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Domestic use of cleaning sprays and asthma activity in women

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ABSTRACT

We aimed to study the associations between the household use of cleaning sprays and asthma symptoms and control of asthma, in women from the Epidemiological study on the Genetics and Environment of Asthma (EGEA).

Data were available for 683 women (44 years, 55% never smokers, 439 without asthma and 244 with current asthma). Both domestic exposures and asthma phenotypes (asthma symptom score, current asthma, poorly-controlled asthma (56%)) were evaluated as previously described in the European Community Respiratory Health Survey. Associations between the use of sprays and asthma phenotypes were evaluated using logistic and nominal regressions, adjusted for age, smoking, body mass index and occupational exposures.

Significant associations were observed between the weekly use of at least 2 types of sprays and a high asthma symptom score (odds ratio (OR) [95% confidence interval] 2.50[1.54-4.03]) compared to a null score. Consistent results were observed for current asthma (1.67[1.08-2.56]) and poorly-controlled asthma (2.05[1.25-3.35]) compared to women without asthma. The association for current asthma was higher in women without avoidance of polluted places (2.12[1.27-3.54]) than in those reporting avoidance (0.99[0.53-1.85]).

The common use of household cleaning sprays is positively associated with a high asthma symptom score, current asthma and poorly-controlled asthma in women.

Keywords: asthma control; asthma symptom; cleaning sprays; EGEA; epidemiology; household exposure

INTRODUCTION

Previous studies have reported an excess risk for asthma in cleaners working in offices, hospitals or employed in private houses [1]. Results are consistent with an effect of cleaning agents both in the aggravation and new onset of asthma [1, 2]. Household cleaning substances are classified in the top 5 substances most frequently involved in exposure complaints in the 2009 report of the American National Poison Data System [3]. Bello et al [4], who studied detailed tasks among hospital cleaners, classified the use of cleaning sprays as high risk for inhalation exposure. The use of cleaning products in spray form, at work and at home, may be an important risk factor for asthma [1, 5, 6]. One study has reported a dose-response relationship between the frequency of use and number of cleaning sprays used at home and asthma incidence [6].

Exposure to cleaning agents may represent an important public health issue, especially in women. Involvement in domestic tasks and home cleaning is a gender-related behavior [7, 8]. Uncontrolled-asthma was more frequent in women than in men [9], and domestic exposures might partly explain gender differences in asthma control [10]. Both at work and at home, women are likely to be at high risk based on the potential deleterious effect of cleaning products, including those in spray form [11]. Other studies are necessary to confirm this deleterious role of household cleaning sprays on asthma activity and clinical expression of the disease.

The “healthy worker effect” is an important bias in occupational asthma [12, 13]. For domestic exposures, we hypothesize that a similar phenomenon of selection might be present but has not yet been studied. A “healthy home-cleaning effect” would be induced by the fact that people with cleaning task-related asthma symptoms may modify their behavior to reduce the use of cleaning products, sprays or tasks.

In the Epidemiological study on the Genetics and Environment of Asthma (EGEA), a detailed questionnaire regarding current domestic tasks was used along with precise asthma phenotypes. The aim of the present analysis was to assess, in women from the EGEA study, the associations between home cleaning, particularly the use of household cleaning sprays, and asthma activity. Specific hypotheses were: the use of household sprays as a risk factor for (1) poorly-controlled asthma, (2) a high asthma symptom score; and (3) a potential 'healthy home-cleaning effect', evaluated by the avoidance of polluted places, in the association between domestic exposures and asthma.

MATERIAL AND METHODS

Population

EGEA is a cohort study based on an initial group of patients with asthma recruited (1991-1995) in chest clinics (probands, n=388) along with their first-degree relatives (n=1244), and a group of population-based subjects (n=415). At the second survey (1601 subjects with detailed questionnaires), detailed phenotyping was performed with lung function tests including methacholine challenge, skin prick tests (SPT) to 12 aeroallergens and total serum IgE (see flow chart and descriptive data in the online supplement) [9, 14]. The analysis is based on 683 women examined at the second survey, for whom detailed information regarding domestic exposures, in particular to sprays, was collected in 2003-2007 (244 with current asthma and 439 without asthma, with detailed phenotyping). The main analysis was focused on women, because few men used cleaning products and no associations were observed in men (online supplement).

Asthma and related phenotypes

Based on five asthma symptoms over the past 12 months (wheezy breathlessness, woken up by chest tightness and by an attack of shortness of breath, attack of shortness of breath at rest and after exercise), the asthma symptom score was computed, as previously proposed [15,

16]. A high score was defined by ≥2 symptoms. As in the European Community Respiratory Health Survey (ECRHS) [17, 18], current asthma referred to the report of asthma attacks or asthma treatment or asthma-like symptoms in the past 12 months [9]. Asthma control was assessed as described by Cazzoletti et al [17] and already used in EGEA by Siroux et al [9], based on the GINA 2006-2010 guidelines combining diurnal and nocturnal respiratory symptoms, asthma attacks, lung function, hospitalization for asthma and the use of reliever medication. Women with current asthma were classified as poorly-controlled (i.e. uncontrolled or partly-controlled) or controlled. Sensitivity analyses were performed for the following asthma sub-phenotypes: asthma severity, low lung function (FEV1 <80%pred), bronchial hyperresponsiveness (PD20<4mg methacholine), positive skin prick tests (SPT+, any of 12 allergens), high total IgE (≥100IU/ml) and blood eosinophilia (≥ 250/mm3). See online supplement for more details.

Assessment of exposure

Current domestic exposures (last 12 months) were recorded as in ECRHS [6], based on 24 domestic exposure variables including 9 cleaning tasks and 15 cleaning agents (see online supplement). Exposure to home cleaning referred to the report of this task ≥1/week as in Zock et al [6]. Exposure to sprays was defined by the exposure to any of the 8 types of sprays (furniture, glass-cleaning, carpet, mopping the floor, oven, ironing, air-refreshing, other use) ≥1/week. Detailed analyses of those exposed (≥1/week) to 2 types of sprays were performed.

For a more comprehensive approach, domestic exposure patterns were defined through principal component analysis (PCA) based on the 24 exposure variables. PCA evidenced three domestic exposure patterns entitled ‘Essential tasks’, ‘Domestic wizard’, and ‘Chemical products’ (see Table 2).

In order to assess a potential "healthy home-cleaning effect", we analyzed a proxy of avoidance of cleaning products, i.e. 'avoidance of polluted places', assessed by four questions on the activity limitation domain (passive smoking, dust, pollution, perfume/odor) from the Asthma Quality-of-Life Questionnaire [19]. Participants with asthma were classified as 'without avoidance of polluted places' if, from the 7-point scale of each of the questions, they reported 'none of the time', 'hardly/any of the time', or 'a little of the time'. Working as a cleaner or occupationally exposed to cleaning agents, assessed through an asthma job exposure matrix with an expert re-evaluation step [13, 20], was used for sensitivity analysis.

Statistical analysis

Associations between reported domestic exposures, exposure patterns and asthma-related phenotypes were evaluated using logistic regression, taking into account the familial structure of the data (Genmod, SAS) and nominal logistic regression analyses. In all of the analyses on asthma sub-phenotypes, the women with a given asthma phenotype were compared to those without asthma. All analyses were adjusted for age, smoking status, BMI, and occupational exposure to asthmogens.

RESULTS

The average age of the women was 44 years, 55% were never smokers, and 36% had current asthma, of which 56% poorly-controlled asthma (Table 1). Home cleaning, but not spray use, was significantly associated with age, BMI, diploma level but not with other covariates.

Most of the women with asthma had childhood-onset asthma (<16 years). As expected, women with asthma had significantly more often low FEV_1, BHR, SPT+, high IgE, eosinophilia compared to women without asthma (Table E1).

Avoidance of polluted places

Among the women with current asthma (n=244), 83 avoided passive smoking, dust, pollution, and perfume/odors (60, 41, 24, and 24, respectively), half of them for at least two reasons. The avoidance of polluted places was not significantly associated with home cleaning but was significantly associated with the use of sprays (Table 1). The subjects who reported avoiding exposure to inhaled irritants also weekly used sprays less frequently than those who did not avoid polluted places (39% vs 57%). A significant higher prevalence of avoidance of polluted places was observed in non users of sprays (44% in non vs 27% in weekly users, p=0.01), in non smokers (41% in non vs 14% in current smokers, p=0.001) and in women with adult-onset asthma (44% in adult- vs 31% in childhood-onset asthma, p=0.04). No associations between avoidance of polluted places with atopy and diploma level were observed.

Home cleaning

Using self-report assessment of home cleaning, no significant associations were observed (OR [95% Confidence Interval], 1.38[0.91-2.11]) with the asthma symptom score in univariate analysis. After adjustment for age, smoking habits, BMI, and occupational exposure, home cleaning (1.85 [1.16-2.94]) was significantly related to a high asthma symptom score (Table 3).

No significant associations were observed between home cleaning and current asthma or asthma control (Table 3), nor with any of the other studied asthma phenotypes (data not shown). Using PCA exposure assessment, ‘essential tasks’ (second tertile, Table 3) were positively and significantly associated with a high asthma symptom score and poorly-controlled asthma. A significant negative association was observed for moderate exposure to the category of ‘Domestic wizard’ and current asthma (OR 0.61 [0.39-0.97]) whereas no associations were observed for the third derived factor.

Spray use

The use of at least two types of sprays per week was significantly associated to a high asthma symptom score before (2.68 [1.70-4.24]) and after adjustment (2.50 [1.54-4.03], Table 3). For the use of at least two types of sprays, there was a significant trend according to the frequency of use (p value for trend=0.0002, Table 4). Exclusion of the 40 women occupationally exposed to cleaning agents led to a significant association of similar magnitude (2.47 [1.50-4.07]). Odds ratios were close to 1 for participants with only one symptom. Stronger significant associations were observed between both the use of one and at least two types of sprays and a high asthma symptom score (3.20 [1.48-6.91] and 4.20 [1.78-9.93], respectively) when the analyses were performed only in women without asthma (n=54 women with a high symptom score and without asthma).

For current asthma, no significant associations were observed with the use of one spray weekly with an OR lower than one (0.68 [0.44-1.04]), whereas a significant association was observed for the weekly use of at least two types of sprays (1.67 [1.08-2.56]). The association was of borderline significance (1.50 [0.97-2.32]), p=0.07) after exclusion of the women occupationally exposed.

For asthma control, similar results were observed: ORs were higher for poorly-controlled asthma (Table 3) and associations remained significant after exclusion of the women occupationally exposed with similar magnitudes.

Analyses were also performed using the 3 most commonly-used sprays. Significant associations were observed between exposure to furniture (n=92) and air refreshing (n=160) sprays and a high symptom score (2.06[1.20-3.55] and 1.77[1.14-2.73], respectively) and between glass cleaning sprays (n=161) and current asthma (1.46[1.00-2.13]). No significant associations were observed with asthma control.

Selection bias

To evaluate selection bias, we classified women with asthma according to 'avoidance of a polluted place' (yes/no, Table 5). For current asthma, ORs were higher in women without avoidance of polluted places than in those with avoidance, especially for the use of at least two types of sprays (ORs 2.12 [1.27-3.54] vs 0.99 [0.53-1.85]). A significant negative association was observed for the use of only one spray per week in women with current asthma and with an avoidance of polluted places as compared to women without asthma (OR 0.38 [0.19-0.74]). Similar trends were observed for asthma control (Table 4).

Spray use and asthma sub-phenotypes

Sensitivity analyses regarding the associations between the use of at least two types of sprays and asthma sub-phenotypes are presented in Figures 1 and 2. Compared to the OR for current asthma (OR 1.67 [1.08-2.56]), the ORs were higher for asthma with low FEV_1 (2.67 [1.31-5.48]), for severe asthma (2.20 [1.20-4.04]), for asthma with high IgE (2.11 [1.25-3.57]), for asthma with a high symptom score (2.04 [1.30-3.22]) and for non-eosinophilic asthma (1.88 [1.16-3.06]). The weekly use of at least two types of sprays was significantly related to SPT+ asthma (1.66[1.03-2.68]), with an OR of similar magnitude for SPT- asthma (1.63 [0.78-3.39]), as compared to women without asthma. Whatever the neutrophil levels, similar ORs were observed with the weekly use of at least two sprays (1.66 [1.05-2.65], 1.54 [0.75-3.13], for $\leq$5000/mm^3 and >5000/mm^3, respectively).

Significant or borderline significant associations were observed between the weekly use of at least 2 sprays and childhood- and adult-onset asthma (2.02 [1.20-3.40], 1.60 [0.91-2.81], respectively), with a higher OR for poorly-controlled adult-onset asthma (2.29[1.15-4.54]).The associations between asthma symptom score, asthma status and the use of sprays have been investigated after stratifying on smoking habits, diploma and SPT, and led to

similar results. Significant associations were observed between the use of at least two types of sprays (vs. no spray) and a high asthma symptom score (vs. no symptom) in never smokers (3.17 [1.60-6.29]) and in smokers (2.54 [1.57-4.10]), in women without (3.69 [1.82-7.48]) and with university diploma (1.87 [0.94-3.71], p=0.07), as well as in women without (2.59 [1.19-5.67]) and with atopy (2.76 [1.32-5.78]). Significant associations were observed between the use of at least two types of sprays (vs. no spray) and current asthma in never smokers (1.96 [1.08-3.55]) and in smokers (2.79 [1.12-6.99]), in women without university diploma level (1.91 [1.06-3.44]) and with a lower OR (1.55 [0.83-2.91]) for university level. Associations remained similar after adjustment for diploma level (instead of occupational exposure).

DISCUSSION

The domestic use of at least two types of sprays per week was significantly and positively associated with a high asthma symptom score, and asthma activity (assessed either by current asthma or poorly-controlled asthma). Consistent results were observed after stratification on smoking habits, diploma level and atopy. Our results also suggest a selection bias in the use of domestic sprays which may mask or underestimate the associations between sprays and asthma phenotypes. Our results are consistent with those from the single previous epidemiological survey, in which a dose response relationship was observed between household cleaning sprays and adult-onset asthma [6]. No association was observed among men, probably because only a small number of them (7%) use at least two sprays per week, with an OR of 0.90 for current asthma. The present work suggests that domestic exposure to cleaning sprays, for which an increasing use has been observed [21], may represent a public health issue in women.

Domestic use of sprays and asthma in women

Our results are consistent with a deleterious effect in the use of cleaning sprays on asthma phenotypes and with previous results on household exposure [6], from nurse cohorts [5], and cleaners in offices or private homes [1]. The lack of association between home cleaning, evaluated both by self-report and by PCA, and asthma phenotypes is an argument in favor of the specific effect of products in spray form.

The use of cleaning sprays involved a high risk for inhalation exposure [4]. Peak concentrations of 2-buthoxyethanol (major ingredient of their selected sprayed products) may approach occupational exposure limits and remain in the air after tasks' completion [22]. The deleterious effect of products in spray form such as waterproofing sprays [23], pesticide/insecticide sprays [24, 25] or hair sprays [26] has been established for several diseases.

We observed an association between the use of at least two sprays and IgE-dependent asthma and non-eosinophilic asthma. Further analyses are needed to clarify the underlying mechanisms that may lead to a deleterious effect of sprays on asthma.

Exposure assessment

One limitation of our study relates to the self-reporting of spray exposure which may lead to misclassification errors, recall bias and biased estimates [2]. One could hypothesize that those with asthma and bronchial hyperactivity may feel uncomfortable using sprays and may therefore remember more details and provide a more precise report or also exaggerate on the use of sprays (self-report). However, in a recent paper comparing self-reported occupational exposure to cleaning/disinfecting agents and an expert assessment in the EGEA study, we observed that the validity of self-reported exposure to sprays was good (Cohen's Kappa coefficient: 0.84; sensitivity: 95%; specificity: 91%) [27]. For home cleaning, results were

similar whatever the exposure assessments (self-report, 'essential tasks') and asthma phenotypes. No associations were observed between the 3 most common sprays taken separately and uncontrolled asthma. It was not possible to study specific types of sprays any further due to sample size.

Selection bias or protective effect

Recent European studies [13, 28, 29] support the importance of the healthy worker effect in occupational asthma [12]. Such phenomenon might even be more important for domestic exposures because it is easier to alter behavior regarding domestic habits as opposed to occupational ones. A "healthy home-cleaning effect" implies that women with asthma might use fewer sprays or cleaning products than those without asthma.

For home cleaning, a significant association was only observed with a high asthma symptom score, and the lack of association for asthma might be explained by a healthy home-cleaning effect (which might be more important for diagnosed asthma than for symptoms). ORs for associations between exposures and disease were always higher for a high asthma symptom score than for current asthma, consistent with a selection bias. It was not possible to study the association between health status and avoidance of polluted places only recorded for participants with asthma, which is a limitation of our study.

For exposure to at least two types of sprays, ORs were higher in women without avoidance of polluted places than in those with avoidance. The potential selection bias might be higher for sprays than for home cleaning in general. Women may choose which type of products they will use to clean their home. The Asthma Quality-of-life Questionnaire (AQLQ), not originally designed to study avoidance, has been shown to be valid and reproducible [19]. However, to study selection bias in an optimal way all domestic exposure histories need to be taken into account, as performed previously to study the healthy hire effect in the EGEA

survey [13]. We hypothesize that a selection bias could explain the lack of association of asthma characteristics with the use of one spray. Such a selection bias could also occur, at lesser extent, for the use of 2 sprays and underestimate the association. As it has not been explored before, the hypothesis of a selection bias needs to be considered with caution.

An alternative hypothesis is the protective effect of a moderate use of cleaning products on asthma. Individuals with asymptomatic asthma or poorly-controlled asthma might use, in order to keep their home clean, cleaning products and sprays more often than those without asthma. Studies among children with asthma have shown that an improvement of cleaning practices (to have a "clean" home) reduces asthma symptoms [30]. In our study, OR lower than one, for the use of one spray per week and the first tertile of "Domestic wizard" and "Chemical products", is consistent with this hypothesis. It remains possible that an unstudied confounding factor may explain the finding. Further studies are needed to clarify this point.

Asthma phenotypes

One strength of the EGEA survey is that participants with asthma were well phenotyped. Asthma status at follow-up has been checked carefully by respiratory epidemiologists and clinicians (F Kauffmann, V Siroux, I Pin) and was defined to favor specificity (in doubt, the participant was classified as being without asthma). The asthma symptom score showed a good ability to detect risk factors [15, 16] and was used in both the ECRHS [31] and the EGEA surveys [13]. Current asthma and asthma control were defined as previously in both the EGEA [9] and ECRHS surveys [17]. For the use of at least two sprays, consistent results were observed with sub-phenotypes such as severe asthma, high symptomatic asthma, asthma with low FEV_1, IgE-dependent asthma, and non-eosinophilic asthma. However, in the current study, due to the sample size issue, it is difficult to disentangle whether the use of domestic

sprays is associated more to a high asthma symptom score, poorly-controlled or more severe asthma, as all phenotypes are strongly correlated.

Public Health Implications

An excess risk of asthma in cleaners has been reported for cleaners in offices, hospitals, private homes and in homemakers doing their own domestic work [1], with a potentially high risk in women typically exposed to household cleaning products [11]. Many people are exposed worldwide, both at work and at home, to cleaning agents in spray form, with an increase of use in the last decade [21]. Personnel care and household products represented three quarters of the aerosol products in Europe, which is the world's largest producer, with 5,1 billion aerosols produced in 2009 out of the 12 billion worldwide [21]. Domestic products might be less toxic than industrial cleaning agents. However, household cleaning substances are classified in the top 5 substances most frequently involved in all human exposure complaints [3]. Whereas occupational exposure is controlled and monitored, this is not the case for the general consumer [32]. Furthermore, homemakers have no training on the potential toxicity of the products used. In conclusion, more research is needed on hazards related to domestic use of cleaning sprays.

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Table 1. Characteristics of the population according to the use of sprays

	All	Spray use			
		< 1day/week	≥ 1day/week		
	n=683	n=346	1 spray n=184	≥ 2 types of sprays n=145	p value
Age, mean ± sd	43.8 ± 15.5	43.6 ± 15.3	44.1 ± 16.2	43.0 ± 15.2	p>0.10
BMI					
< 25 kg/m^2	450 (69.4)	239 (72.9)	120 (68.6)	88 (64.2)	
≥ 25 kg/m^2	198 (30.6)	89 (27.1)	55 (31.4)	49 (35.8)	p>0.10
Smoking habits					
Non smokers	376 (55.1)	191 (55.4)	112 (60.9)	68 (46.9)	
Ex-smokers	168 (24.6)	91 (26.4)	35 (19.0)	40 (27.6)	
Smokers	138 (20.2)	63 (18.3)	37 (20.1)	37 (25.5)	0.07
Diploma level					
Primary	154 (22.6)	74 (21.5)	36 (19.6)	41 (28.3)	
Secondary	177 (26.0)	87 (25.3)	47 (25.5)	40 (27.6)	
University	350 (51.4)	183 (53.2)	101 (54.9)	64 (44.1)	p>0.10
Status at the first survey					
Cases	109 (16.0)	50 (14.5)	20 (10.9)	36 (24.8)	
Relatives	388 (56.8)	209 (60.4)	105 (57.1)	72 (49.7)	
Spouses	49 (7.2)	20 (5.8)	17 (9.2)	10 (6.9)	
Controls	137 (20.1)	67(19.3)	42 (22.8)	27 (18.6)	0.01
Asthma symptom score*					
0	284 (41.6)	155 (44.8)	82 (44.6)	42 (29.0)	
1	171 (25.0)	92 (26.6)	48 (26.1)	31 (21.4)	
2 and +	228 (33.3)	99 (28.6)	54 (29.3)	72 (49.6)	0.0001
Asthma					
Never	439 (64.3)	227 (65.6)	130 (70.7)	77 (53.1)	
Current	244 (35.7)	119(34.4)	54 (29.4)	68 (46.9)	0.003
Asthma control	n=227	n=113	n=47	n=65	
Controlled	99 (43.6)	53 (46.9)	22 (46.8)	24 (36.9)	
Poorly controlled	128 (56.4)	60 (53.1)	25 (53.2)	41 (63.1)	0.003
Avoidance of a polluted place#	n=236	n=115	n=55	n=63	
No	153 (64.8)	64 (55.6)	41 (74.6)	45 (71.4)	
Yes	83 (35.2)	51 (44.4)	14 (25.5)	18 (28.6)	0.02
Occupational exposure, last job					
Asthma job exposure matrix(JEM)					
Asthmogens (high probability)	94 (14.2)	47 (14.2)	31 (17.2)	16 (11.3)	p>0.10
Cleaning agents	23 (3.5)	10 (3.0)	7 (3.9)	6 (4.2)	p>0.10
Employed in a cleaning job	20 (2.9)	6 (1.7)	6 (3.3)	8 (5.5)	0.08
Cleaning products (JEM or job)	40 (5.9)	14 (4.1)	12 (6.5)	14 (9.7)	0.05

Figures are n (%); p value is indicated if p ≤ 0.10, p>0.10 is indicated for other non significant associations.

***** Women with current asthma (n=244) had a higher symptom score than those without (n=439) and percentages of women with 0, 1 or at least 2 symptoms were respectively, 7.8, 20.9, 71.3 *vs* 60.4, 27.3, 12.3, p<0.001.

Avoidance of an exposed situation or place, available only in participants with asthma, was evaluated by a positive response to at least one of the four questions (passive smoking, dust, pollution, perfume or odor) on avoidance from the Asthma Quality-of-Life Questionnaire (AQLQ) [19].
There were 8 missing values for the number of sprays used per week, 35 for BMI, 1 for smoking habits, 3 for diploma level. In women with current asthma, there were 17 missing values for asthma control and 8 for avoidance of polluted places.

Table 2. Factor-loading matrix for domestic exposure patterns in women

Questions on tasks, cleaning products or sprays used	**Factor 1** 'Essential tasks'	**Factor 2** 'Domestic wizard'	**Factor 3** 'Chemical products'
Cleaning the house	0.80		
Dusting, sweeping, hoovering, rug beating	0.80		
Mopping, wet cleaning, damp wiping	0.79		
Cleaning the toilet bowl	0.72		
Cleaning the kitchen	0.68		
Liquid multi-use cleaning products	0.64		
Washing clothes by machine	0.56		
Washing powders	0.50		
Bleach	0.48		0.45
Furniture sprays		0.77	
Cleaning windows or mirrors		0.70	
Polishes, waxes		0.69	
Polishing, waxing, shampooing		0.66	
Glass cleaning sprays		0.61	
Ammonia			0.75
Decalcifiers, acids			0.68
Solvents, stain removers			0.64
Sprays for carpets, rugs, or curtains		0.52	0.54

Values < 0.40 after orthogonal transformation are not listed in the table for clarity.

Principal component analysis (PCA) evidenced three domestic exposure patterns for the women. They were labeled 'Essential tasks', 'Domestic wizard', 'Chemical products' (table E2). The first factor ('Essential tasks') was defined by domestic tasks or the use of cleaning products essential for common home cleaning. The second factor ('Domestic wizard') was defined by specific tasks to dust the home perfectly. The third factor ('Chemical products') was defined by the use of chemical products. The score obtained for each domestic exposure pattern was divided into tertiles to study the associations between exposure and asthma phenotypes.

Table 3. Domestic cleaning exposures and asthma phenotypes

	Self-reported exposure, OR [95%CI]			Principal component analysis, OR [95%CI]					
	Home cleaning	Spray use (≥ 1 day/week)		Factor 1 'Essential tasks'		Factor 2 'Domestic wizard'		Factor 3 'Chemical products'	
	≥ 1 day/week	1 type of spray	≥ 2 types of sprays	2nd tertile	3rd tertile	2nd tertile	3rd tertile	2nd tertile	3rd tertile
Symptom score									
0 (n=284)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1 (n=171)	1.17	0.93	0.99	1.32	1.45	0.89	0.85	0.89	0.97
	[0.73-1.88]	[0.59-1.47]	[0.56-1.73]	[0.78-2.26]	[0.85-2.48]	[0.54-1.47]	[0.50-1.44]	[0.53-1.49]	[0.58-1.62]
≥ 2 (n=228)	**1.85**	0.92	**2.50**	**1.68**	1.57	0.75	1.21	0.90	0.97
	[1.16-2.94]	[0.59-1.45]	**[1.54-4.03]**	**[1.02-2.76]**	[0.93-2.64] *	[0.46-1.22]	[0.75-1.96]	[0.56-1.45]	[0.59-1.59]
Current asthma									
Never (n=439)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
All (n=244)	1.34	0.68	**1.67**	1.42	1.27	**0.61**	1.17	0.97	0.84
	[0.87-2.05]	[0.44-1.04] *	**[1.08-2.56]**	[0.92-2.20]	[0.78-2.06]	**[0.39-0.97]**	[0.76-1.81]	[0.64-1.46]	[0.54-1.30]
Controlled	1.12	0.67	1.32	0.78	1.24	**0.52**	1.04	0.85	0.87
(n=99)	[0.66-1.90]	[0.38-1.18]	[0.75-2.34]	[0.42-1.46]	[0.66-2.30]	**[0.28-0.97]**	[0.54-1.84]	[0.47-1.52]	[0.48-1.59]
Poorly controlled	1.50	0.65	**2.04**	**2.06**	1.25	0.72	1.36	1.08	0.84
(n=128)	[0.88-2.52]	[0.38-1.12]	**[1.25-3.32]**	**[1.19-3.54]**	[0.69-2.26]	[0.42-1.25]	[0.81-2.28]	[0.64-1.82]	[0.48-1.45]

Odds ratios were adjusted for age, smoking habits, body mass index, and occupational exposure.

Principal component analysis (PCA) evidenced 3 domestic exposure patterns for the women (See table E1, online supplement) labeled 'Essential tasks' (factor1), 'Domestic wizard' (factor 2), and 'Chemical products' (factor 3).

*p=0.09 (for 'Essential tasks' and asthma symptom score) and p=0.07 (for one spray and asthma)

In women with current asthma, there were 17 missing values for asthma control.

Table 4. Self-reported exposure to sprays and asthma symptom score

	Exposure to <u>one spray</u>		**Exposure to <u>at least 2 types of sprays</u>**	
	≥ 1 day/week		**≥ 1 day/week**	
	OR [95%CI]		**OR [95%CI]***	
Symptom score	1 to 3 days/ week	4 to 7 days/ week	1 to 3 days/ week	4 to 7 days/ week
0 (n=284)	1.00	1.00	1.00	1.00
1 (n=171)	0.84 [0.51-1.40]	1.26 [0.58-2.72]	0.87 [0.43-1.77]	1.18 [0.52-2.67]
≥ 2 (n=228)	0.92 [0.56-1.51]	0.91 [0.40-2.10]	**2.04 [1.13-3.68]**	**3.27 [1.65-6.45]**

Odds ratio were adjusted for age, smoking habits, body mass index, and occupational exposure.

*p value for trend = 0.0002 for the use weekly of at least 2 type of sprays

Table 5. Role of avoidance of polluted places on the association of domestic cleaning exposures and current asthma

	Exposed, n home cleaning/ ≥1 / 1/≥2 sprays	Self-reported exposure: Home cleaning ≥ 1 day/week OR [95%CI]	Spray use (≥ 1 day/week): At least 1 spray OR [95%CI]	1 spray/week OR [95%CI]	2 sprays/week OR [95%CI]
Never asthma (reference), n=439		1.00	1.00	1.00	1.00
Current asthma, no avoidance					
All, n=149	112/82/37/45	1.39[0.82-2.34]	1.33[0.89-1.98]	0.90[0.55-1.47]	**2.12[1.27-3.54]**
Controlled asthma, n=70	49/36/17/19	1.04[0.57-1.90]	1.15[0.68-1.96]	0.84[0.44-1.61]	1.72[0.89-3.32]
Poorly controlled, n=67	54/39/14/25	1.80[0.90-3.63]	1.61[0.93-2.79]	0.89[0.43-1.81]	**2.87[1.53-5.40]**
Current asthma, avoidance					
All, n=83	66/32/14/18	1.19[0.64-2.22]	**0.59[0.36-0.98]**	**0.38[0.19-0.74]**	0.99[0.53-1.85]
Controlled asthma, n=22	18/6/2/4	1.59[0.51-5.02]	0.39[0.15-1.03]†	**0.20[0.04-0.89]**	0.75[0.24-2.34]
Poorly controlled, n=57	46/24/11/13	1.14[0.55-2.35]	0.77[0.43-1.37]	0.52[0.24-1.10]†	1.21[0.59-2.48]

Odds ratios were adjusted for age, smoking habits, body mass index, and occupational exposure.

Avoidance of an exposed situation or place was evaluated by a positive response to at least one of the 4 questions on avoidance in AQLQ for participants with asthma (passive smoking, dust, pollution, perfume or odor). Women with asthma, with (n=83) and without (n=153) avoidance, were compared to those who had never had asthma (n=439).

†p=0.06 (for at least one spray and controlled asthma) and p=0.09 (for one spray and poorly controlled asthma)

In women with current asthma, there were 17 missing values for asthma control**,** 8 for avoidance of polluted places.

Figure 1. Association of domestic exposures to two sprays with current asthma subphenotypes

Odds ratios (95% confidence interval), expressed with 'never asthma' as reference, were adjusted for age, smoking habits, BMI and occupational exposure to asthmogens.

Symptom score was defined following Pekkanen and Sunyer et al [15, 16]. Low/high symptom score referred to score below/equal or above 2 asthma-like symptoms (out of a maximum of five, see methods)

FEV_1 %predicted were based on Stanojevic et al values (Am J Respir Crit Care Med 2008; see online supplement)

Missing data for PD_{20} to methacholine challenge were mostly due to low FEV_1values (challenge not performed when FEV_1%pred < 80%)

Skin prick test positivity refers to a wheal > 3mm for any of 12 allergens

Blood eosinophilia ($\geq 250/mm^3$) was defined as previously reported in EGEA by Nadif et al (Thorax 2009; see online supplement).

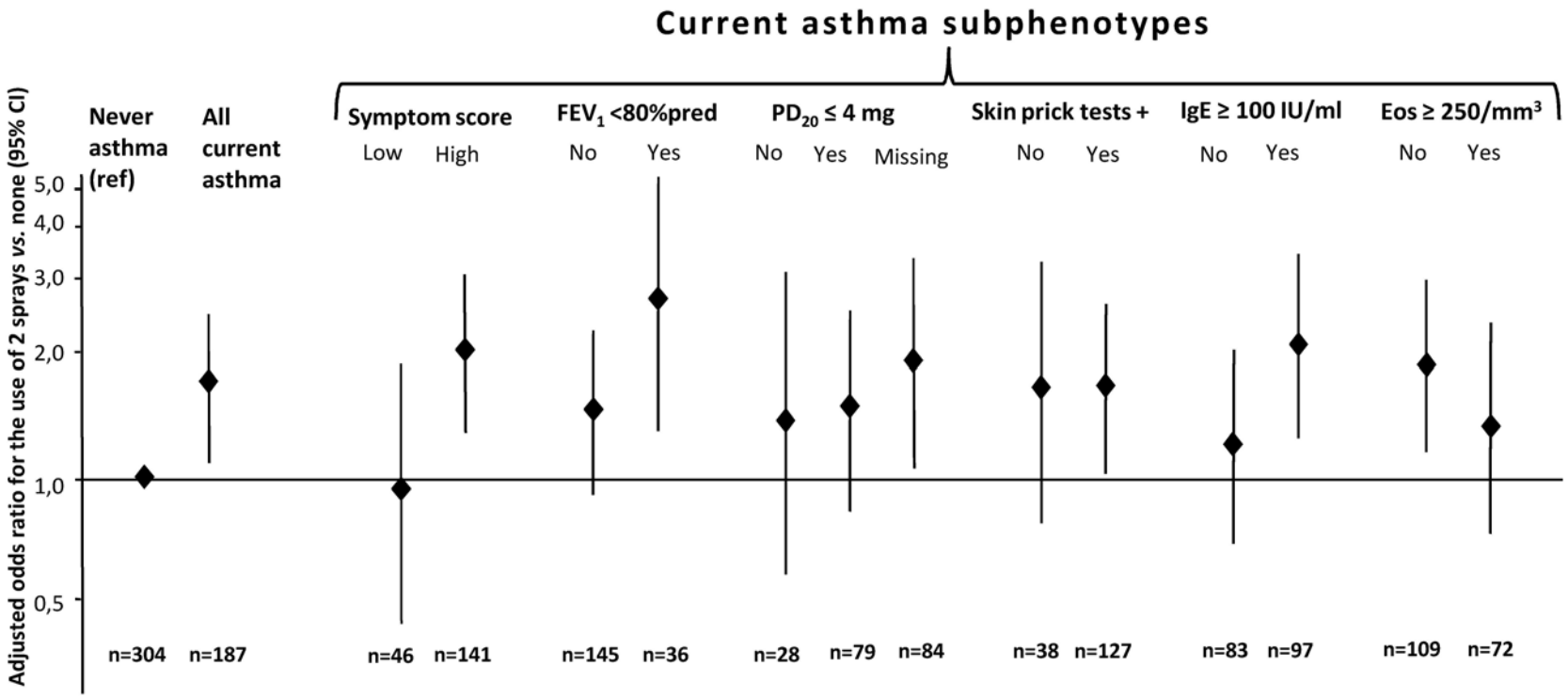
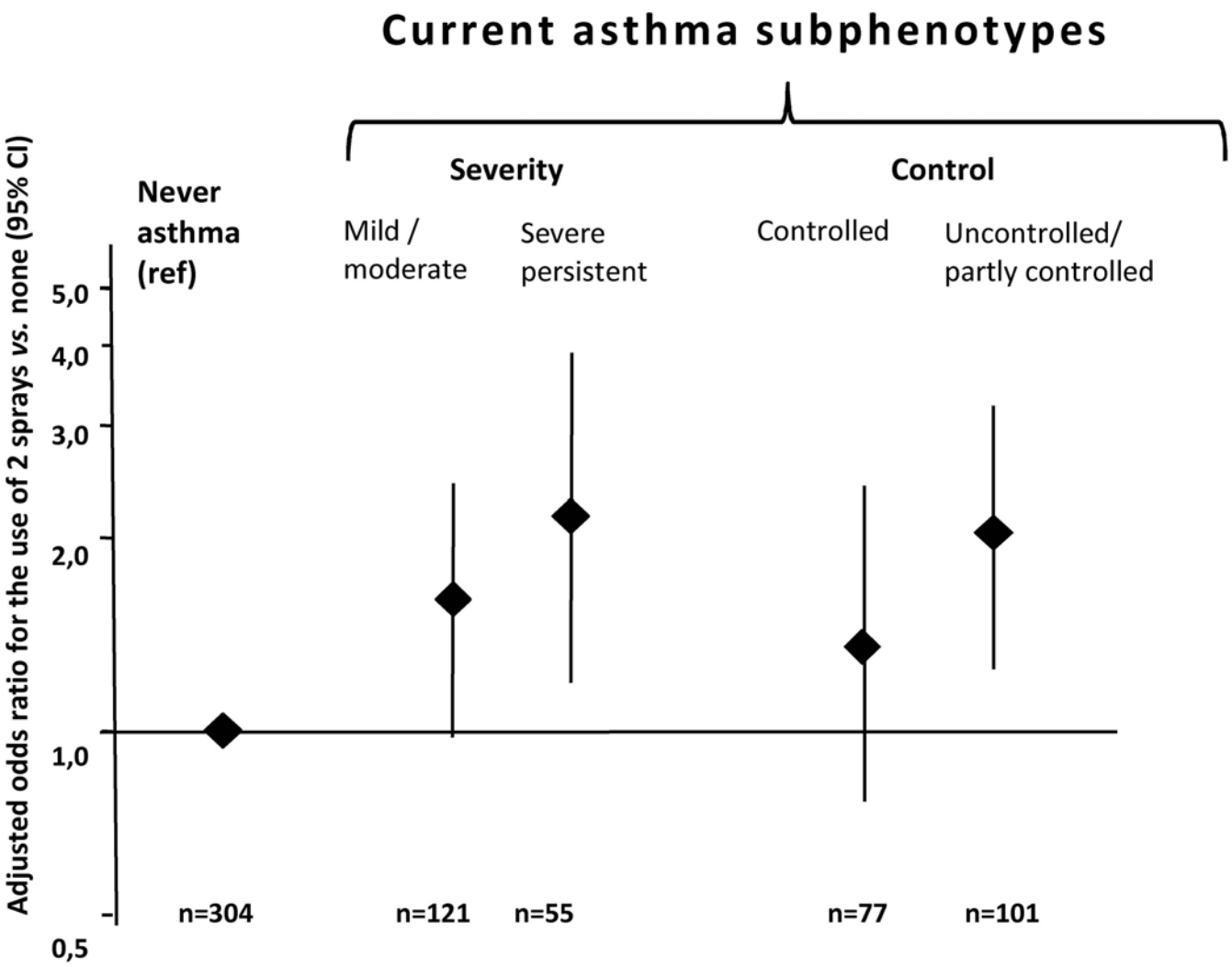

Current asthma subphenotypes
Adjusted odds ratio for the use of 2 sprays vs. none (95% CI)
5,0
4,0
3,0
2,0
1,0
0,5
Never asthma (ref)
All current asthma
Symptom score
Low
High
FEV1 <80%pred
No
Yes
PD20 ≤ 4 mg
No
Yes
Missing
Skin prick tests +
No
Yes
IgE ≥ 100 IU/ml
No
Yes
Eos ≥ 250/mm3
No
Yes
n=304
n=187
n=46
n=141
n=145
n=36
n=28
n=79
n=84
n=38
n=127
n=83
n=97
n=109
n=72

Figure 2. Association of domestic exposures to at least two sprays with current asthma subphenotypes, defined by composite scores (severity and control)

Odds ratio (95% confidence interval), expressed with ‘never asthma’ as reference, were adjusted for age, smoking habits, BMI and occupational exposure to asthmogens.

Asthma severity was assessed, as previously described in detail by de Marco et al [18], following the 2002-2006 GINA principles, combining clinical feature of the patients and asthma treatment level at the time of examination.

Asthma control was assessed, as described by Cazzoletti et al [17] and already used in EGEA by Siroux et al [9], based on the GINA 2006-2010 guidelines, combining diurnal and nocturnal respiratory symptoms, asthma attacks, lung function, hospitalization for asthma and use of reliever medication.


Current asthma subphenotypes
Severity
Control
Never asthma (ref)
Mild / moderate
Severe persistent
Controlled
Uncontrolled/ partly controlled
Adjusted odds ratio for the use of 2 sprays vs. none (95% CI)
5,0
4,0
3,0
2,0
1,0
0,5
n=304
n=121
n=55
n=77
n=101

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