A. Virji, K. J. Cummings, A. Johnson, and J. Cox-Ganser, "Respiratory Symptoms in Hospital Cleaning Staff Exposed to a Product Containing Hydrogen Peroxide, Peracetic Acid, and Acetic Acid," *Annals of Work Exposures and Health* 62, no. 1 (2017): 28–40, https://doi.org/10.1093/annweh/wxx087.

54. O. Dumas, "Cleaners and Airway Diseases," *Current Opinion in Allergy & Clinical Immunology* 21, no. 2 (2021): 101–109, https://doi.org/10.1097/ACI.0000000000000710.

55. J. P. Zock, M. Kogevinas, J. Sunyer, et al., "Asthma Risk, Cleaning Activities and Use of Specific Cleaning Products Among Spanish Indoor Cleaners," *Scandinavian Journal of Work, Environment & Health* 27, no. 1 (2001): 76–81, https://doi.org/10.5271/sjweh.590.

56. M. Kogevinas, J. P. Zock, D. Jarvis, et al., "Exposure to Substances in the Workplace and New-Onset Asthma: An International Prospective Population-Based Study (ECRHS-II)," *Lancet* 370, no. 9584 (2007): 336–341, https://doi.org/10.1016/S0140-6736(07)61164-7.

57. I. Lindström, J. Lantto, K. Karvala, et al., "Occupations and Exposure Events in Acute and Subacute Irritant-Induced Asthma," *Occupational and Environmental Medicine* 78, no. 11 (2021): 793–800, https://doi.org/10.1136/oemed-2020-107323.

58. A. Eng, A. 't Mannetje, D. McLean, L. Ellison-Loschmann, S. Cheng, and N. Pearce, "Gender Differences in Occupational Exposure Patterns," *Occupational and Environmental Medicine* 68, no. 12 (2011): 888–894, https://doi.org/10.1136/oem.2010.064097.

59. N. Le Moual, F. Kauffmann, E. A. Eisen, and S. M. Kennedy, "The Healthy Worker Effect in Asthma: Work May Cause Asthma, but Asthma May Also Influence Work," *American Journal of Respiratory and Critical Care Medicine* 177, no. 1 (2008): 4–10, https://doi.org/10.1164/rccm.200703-415PP.

60. O. Dumas, R. Varraso, J. P. Zock, et al., "Asthma History, Job Type and Job Changes Among Us Nurses," *Occupational and Environmental Medicine* 72, no. 7 (2015): 482–488, https://doi.org/10.1136/oemed-2014-102547.

61. D. Provost, M. C. Delmas, L. Bénézet, et al., "Impact of Asthma on Working Life: An Analysis of the French Constances Cohort," *Occupational and Environmental Medicine* 80, no. 7 (2023): 392–398, https://doi.org/10.1136/oemed-2022-108671.

62. O. Dumas, N. Le Moual, V. Siroux, et al., "Work Related Asthma. A Causal Analysis Controlling the Healthy Worker Effect," *Occupational and Environmental Medicine* 70, no. 9 (2013): 603–610, https://doi.org/10.1136/oemed-2013-101362.

63. M. M. Quinn, P. K. Henneberger, B. Braun, et al., "Cleaning and Disinfecting Environmental Surfaces in Health Care: Toward an Integrated Framework for Infection and Occupational Illness Prevention," *American Journal of Infection Control* 43, no. 5 (2015): 424–434, https://doi.org/10.1016/j.ajic.2015.01.029.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.