Allergy

WILEY

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

ORIGINAL ARTICLE OPEN ACCESS

Asthma and Lower Airway Disease

Exposure Profiles for the Long-Term Use of Disinfectants and Cleaning Products and Asthma

Emilie Pacheco Da Silva[1,2] | Tobias Weinmann[1] | Jessica Gerlich[1] | Gudrun Weinmayr[3] | Jon Genuneit[3,4] | Dennis Nowak[1] | Erika von Mutius[5,6] | Christian Vogelberg[7] | Katja Radon[1] | Felix Forster[1]

[1]Institute and Clinic for Occupational, Social and Environmental Medicine, LMU University Hospital, LMU Munich, Munich, Germany | [2]Université Paris-Saclay, UVSQ, Univ. Paris-Sud, Inserm, Équipe d'Épidémiologie Respiratoire Intégrative, CESP, Villejuif, France | [3]Institute of Epidemiology and Medical Biometry, Ulm University, Ulm, Germany | [4]Pediatric Epidemiology, Department of Pediatrics, Medical Faculty, Leipzig University, Leipzig, Germany | [5]Institute for Asthma and Allergy Prevention, Helmholtz Center Munich, German Research Center for Environmental Health, Munich, Germany | [6]Department of Pediatrics, Dr. von Hauner Children's Hospital, LMU University Hospital, LMU Munich, Munich, Germany | [7]Department of Pediatrics, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

Correspondence: Emilie Pacheco Da Silva (emilie.pacheco-da-silva@inserm.fr)

Received: 18 July 2024 | **Revised:** 13 November 2024 | **Accepted:** 30 November 2024

Funding: This work was supported by the European Respiratory Society, Société de Pneumologie de Langue Française, German Ministry of Labour and Social Affairs, Deutsche Forschungsgemeinschaft, German Ministry for Economy and Labour, German Federal Institute for Occupational Safety and Health, and German Ministry of Education and Research (01 EE 9411-3).

Keywords: asthma | disinfectants and cleaning products | exposure profiles | latent class analysis | sprays

ABSTRACT

Background: Using disinfectants and cleaning products (DCPs) at home and work is known to influence both the onset and course of asthma, but most epidemiological studies did not consider the multiplicity and correlations of exposures to DCPs. We aimed to identify exposure profiles for the long-term weekly use of DCPs by latent class analysis (LCA) and assess their associations with asthma.

Methods: LCA was conducted on data from 1143 young adults initially recruited in the German centers of Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC) and followed up three times. In our LCA model, we included the use of cleaning sprays, disinfectant sprays, and nonspray disinfection methods, measured at ages 19–24 (first assessment) and 29–34 years (second assessment). Associations between identified exposure profiles and current as well as incident asthma/wheeze were evaluated by logistic regression.

Results: We identified five long-term exposure profiles to DCPs (latent classes): no weekly use of DCPs (55% of participants), use in first assessment (7%), use in second assessment (18%), persistent use (8%), and persistent cleaning sprays use (12%). Compared to "no weekly use," being in the "persistent use" profile was associated with both current asthma (OR = 1.68, 95% CI = [0.48–5.88]) and current wheeze (OR = 1.71, 95% CI = [0.75–3.90]). For incident asthma/wheeze, interval estimates were very wide.

Conclusions: Our study identified five distinct long-term exposure profiles to DCPs. Among those, only a persistent weekly use of multiple DCPs over time seemed to have an adverse effect on asthma. However, large confidence intervals indicate considerable uncertainty.

1 | Introduction

With nearly 300 million individuals affected worldwide [1], asthma is among the most prevalent chronic respiratory diseases resulting in a considerable burden to individuals and societies alike [2]. Various environmental and occupational factors have been identified as influencing both the onset and the course of asthma [3]. Among these factors, disinfectants and cleaning products (DCPs), widely used at home and in some occupational settings, could contribute to the global burden of asthma [4–6].

In epidemiological studies evaluating the respiratory health risks of using DCPs at work [5], occupational exposures to disinfectants [7–9], as well as sprayed DCPs [10–13], were associated with both incident [7, 10, 11] and current asthma [8, 9, 12, 13]. Considering that several DCPs used in the workplace are also commonly used at home, an increasing number of epidemiological studies investigated to what extent household use of DCPs might affect asthma [6]. Overall, these studies have shown an association of a short-term use of DCPs (i.e., one assessment representing the use in the last 12 months) containing respiratory irritants (i.e., bleach, acids, solvents, and ammonia) [14–17] or those used in a spray form [16, 18–20] with both incident [15, 18] and current asthma [14, 16, 17, 19, 20]. So far, only one of them investigated the adverse effects of long-term use of DCPs (i.e., two assessments separated by 8 years apart, both representing the use in the last 12 months) [21]. In the "Epidemiological study on the Genetics and Environment of Asthma" (EGEA), a persistent and increased use of irritants/sprays from the first to the second assessment was associated with a higher risk of asthma symptoms, while a decreased use was associated with a lower risk of asthma symptoms [21].

Cleaning at home and work implies the simultaneous use of multiple DCPs, leading users to be exposed to a mixture of chemical ingredients and application modes (i.e., liquid, spray, and wipe) [5, 22]. However, most epidemiological studies did not consider the multiplicity and correlations of exposures to DCPs because the occupational or household use of DCPs was self-reported by questionnaire [7–10, 12, 14–21], where exposures were not mutually exclusive. Recently, the identification of homogeneous groups of exposures with clustering methods was suggested to consider the multiplicity and correlations of exposures to DCPs [23]. To our knowledge, only one study has been realized to identify exposure profiles for the use of DCPs using a cluster analysis [24], and assessed their associations with asthma [25]. The authors concluded that combined use of several disinfectants could induce a higher risk of asthma symptoms among healthcare workers [25]. Therefore, more longitudinal epidemiological studies using innovative clustering methods to assess and synthesize information regarding occupational and household long-term use of DCPs are needed in order to study more accurate adults' exposure to DCPs and to improve the characterization of their respiratory health effects.

Based on longitudinal data from the Study on Occupational Allergy Risks (SOLAR), the objectives of this study were to (i) identify exposure profiles for the long-term weekly use of DCPs over 10 years by performing a latent class analysis (LCA), and (ii) assess the associations between the identified exposure profiles and current as well as incident asthma/wheeze.

2 | Methods

2.1 | Population

SOLAR is a population-based epidemiological cohort established to investigate the course of asthma and allergies over more than 20 years and their associations with environmental, occupational, and psychosocial health risk factors from childhood to adulthood [26, 27]. At baseline, participants living in the German cities of Munich or Dresden were recruited for Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC Phase 2, 1995–1996, $n = 6399$ German participants aged 9–11 years) [28]. Dresden and Munich were initially selected to compare children from the former East and West of the recently reunified Germany. SOLAR consists of three follow-ups of the ISAAC study: SOLAR 1 (2002–2003, $n = 3785$ participants aged 16–18 years), SOLAR 2 (2007–2009, $n = 2051$ participants aged 19–24 years), and SOLAR 3 (2017–2018, $n = 1359$ participants aged 29–34 years). Standardized questionnaires collected sociodemographic data, information on respiratory health, and occupational and household use of different DCPs (only at SOLAR 2 and 3). Our study was performed on the 1143 adults who participated in all four study phases (Figure 1) because, for those without participation in SOLAR 2 or SOLAR 3, half of the information on DCPs would have been completely missing.

All study phases were approved by the Ethical Committees of the Medical Faculty of the University of Dresden (Number: EK960720 02, EK380220 07, EK2871120 07, and EK163042015) and the Bavarian Chamber of Physicians (Number: 02071,

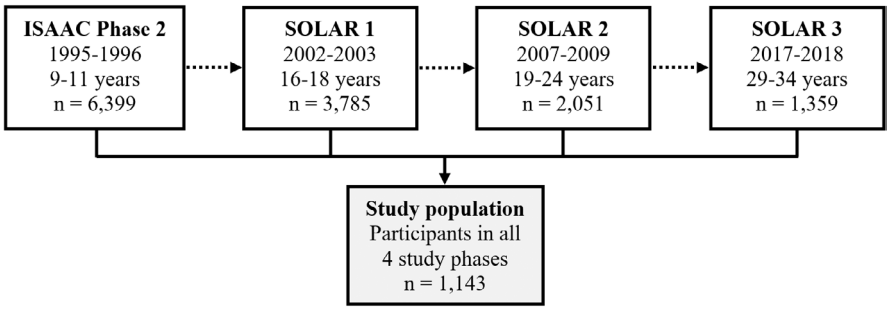

FIGURE 1 | For each of the four study phases, a box describes the time period of data collection, the age range, and the number of participants at data collection.

7/07101, mb BO 17015). Written informed consent, also for linking data across study phases, was obtained from all participants (SOLAR 1 to 3) or their legal guardians (ISAAC Phase 2, SOLAR 1).

2.2 | Weekly Use of DCPs

Occupational and household use of DCPs was recorded at SOLAR 2 and 3 based on questions from the European Community Respiratory Health Survey (ECRHS) [18, 29]. No information was available for ISAAC Phase 2 and SOLAR 1. In the SOLAR 2 and 3 questionnaires, participants declared their current use at home or work of several DCPs in four frequency categories (never, less than 1 day/week, 1–3 days/week, and 4–7 days/week). For each of the two study phases, we specifically estimated the weekly use of cleaning sprays (maximum frequency of use of furniture, glass, carpets/curtains, oven, and ironing), disinfectant sprays, nonspray disinfection methods (maximum frequency of use of hand, machine, surfaces, floor, and other methods), and air freshener sprays. In our analyses, we combined the categories "never" and "less than 1 day/week" to define the reference group "no weekly use", and the categories "1-3 days/week" and "4-7 days/week" to define the exposed group "weekly use", as commonly done [14–21]. These four binary variables ("no weekly use" and "weekly use") per study phase were considered in LCA modeling. Information on nonspray cleaning agents used was not available, nor was the amount of DCPs.

2.3 | Current Asthma/Wheeze and Incident Asthma/Wheeze

We defined current asthma at SOLAR 3 as reporting physician-diagnosed asthma, and either having wheeze without a cold or an asthma treatment in the past 12 months. We also defined current wheeze at SOLAR 3 as reporting wheeze without a cold or an asthma treatment in the past 12 months, regardless of whether they declared or not a physician-diagnosed asthma. Current asthma is therefore a more specific definition and current wheeze is a more sensitive definition of asthma [15]. In our analyses, we compared participants with current asthma/wheeze to those with "no physician-diagnosed asthma"/"no current wheeze" at SOLAR 3, respectively. Participants with remittent asthma at SOLAR 3 (i.e., asthma diagnosed but without wheeze and without asthma treatment) were excluded from the analyses related to current asthma.

Based on the current asthma/wheeze status at each of the four study phases, we studied the incidence of asthma/wheeze between SOLAR 2 and SOLAR 3. Participants who did not report physician-diagnosed asthma/current wheeze from ISAAC Phase 2 to SOLAR 2, but gave a positive answer in the SOLAR 3 questionnaire were classified in the "incident asthma"/"incident wheeze" group, respectively. In our analyses, we compared participants with incident asthma/wheeze to those with "no physician-diagnosed asthma"/"no current wheeze" from ISAAC Phase 2 to SOLAR 3, and those with remittent asthma (physician-diagnosed asthma before SOLAR 3)/wheeze (current wheeze before SOLAR 3) were excluded.

2.4 | Statistical Analysis

An LCA is a statistical approach that allows determination of a set of (not directly observed) latent classes within a heterogeneous population based on response patterns to observed variables (indicators) used in the model [30, 31]. The latent classes identified in our study correspond to exposure profiles for the long-term weekly use of DCPs. When conducting LCA, a final model needs to be selected from various candidate models, which includes the selection of indicator variables and the number of latent classes. Candidate models must be identified, that is, the global maximum-likelihood solution must have been found. We evaluated identification by repeating estimation for every model with 100 random sets of starting values. If at least 50%–60% led to the best solution available from the 100 repetitions, we were reasonably certain to have found the global maximum-likelihood solution (Table S1) [30]. The final model was chosen based on parsimony (if two models are basically the same, choose the simpler one), interpretability (latent classes should make sense), and statistical criteria. Our final model included six binary variables ("weekly use" vs. "no weekly use") as indicators for the use of cleaning sprays, disinfectant sprays, and nonspray disinfection methods measured at SOLAR 2 and 3. Statistical criteria provided a first indication of a reasonable number of latent classes. However, although the four-class solution had the lowest Bayesian information criterion (BIC), we selected the five-class solution as our main model because it allowed us to identify and study one additional relevant and interpretable exposure profile and was the one with the lowest Akaike information criterion (AIC, Table S1). Another LCA candidate model included two additional binary variables for the use of air freshener sprays at both study phases. The use of air fresheners appeared to follow similar usage patterns to those observed for cleaning sprays, so this additional model yielded the same five-class solution previously identified with our main model and we did not select it in favor of parsimony. As multiple imputations were performed to address missing values on the indicators, we recalculated the selected five-class LCA model in each of the 20 imputed datasets and pooled the results. In order to assess the associations between the exposure profiles (latent classes) and asthma, participants needed to be individually assigned to one latent class. To consider the uncertainty of classification, we drew 20 random values from the individual classification probabilities, that is, the probabilities of a certain participant being in a certain latent class, and pooled the results of the 20 draws [32].

Associations between the identified exposure profiles by LCA for the long-term weekly use of DCPs with current asthma/wheeze and incident asthma/wheeze were evaluated by logistic regression models. All models were adjusted for potentially confounding factors based on a scientific literature review [5, 6, 8, 15], that is, sex (men, women), age (continuous), smoking status (never smokers, past smokers, and current smokers), study center (Munich, Dresden), and socioeconomic status (SES: low: <12 years of school attendance and high: ≥ 12 years of school attendance [27]). Models for current asthma/wheeze at SOLAR 3 were further adjusted for current asthma/wheeze at SOLAR 2, respectively. In a sensitivity analysis, associations were additionally adjusted for occupational exposure to other

asthmagens since SOLAR 1 (instead of SES). It was estimated with the occupational asthma-specific job-exposure matrix (OAsJEM) [33] and studied by a binary variable (no occupational exposure to any asthmagens or occupational exposure to only high-level chemical disinfectants/indoor cleaning/bleach, and occupational exposure to other asthmagens including or not high-level chemical disinfectants/indoor cleaning/bleach). Likewise, we additionally adjusted for parental asthma (no parental asthma and maternal and/or paternal asthma). In addition, analyses with current asthma/wheeze were stratified by sex as susceptibility to DCP exposure might be different and to verify if associations were more pronounced in women than in men, considering that women are generally more involved in household tasks [19] and often choose occupations that imply using DCPs (i.e., nurses and cleaners) [5]. Analyses were also stratified by rhinoconjunctivitis symptoms (proxy of allergic status: no or yes) to verify if associations were more pronounced in participants without rhinoconjunctivitis symptoms, considering that DCPs might contain respiratory irritants that can affect asthma through non–immunoglobulin E–related mechanisms [5, 34–37]. We pooled the coefficients and their standard errors for each regression model across imputed datasets to obtain a single estimate, based on Rubin's rules [38], from which we calculated the odds ratio (ORs) and the 95% confidence interval (95% CI).

We carried out an additional analysis to study the observed long-term weekly use of DCPs (instead of underlying LCA exposure profiles) in association with current asthma/wheeze, as previously realized in the French EGEA cohort [21]. For this analysis, we evaluated the long-term weekly use of each DCPs studied at SOLAR 2 and 3 with a three-class variable (no weekly use at both study phases, persistent use, i.e., weekly use at both study phases, and increased use, i.e., weekly use at SOLAR 3 but not at SOLAR 2), and the decreased use with a binary variable (persistent use, as above, and decreased use, i.e., weekly use at SOLAR 2 but not at SOLAR 3) [21].

All analyses were performed using the statistical analysis software R (Version 4.1.1) [39], including LCA (poLCA package [40]) and multiple imputation (MICE package [41]).

3 | Results

Participants were on average 32 years old at SOLAR 3, 63% were women, 25% were current smokers, 63% had a high SES, 57% lived in Dresden, 50% had an occupational exposure to other asthmagens, 35% had rhinoconjunctivitis symptoms, and 9% reported parental asthma (Table S2). As for respiratory health, 7%/10% of participants reported current asthma/wheeze at SOLAR 3 and 3%/5% reported incident asthma/wheeze between SOLAR 2 and SOLAR 3, respectively. Regarding indicators included in our LCA model, between 10% and 30% of participants used DCPs at least weekly (Table 1). The prevalence of current asthma and current wheeze was higher in men than in women (Table S2). In addition, compared with men, women had less often occupational exposure to other asthmagens, but they had a higher weekly use of DCPs at SOLAR 2 and 3 (Table S2).

TABLE 1 | Observed frequency of weekly use of DCPs at SOLAR 2 and 3 in the study population ($n = 1143$).

Variable	SOLAR 2 *n* (%)	SOLAR 3 *n* (%)
Weekly use of cleaning sprays	149 (13.5)	150 (13.4)
Missing values	40	24
Weekly use of disinfectant sprays	145 (12.9)	230 (20.4)
Missing values	20	14
Weekly use of nonspray disinfection methods	180 (16.6)	318 (28.5)
Missing values	60	29

Note: The frequencies of weekly use were calculated on the total number of nonmissing cases.

3.1 | Exposure Profiles for the Long-Term Weekly Use of DCPs

Five long-term exposure profiles to DCPs were identified by LCA (Figure 2 and Table S3), which are defined by the probabilities of weekly use of DCP indicator variables (i.e., cleaning sprays, disinfectant sprays, and nonspray disinfection methods at SOLAR 2 and 3). Latent Class 1 (LC 1, latent class prevalence: 55%) corresponds to an exposure profile in which participants did not have a weekly use of DCPs at both study phases. Latent Class 2 (LC 2, 12%) represents an exposure profile in which participants had a persistent weekly use of only cleaning sprays at both study phases. Latent Class 3 (LC 3, 7%) corresponds to an exposure profile in which participants had decreased their use of DCPs between SOLAR 2 and SOLAR 3. Latent Class 4 (LC 4, 18%) represents an exposure profile in which participants had increased their use of DCPs between SOLAR 2 and SOLAR 3. Latent Class 5 (LC 5, 8%) corresponds to an exposure profile in which participants had a persistent use of DCPs at both study phases.

We observed differences in the distributions of sociodemographic and respiratory health characteristics by latent classes (Table 2). LC 5 ("Persistent use") had the highest proportion of women, current smokers, and participants with occupational exposure to other asthmagens, while SES was the lowest. Furthermore, the prevalence of current asthma/wheeze as well as incident asthma/wheeze was the highest in LC 5. Among the remaining latent classes, the relative frequencies of participants grouped in LC 3 ("Decreased use") were the closest to those of LC 5.

3.2 | Associations Between Exposure Profiles and Asthma

Regarding the associations between the identified exposure profiles, current asthma/wheeze, and incident asthma/wheeze (Figure 3), we found that membership in LC 5 ("Persistent

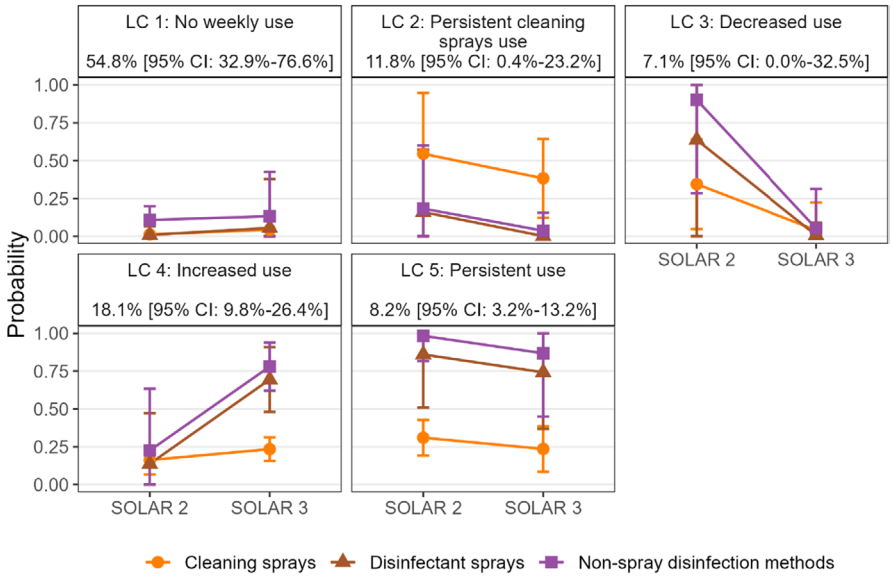

FIGURE 2 | Probabilities of weekly use of DCPs at SOLAR 2 and 3 according to exposure profiles. Each subplot shows the probabilities of weekly use of cleaning sprays, disinfectant sprays, and nonspray disinfection methods with their respective 95% confidence interval at SOLAR 2 and 3 for one latent class. Prevalence of each exposure profile (latent class), with their respective 95% confidence interval, is shown under their label. Numerical values are displayed in Table S3. poLCA calculated an entropy between 2.40 and 2.50 for the models based on the 20 imputed datasets.

use"), compared to LC 1 ("no weekly use"), was associated with both current asthma (OR = 1.68, 95% CI = [0.48–5.88]) and current wheeze (OR = 1.71, 95% CI = [0.75–3.90]), but these associations were not statistically significant. Results were consistent when we further adjusted our models for occupational exposure to other asthmagens and parental asthma (Table S4). Given that most estimates were unreliable (i.e., 95% CI = [0.00-large]) in stratified analyses (Table S5), we could not compare associations obtained in men and women, nor for participants with and without rhinoconjunctivitis symptoms. In stratified analyses by sex, ORs obtained for the associations between LC 4 and current wheeze were smaller in women than in men with wide CI.

In the additional analysis considering the observed long-term weekly use of DCPs (instead of underlying LCA exposure profiles) and asthma (Table S6a,b), only a persistent use of nonspray disinfection methods was associated with current wheeze (OR = 1.59, 95% CI = [0.80–3.16]), albeit not statistically significantly.

4 | Discussion

In the present study, LCA conducted on SOLAR longitudinal data identified five exposure profiles for the long-term weekly use of cleaning sprays, disinfectant sprays, and nonspray disinfection methods over a period of 10 years, namely, no weekly use of DCPs, persistent weekly use of cleaning sprays, decreased weekly use of DCPs, increased weekly use of DCPs, and persistent weekly use of DCPs. Among the identified exposure profiles, only a persistent weekly use of multiple DCPs over time seemed to be associated with current asthma, while the other exposure profiles were not. However, large CIs indicate considerable uncertainty. Associations remained similar after further adjustments for occupational exposure to other asthmagens and parental asthma. Regarding associations with incident asthma/wheeze, we observed wide interval estimates which did not allow us to draw any conclusions. Similarly, from the stratified analyses, we could not conclude a difference across sex and allergic status (i.e., rhinoconjunctivitis symptoms) due to wide CIs.

4.1 | Comparison With Similar Studies

Most previous epidemiological studies examined the impact on asthma attributed to the observed (instead of the underlying patterns) short-term use of DCPs (i.e., one assessment representing the use in the last 12 months) [7–10, 12, 14–20]. Only a few studies assessed the underlying profiles for the short-term exposure to DCPs [25] or the observed long-term use of DCPs [21]. In our study, we identified underlying exposure profiles for the long-term use of DCPs with two assessments 10 years apart using LCA and investigated their associations with asthma.

The underlying profiles for short-term exposure to DCPs were studied by Su and colleagues through the identification of five exposure profiles for cleaning and disinfecting activities by cluster analysis among healthcare workers [25]. These exposure profiles (clusters) were characterized by "no products," "housekeeping/chlorine," "patient care," "general cleaning/laboratory," and "disinfection products". In contrast, our exposure profiles included both occupational and household use of DCPs and were established based on longitudinal data from a population-based cohort. Due to these differences, the underlying exposure profiles are difficult to compare. Nevertheless, despite the differences in methods, both studies suggested that the use of multiple DCPs may negatively impact asthma.

In another population-based cohort [21], the observed long-term household use of DCPs (i.e., two assessments separated by 8 years apart, both representing the use in the last 12 months) was

TABLE 2 | Description of the study population by exposure profiles (i.e., latent classes), nonimputed data.

	Missing values	Study population	LC 1	LC 2	LC 3	LC 4	LC 5
Variable	***n* (%)**	**Mean SD**	**Mean SD**	**Mean SD**	**Mean SD**	**Mean SD**	**Mean SD**
Age (years)	0 (0.0)	31.7 (0.6)	31.7 (31.7–31.7) 0.6 (0.6–0.6)	31.7 (31.6–31.8) 0.6 (0.6–0.6)	31.9 (31.8–31.9) 0.5 (0.5–0.5)	31.8 (31.7–31.8) 0.6 (0.6–0.6)	31.8 (31.8–31.9) 0.7 (0.7–0.7)
	***n* (%)**	***n* (%)**	**%**	**%**	**%**	**%**	**%**
Sex (women)	0 (0.0)	716 (62.6)	56.4 (55.8–57.3)	65.5 (63.0–68.7)	74.3 (70.5–79.1)	69.1 (66.9–71.4)	80.3 (77.4–83.1)
Smoking status							
Never smokers	8 (0.7)	638 (56.2)	61.0 (60.2–62.0)	54.3 (49.9–57.5)	42.0 (35.3–48.9)	52.7 (50.7–55.1)	41.0 (37.3–43.4)
Past smokers		217 (19.1)	18.2 (17.4–18.9)	18.3 (14.8–21.8)	21.3 (15.5–27.9)	20.9 (18.8–23.7)	21.8 (19.4–24.0)
Current smokers		280 (24.7)	20.8 (20.0–21.3)	27.4 (24.4–31.1)	36.7 (30.2–42.1)	26.4 (24.5–27.9)	37.2 (33.9–41.2)
Socioeconomic status (high)	4 (0.3)	720 (63.2)	72.3 (71.5–73.0)	56.6 (54.0–60.3)	50.3 (45.8–56.3)	54.0 (51.9–56.5)	39.1 (35.7–41.3)
Study center (Dresden)	0 (0.0)	647 (56.6)	56.6 (55.6–57.8)	45.3 (42.1–49.1)	64.6 (59.3–69.7)	59.9 (57.0–62.8)	63.7 (61.4–66.1)
Occupational exposure to other asthmagens[a]	208 (18.2)	464 (49.6)	49.4 (48.4–50.2)	42.0 (38.8–46.0)	58.4 (53.2–64.0)	49.2 (46.8–51.7)	59.2 (55.8–62.9)
Asthma							
Current asthma	133 (11.6)	73 (7.2)	6.7 (6.1–7.2)	6.6 (4.8–8.3)	8.3 (5.6–12.2)	6.9 (5.6–8.7)	11.4 (10.3–13.4)
Incident asthma	409 (35.8)	19 (2.6)	2.5 (2.2–2.8)	1.1 (0.0–2.2)	3.7 (0.0–4.5)	2.8 (1.8–3.9)	4.4 (3.9–4.7)
Wheeze							
Current wheeze	2 (0.2)	115 (10.1)	9.5 (9.0–10.0)	9.6 (8.0–11.9)	13.0 (9.1–16.2)	7.9 (6.6–9.5)	16.7 (15.0–18.5)
Incident wheeze	454 (39.7)	36 (5.2)	5.4 (4.6–5.9)	3.1 (1.2–5.7)	5.1 (0.0–6.4)	5.4 (3.7–7.2)	6.6 (5.4–7.4)
Rhinoconjunctivitis symptoms	11 (1.0)	395 (34.9)	33.6 (32.3–34.7)	33.8 (31.0–37.2)	39.8 (36.1–44.3)	39.1 (36.1–42.0)	35.0 (32.0–38.0)
Parental asthma	88 (7.7)	98 (9.3)	8.2 (7.4–8.6)	9.4 (7.4–12.2)	15.6 (13.4–18.2)	10.0 (8.2–11.5)	12.7 (11.4–14.2)

Note: LC 1: No weekly use; LC 2: persistent cleaning spray use; LC 3: decreased use; LC 4: increased use; and LC 5: persistent use. Because there is uncertainty in which participant belongs to which latent class, we randomly drew latent class membership 20 times from the available information to account for this uncertainty. For columns LC 1 to LC 5, means, standard deviations (SD), and relative frequencies (%) are averaged over 20 draws of latent class membership with the 5th and 95th percentiles in parentheses, that is, the second lowest and the second highest value (since there are 20 values). Mean, SD, and % change between the 20 draws because participants are not always assigned the same latent class. Since there is no assignment uncertainty in the overall study population, there is only one mean, one SD, one *n*, and one % value.

[a]Occupational exposure to other asthmagens since SOLAR 1 was estimated with the OAsJEM [33]. Participants with current asthma/wheeze were compared to those with no current asthma/wheeze at SOLAR 3. Participants with incident asthma/wheeze were compared to those with no asthma/wheeze from ISAAC Phase 2 to SOLAR 3.

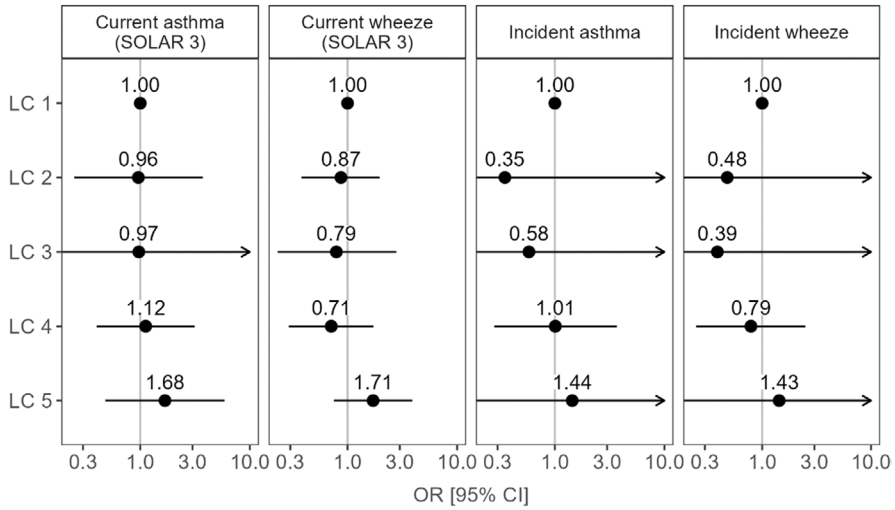

FIGURE 3 | Associations of the identified exposure profiles with current asthma/wheeze and incident asthma/wheeze. LC 1: No weekly use; LC 2: Persistent cleaning sprays use; LC 3: Decreased use; LC 4: Increased use; LC 5: Persistent use. Adjusted odds ratios (ORs) for sex, age, smoking status, study center, and socioeconomic status, presented with their 95% confidence interval [95% CI] were estimated by logistic regression models. Models for current asthma/wheeze at SOLAR 3 were further adjusted for current asthma/wheeze at SOLAR 2, respectively. The arrow on the upper CI means that the value is larger than 10, that is, the x-axis upper limit. Associations with current asthma were performed on 1003 to 1008 participants (from the 20 imputed datasets) with the remaining ones being excluded due to remittent asthma. Associations with current wheeze were performed on 1143 participants. Associations with incident asthma were performed on 911 to 920 participants (from the 20 imputed datasets), and those with incident wheeze were performed on 860 to 870 participants (from the 20 imputed datasets) with the remaining ones being excluded due to remittent asthma/wheeze, respectively. Participants with current asthma/wheeze were compared to those with no current asthma/wheeze at SOLAR 3. Participants with incident asthma/wheeze were compared to those with no asthma/wheeze from ISAAC Phase 2 to SOLAR 3.

evaluated, considering no use, decreased use, persistent use, and increased use over time. In that study, a persistent and increased use of irritants and sprays (compared to no weekly use) elevated the risk of asthma symptoms, while a decreased use (compared to a persistent use) lowered the risk. We also observed limited evidence for an association between a latent class describing a persistent use of DCPs and current asthma. However, since we studied underlying exposure profiles using LCA, comparability was limited. Therefore, we performed an additional analysis with similar exposure variable definitions. We observed that a persistent use of nonspray disinfection methods (compared to no weekly use) was associated with current wheeze, but we did not find an association between a persistent use of cleaning sprays and current asthma/wheeze. This difference may be attributed to a lower prevalence of cleaning sprays use in SOLAR (partly explained by sociodemographic characteristics) and the use of a slightly different definition of cleaning sprays, which includes also occupational use and did not consider some types of sprays (e.g., cleaning floor sprays and air fresheners sprays) [21]. Still, both studies suggested that a persistent use of DCPs over time may have adverse effects on asthma.

4.2 | Strengths and Limitations

The main strength of our study is the use of longitudinal data from the SOLAR study in which we studied a relevant time period to assess the long-term weekly use of DCPs and its impact on asthma. Indeed, participants might start using DCPs when having their first job and living on their own in their 20s [15], whereas they might have a regular use for years when they are in their 30s. However, the exposure to DCPs relied on self-reported data collected by questionnaire, which could have both induced differential and nondifferential misclassification bias [42]. On the one hand, participants with asthma are generally more vigilant toward exposures that can affect their health, so they report more precisely the DCPs they use than participants without asthma, which could lead to differential misclassification bias. On the other hand, participants, whether they have asthma or not, do not properly report their exposure to certain DCPs because they do not know their exact composition, which could lead to a nondifferential misclassification bias resulting in an underestimation of the ORs evaluated. Using an LCA helped to a certain extent to deal with exposure misclassification, as a latent class model assumes that the observed use of DCPs is caused by the underlying latent variable (i.e., exposure profiles), as well as error terms [30]. Nonetheless, it would be essential to develop more objective methods to assess both household and occupational exposure to DCPs. In addition, the assessment of asthma and the use of DCPs at only two surveys separated by 10 years did not allow us to account for potential changes in the meantime, which could lead to misclassification errors in both outcome and exposure. Also, it was not possible to distinguish household and occupational use of DCPs, so we cannot conclude the contribution of household and occupational use to the current asthma risk. Although we selected a relatively large study population for our analyses ($n = 1143$), the primary findings regarding the associations between exposure profiles for the long-term weekly use of DCPs and asthma outcomes are not statistically significant. We believe the low prevalence of weekly use of DCPs (ranging between 13% and 28%) contributed to the lack of statistical significance in several analyses. Also, due to low numbers, we could not investigate associations with persistent or remittent asthma [15]. Over the decades, SOLAR

experienced a substantial loss in follow-up. Indeed, from initially 6399 participants in the ISAAC Phase 2 cohort, only 1359 participated in the third follow-up SOLAR 3 (Figure 1). We further had to restrict our analysis to the 1143 cohort members who participated in both SOLAR 2 and SOLAR 3 in order to be able to estimate long-term exposure profiles. In nonresponder analyses, follow-up participants were more often women, with a higher socioeconomic status, smoked less, and tended to have more asthma and allergic symptoms [26, 27]. Finally, as our study population included German young adults, with a relatively high socioeconomic status, and recruited only in the cities of Munich or Dresden, our results must be extrapolated to the general population with caution. Therefore, it would be interesting to assess the associations between exposure profiles for the long-term weekly use of DCPs and asthma in other population-based cohorts in which participants have a higher prevalence of weekly use of DCPs at different surveys.

We were the first to identify distinct and relevant long-term exposure profiles to DCPs by LCA, which constitutes a promising approach to provide a more accurate understanding of individuals' exposure to DCPs. Although LCA is sometimes called a hypothesis-free method [30, 31], the latent classes established are influenced by the indicators included in the LCA models. Therefore, we considered several sets of indicators to assess the variability between different sets. Another strength is the draw of 20 random values to consider the uncertainty of class assignment, as well as the use of multiple imputations to account for missing data. Lastly, despite observing quantitative differences between men and women in the weekly use of DCPs, our selected LCA model contains the assumption that the same exposure profiles should be observed in both sexes.

5 | Conclusion

In conclusion, distinct exposure profiles for the long-term weekly use of DCPs were identified by LCA, which constitutes a promising approach to enhance our understanding of adults' exposure to DCPs. Among the identified exposure profiles, only a persistent weekly use of multiple DCPs over time seemed to have an adverse effect on asthma. However, large CIs indicate considerable uncertainty. Future longitudinal studies in other population-based cohorts should focus on repeated assessment of the use of DCPs at surveys separated by shorter time periods, in order to better characterize the long-term deleterious effects of using DCPs on asthma.

Author Contributions

E.P.D.S.: conceptualization, formal analysis, and writing – original draft; T.W.: conceptualization, supervision, and writing – review and editing; J. Gerlich: conceptualization, data curation, funding acquisition, and writing – review and editing; G.W.: conceptualization, data curation, funding acquisition, and writing – review and editing; J. Genuneit: conceptualization, data curation, funding acquisition, and writing – review and editing; D.N.: conceptualization, funding acquisition, and writing – review and editing; E.vM.: conceptualization, funding acquisition, supervision, and writing – review and editing; C.V.: conceptualization, funding acquisition, supervision, and writing – review and editing; K.R.: conceptualization, funding acquisition, supervision, and writing – review and editing; and F.F.: conceptualization, data curation, formal analysis, and writing – review and editing.

Acknowledgments

The authors cordially thank all study participants and the students who helped enter paper questionnaires. The ISAAC Phase 2 study in Dresden and Munich was supported by the German Ministry of Education and Research (01 EE 9411-3). The SOLAR I study was supported by the German Ministry for Economy and Labour. The SOLAR II study was supported by the German Federal Institute for Occupational Safety and Health and the German Ministry of Labour and Social Affairs. The SOLAR III study was supported by the German Research Foundation (DFG) under project number GZ: RA 857/12-1; AOBJ: 629972; GZ: VO 839/2-1; and AOBJ: 629973. Emilie Pacheco Da Silva is the recipient of an ERS/SPLF Joint Short-Term Research Fellowship—Number n°202310-01107. The research leading to these results has received funding from the European Respiratory Society (ERS) and the Société de Pneumologie de Langue Française (SPLF).

Conflicts of Interest

E.vM. reports grants from OM Pharma; consulting fees from OM Pharma, AstraZeneca; payment or honoraria from ALK-Abello Arzneimittel GmbH, AstraZeneca, OM Pharma, and Abbott Laboratories; support for attending meetings and/or travel from Fabio Luigi Massimo Ricciardolo/Contatto S.r.l., Karl-Landsteiner Private University for Health Sciences, Gordon Research Conferences, Arla, OM Pharma; participation on the BEAMS External Scientific Advisory Board (ESAB) and Abbott Allergy Risk Reduction Advisory Board. E.vM. has Patent No. PCT/EP2019/085016 (barn dust extract for the prevention and treatment of diseases) pending, royalties paid to ProtectImmun for patent EP2361632 (Specific environmental bacteria for the protection from and/or the treatment of allergic, chronic inflammatory and/or autoimmune disorders, granted on 19 March 2014), and patents EP1411977 (composition containing bacterial antigens used for the prophylaxis and the treatment of allergic diseases, granted on April 18, 2007), EP1637147 (stable dust extract for allergy protection, granted on December 10, 2008), and EP1964570 (pharmaceutical compound to protect against allergies and inflammatory diseases, granted on November 21, 2012) licensed to ProtectImmun. Patent EP21189353.2. 2021. von Mutius E, Rankl B, Bracher F, Müller C, Walker A, Hauck SM, Merl-Pham J, and inventors; PROTEINS IDENTIFIED FROM BARN DUST EXTRACT FOR THE PREVENTION AND TREATMENT OF DISEASES. Patent PCT/US2021/016918. 2021. Martinez FD, Vercelli D, Snyder SA, von Mutius E, Pivniouk V, Marques dos Santos M, and inventors; THERAPEUTIC FRACTIONS AND PROTEINS FROM ASTHMA-PROTECTIVE FARM DUST. Patent EP21189353.2. 2021. von Mutius E, Rankl B, Bracher F, Müller C, Walker A, Hauck SM, Merl-Pham J, Adler H, Yildirim A.Ö., Sattler M, Santos Dias Mourao A, Borggräfe J, O'Connor P.D., Plettenburg O, and inventors; PROTEINS IDENTIFIED FROM BARN DUST EXTRACT FOR THE PREVENTION AND TREATMENT OF DISEASES.

C.V. reports a research grant from Boehringer Ingelheim; consulting fees from Sanofi Aventis; and payment or honoraria from Sanofi Aventis, AstraZeneca, and Novartis Pharma.

E.P.D.S., T.W., J. Gerlich, G.W., J. Genuneit, D.N., K.R., and F.F. declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. 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.

2. 2024 GINA Main Report, "Global Initiative for Asthma," accessed May 17, 2024, https://ginasthma.org/2024-report/.

3. B. Leynaert, N. Le Moual, C. Neukirch, V. Siroux, and R. Varraso, "Environmental Risk Factors for Asthma Developement," *La Presse Médicale 1983* 48, no. 3 Pt 1 (2019): 262–273, https://doi.org/10.1016/j.lpm.2019.02.022.

4. I. Agache, C. Canelo-Aybar, I. Annesi-Maesano, et al., "The Impact of Indoor Pollution on Asthma-Related Outcomes: A Systematic Review for the EAACI Guidelines on Environmental Science for Allergic Diseases and Asthma," *Allergy* 17 (2024): 1761–1788, https://doi.org/10.1111/all.16051.

5. 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* S2213-2198, no. 24 (2024): 214–219, https://doi.org/10.1016/j.jaip.2024.02.036.

6. L. Casas, O. Dumas, and N. Le Moual, "Indoor Air and Respiratory Health: Volatile Organic Compounds and Cleaning Products," in *Asthma in the 21st Century*, ed. R. Nadif (London, UK: Academic Press, 2023), 135–150, https://doi.org/10.1016/B978-0-323-85419-1.00002-5.

7. 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.

8. T. Weinmann, F. Forster, E. von Mutius, et al., "Association Between Occupational Exposure to Disinfectants and Asthma in Young Adults Working in Cleaning or Health Services: Results From a Cross-Sectional Analysis in Germany," *Journal of Occupational and Environmental Medicine* 61, no. 9 (2019): 754–759, https://doi.org/10.1097/JOM.0000000000001655.

9. C. Brooks, T. Slater, M. Corbin, et al., "Respiratory Health in Professional Cleaners: Symptoms, Lung Function, and Risk Factors," *Clinical and Experimental Allergy* 50, no. 5 (2020): 567–576, https://doi.org/10.1111/cea.13597.

10. 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.

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

12. K. De Troeyer, J. De Man, E. Vandebroek, et al., "Identifying Cleaning Products Associated With Short-Term Work-Related Respiratory Symptoms: A Workforce-Based Study in Domestic Cleaners," *Environment International* 162 (2022): 107170, https://doi.org/10.1016/j.envint.2022.107170.

13. 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.

14. B. Matulonga, M. Rava, V. Siroux, et al., "Women Using Bleach for Home Cleaning Are at Increased Risk of Non-allergic Asthma," *Respiratory Medicine* 117 (2016): 264–271, https://doi.org/10.1016/j.rmed.2016.06.019.

15. T. Weinmann, J. Gerlich, S. Heinrich, et al., "Association of Household Cleaning Agents and Disinfectants With Asthma in Young German Adults," *Occupational and Environmental Medicine* 74, no. 9 (2017): 684–690, https://doi.org/10.1136/oemed-2016-104086.

16. 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.

17. P. Lemire, O. Dumas, S. Chanoine, et al., "Domestic Exposure to Irritant Cleaning Agents and Asthma in Women," *Environment International* 144 (2020): 106017, https://doi.org/10.1016/j.envint.2020.106017.

18. J. P. Zock, E. Plana, D. Jarvis, et al., "The Use of Household Cleaning Sprays and Adult Asthma: An International Longitudinal Study," *American Journal of Respiratory and Critical Care Medicine* 176, no. 8 (2007): 735–741, https://doi.org/10.1164/rccm.200612-1793OC.

19. N. Le Moual, R. Varraso, V. Siroux, et al., "Domestic Use of Cleaning Sprays and Asthma Activity in Females," *European Respiratory Journal* 40, no. 6 (2012): 1381–1389, https://doi.org/10.1183/09031936.00197611.

20. A. Bédard, R. Varraso, M. Sanchez, et al., "Cleaning Sprays, Household Help and Asthma Among Elderly Women," *Respiratory Medicine* 108, no. 1 (2014): 171–180, https://doi.org/10.1016/j.rmed.2013.10.018.

21. E. Pacheco Da Silva, M. Ngutuka, O. Dumas, et al., "Longitudinal Associations of Household Use of Cleaning Agents and Asthma Symptoms in Women: The EGEA Study," *Occupational and Environmental Medicine* 80, no. 4 (2023): 218–224, https://doi.org/10.1136/oemed-2022-108513.

22. Z. Stanfield, C. K. Addington, K. L. Dionisio, et al., "Mining of Consumer Product Ingredient and Purchasing Data to Identify Potential Chemical Coexposures," *Environmental Health Perspectives* 129, no. 6 (2021): 67006, https://doi.org/10.1289/EHP8610.

23. 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.

24. F. C. Su, M. C. Friesen, A. B. Stefaniak, et al., "Exposures to Volatile Organic Compounds Among Healthcare Workers: Modeling the Effects of Cleaning Tasks and Product Use," *Annals of Work Exposures and Health* 62, no. 7 (2018): 852–870, https://doi.org/10.1093/annweh/wxy055.

25. 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.

26. S. Heinrich, A. Peters, J. Kellberger, et al., "Study on Occupational Allergy Risks (SOLAR II) in Germany: Design and Methods," *BMC Public Health* 11 (2011): 298, https://doi.org/10.1186/1471-2458-11-298.

27. F. Forster, S. Kreißl, L. Wengenroth, et al., "Third Follow-Up of the Study on Occupational Allergy Risks (SOLAR III) in Germany: Design, Methods, and Initial Data Analysis," *Frontiers in Public Health* 9 (2021): 591717, https://doi.org/10.3389/fpubh.2021.591717.

28. M. I. Asher, U. Keil, H. R. Anderson, et al., "International Study of Asthma and Allergies in Childhood (ISAAC): Rationale and Methods," *European Respiratory Journal* 8, no. 3 (1995): 483–491, https://doi.org/10.1183/09031936.95.08030483.

29. Ø. Svanes, R. J. Bertelsen, S. H. L. Lygre, et al., "Cleaning at Home and at Work in Relation to Lung Function Decline and Airway Obstruction," *American Journal of Respiratory and Critical Care Medicine* 197, no. 9 (2018): 1157–1163, https://doi.org/10.1164/rccm.201706-1311OC.

30. L. M. Collins and S. T. Lanza, *Latent Class and Latent Transition Analysis* (Hoboken, New Jersey: John Wiley & Sons Ltd., 2009), 1–22, https://doi.org/10.1002/9780470567333.

31. P. Sinha, C. S. Calfee, and K. L. Delucchi, "Practitioner's Guide to Latent Class Analysis: Methodological Considerations and Common Pitfalls," *Critical Care Medicine* 49, no. 1 (2021): e63–e79, https://doi.org/10.1097/CCM.0000000000004710.

32. F. Forster, M. J. Ege, J. Gerlich, et al., "Trajectories of Asthma and Allergy Symptoms From Childhood to Adulthood," *Allergy* 77, no. 4 (2022): 1192–1203, https://doi.org/10.1111/all.15075.

33. 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.

34. E. Pacheco Da Silva, R. Nadif, E. Dohoukpe, et al., "Household Use of Irritant and Sprayed Cleaning Products and Asthma Endotypes. A Brief Report," *Journal of Occupational and Environmental Medicine* 66 (2024): e375–e378, https://doi.org/10.1097/JOM.0000000000003139.

35. 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.

36. S. Quirce and P. Barranco, "Cleaning Agents and Asthma," *Journal of Investigational Allergology & Clinical Immunology* 20, no. 7 (2010): 542–550.

37. O. Vandenplas, M. Wiszniewska, M. Raulf, et al., "EAACI Position Paper: Irritant-Induced Asthma," *Allergy* 69, no. 9 (2014): 1141–1153, https://doi.org/10.1111/all.12448.

38. D. B. Rubin, "Procedures With Ignorable Nonresponse," in *Multiple Imputation for Nonresponse in Surveys* (New York: John Wiley & Sons Ltd., 1987), 154–201, https://doi.org/10.1002/9780470316696.ch5.

39. R Core Team, "A Language and Environment for Statistical Computing," accessed May 17, 2024, https://www.r-project.org/.

40. D. A. Linzer and J. B. Lewis, "poLCA: An R Package for Polytomous Variable Latent Class Analysis," *Journal of Statistical Software* 42 (2011): 10, https://doi.org/10.18637/jss.v042.i10.

41. S. van Buuren and K. Groothuis-Oudshoorn, "Mice: Multivariate Imputation by Chained Equations in R," *Journal of Statistical Software* 45 (2011): 1–67, https://doi.org/10.18637/jss.v045.i03.

42. 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.

Supporting Information

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