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Household use of green and home-made cleaning products, wipe application mode and asthma among French adults from the CONSTANCES cohort

Emilie Pacheco Da Silva^a, Guillaume Sit^a, Marcel Goldberg^b, Bénédicte Leynaert^a, Rachel Nadif^a, Céline Ribet^b, Nicolas Roche^c, Marie Zins^b, Raphaëlle Varraso^a, Orianne Dumas^a, Nicole Le Moual^a

^a Université Paris-Saclay, UVSQ, Univ. Paris-Sud, Inserm, Équipe d'Épidémiologie Respiratoire Intégrative, CESP, 94807 Villejuif, France

^b Université de Paris, Unité "Cohortes en Population" INSERM, Université Paris Saclay, UVSQ, UMS 011, Paris, France

^c Pneumologie, Hôpital Cochin, APHP.Centre – Université de Paris, Paris, France

Corresponding author:

Emilie Pacheco Da Silva
Inserm, CESP, Équipe d'Épidémiologie Respiratoire Intégrative
16, avenue Paul Vaillant Couturier
94807 Villejuif, France

e-mail: emilie.pacheco-da-silva@inserm.fr

1 Abstract

2

3 While exposure to irritant and sprayed cleaning products at home is known to have a harmful
4 role in asthma, the potential health effect of other categories or forms has not been investigated.

5

6 We studied the associations of household use of cleaning products, including green, home-made
7 products and disinfecting wipes, with asthma based on data from the large French population-
8 based Constances cohort.

9

10 Participants completed standardized questionnaires on respiratory health and household use of
11 cleaning products. Cross-sectional associations of cleaning products with current asthma,
12 adjusted for gender, age, smoking status, BMI and educational level, were evaluated by logistic
13 regressions.

14

15 Analyses were conducted in 41,570 participants (mean age: 47 years, 56% women, weekly use
16 of the six specific products/forms studied varied from 11% to 37%). Weekly use of irritants
17 (OR=1.23[1.13-1.35]), scented (OR=1.15[1.06-1.26]), green (OR=1.09[1.00-1.20]) and home-
18 made products (OR=1.19[1.06-1.34]), as well as sprays (OR=1.18[1.08-1.29]), disinfecting
19 wipes (OR=1.21[1.09-1.34]) were significantly associated with asthma, with significant trends
20 according to the frequency of use. When they were not co-used with irritants/sprays,
21 associations were reduced and persisted only for disinfecting wipes.

22

23 Weekly use of disinfecting wipes at home was associated with current asthma, but fewer risks
24 were observed for the use of green and home-made products.

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30 **Keywords:** Asthma; Household cleaning; Disinfecting wipes; Green products; Home-made
31 cleaning products; Irritants

Practical implications:

- Green and home-made products or disinfecting wipes, are increasingly attracting the interest of consumers, at the expense of conventional products, but their respiratory health risks have not been investigated.
- Weekly use of disinfecting wipes at home was associated with asthma, similarly to irritants and sprays, in this study of 41,570 French adults from the CONSTANCES cohort.
- These associations persisted only for disinfecting wipes and were no longer observed for green and home-made products, when considering the co-use of irritants and sprayed products at home.
- Our results suggest that using green and home-made products may induce fewer risk for respiratory health than using conventional ones.

1. Introduction

Cleaning products are widely used, at home and in the workplace, and contribute significantly to chemical exposure in the indoor environment ^{1,2}. These products consist of a complex and diverse mixture of ingredients, with various physical and chemical properties, which can have irritant or sensitizing effects ^{1,3-7}. Evidence of the harmful role of these products on respiratory health, especially on asthma, comes largely from epidemiological studies carried out in populations highly exposed at work ^{3,8}. Over the past fifteen years, a growing number of studies have investigated the effects of indoor exposure to household cleaning products and similar results have been observed. Most studies so far have considered the potential impact of the personal use of cleaning products containing irritant agents ⁹⁻¹³ or applied in a spray form ^{9,11,13-18}. Personal use of these two categories of cleaning products at home has been shown to be associated with the development ^{13,18}, clinical expression ^{10-12,14,16} and poor control of asthma ^{9,16}. The clinical expression of asthma was mainly studied through the evaluation of current asthma ^{10,12,14,16} and the asthma symptom score ^{11,12,14,16}. Studies have suggested that risks for respiratory health could be even more important for women who are more involved in household tasks, and therefore also more exposed to cleaning products ¹⁹. In addition, the female lungs might be more susceptible to the harmful damages of environmental exposures ²⁰. However, only few studies have assessed the associations between the use of cleaning products and asthma on mixed gender populations ^{13,18}.

A wide variety of cleaning products, in several application modes and for various uses, are available to consumers ². More recently, “eco-friendly” certified cleaning products are increasingly attracting the interest of consumers, manufacturers and distributors. However, although the formulations of these products are considered to be less harmful, especially for the environment, their potential health effects have not been studied for household use ^{6,8,21}. An occupational study investigated for the first time the health effects of environmentally preferable products and did not show increased respiratory symptoms associated with this exposure, in contrast to exposure to traditional products ²². More recently, an experimental study found that green products used during bathroom cleaning generated less total volatile organic compounds than other conventional products ²³. In addition, an interventional study showed a significant decrease in air concentrations of multiples volatile organic compounds when using green products, instead of using conventional ones ²⁴. While an increasing number of people are making their own products for home cleaning, e.g. from white vinegar ²⁵, baking soda, soap and sometimes essential oils, their health consequences have not yet been assessed.

35 Exposure to cleaning products depends on both the physico-chemical characteristics of the
36 product and its application mode ^{1,6,21,26}. Spray formulations increase the risk of inhalation and
37 facilitates the penetration of sprayed particles into the lower respiratory tract ^{19,27,28}. Respiratory
38 health risks associated with spraying application mode have been well-established and studies
39 found consistent associations with asthma both at home ^{9,14,16,18} and at work ²⁹⁻³³. While a
40 German study showed an association between a high level use of disinfectants at home,
41 regardless of application mode, and a risk of incident asthma in young adults ¹³, no study has
42 investigated the potential impact of applying disinfectants in wipes form. Because ready-to-use
43 wipes consist of towels saturated with diluted disinfectant and other chemical products ³⁴, with
44 both irritant and sensitizing properties ³, they may contain much more products compared to a
45 product applied with a cloth and then wiped.

46 Thus, despite the accumulation of evidence on the adverse effects of the household use of
47 cleaning products on asthma, evidence is lacking for some products including green and home-
48 made products, and for some application modes, such as wipes, which are all increasingly used
49 but their impact has never been studied to date in epidemiological surveys. We aimed to
50 investigate the associations between household use of six large categories of cleaning products,
51 current asthma and the asthma symptom score among French adults from the CONSTANCES
52 cohort, after considering potential co-exposures at home to irritants and sprays for which
53 respiratory health effects have been shown. We hypothesized that applying disinfectants in a
54 wipe form would have adverse effect on respiratory health and using green and home-made
55 products would have less adverse effect on respiratory health, compared to conventional
56 products.

57 2. Methods

58

59 2.1. Population

60

61 The CONSTANCES study is a French prospective and generalist epidemiological cohort
62 initiated in 2012, which focuses on occupational, behavioral and social factors related to chronic
63 diseases and aging ³⁵. The study enrolled 214,816 adults, aged between 18 and 69 years at
64 inclusion, randomly selected among the insured subjects of the general social security scheme
65 of 21 departments of metropolitan France. Information on respiratory health, including asthma,
66 was collected by self-administered standardized questionnaires at inclusion. Follow-up
67 questionnaires are sent every year. Household exposure to cleaning products was estimated
68 during the follow-up in 2019, by a standardized questionnaire.

69 As respiratory health and household exposures were evaluated at different time-points, we
70 only included participants who completed the baseline (including respiratory health) and 2019
71 (including household exposures) questionnaires within a timeframe of two years or less. Thus,
72 the analyses focused on participants included in the cohort in 2017 and 2018 with available data
73 on household exposure in 2019. In our study, we assume no major change in household cleaning
74 habits in two years.

75

76 2.2. Current asthma and the asthma symptom score

77

78 Participants who answered positively to the question “Have you ever had asthma?” were
79 considered as “ever asthma”, and otherwise as “never asthma”. Among participants with “ever
80 asthma”, those who reported asthma symptoms (wheezing, woken up by a feeling of chest
81 tightness or an attack of shortness of breath, attack of shortness of breath at rest or after
82 exercise), asthma attacks or asthma treatment in the past 12 months were classified as “current
83 asthma” ^{10,12,14,16}. Participants with remission asthma were excluded from these analyses
84 (Figure 1).

85 The asthma symptom score was calculated as described in the literature ^{36,37}, regardless of
86 asthma status. It corresponds to the number of asthma symptoms out of five reported in the
87 standardized questionnaire in the past 12 months (wheezing with shortness of breath, woken up
88 by a feeling of chest tightness or an attack of shortness of breath, attack of shortness of breath
89 at rest or after exercise). It was studied as a continuous variable (0 to 5).

90

2.3. Household use of cleaning products

The household exposure questionnaire evaluated the participants' weekly use of various products at home in the past 12 months. We studied household exposure to six large categories including four type of compounds: irritants (maximum frequency reported for bleach, ammonia, acids and solvents), scented products (maximum frequency reported for scented cleaning products, home fragrances, scented candles, electric or spray air freshener), green products and home-made products, and two application modes: sprays (maximum frequency reported for furniture, glass, floor, bath, oven, ironing, air freshener, insecticide, or other use) and disinfecting wipes.

The frequency of use of home cleaning products was reported according to four categories: never, less than one day a week, 1-3 days a week or 4-7 days a week. In the analyses, "never" and "less than one day a week" were grouped together to define the "unexposed" group, as it is commonly done^{10-12,14,16,18}. For a given cleaning product, participants classified as "unexposed" but who are weekly exposed to one of the others five large categories studied were excluded from the analyses. Thus, the reference group (not weekly exposed to any of the six large categories) was the same for all analyses, as previously done^{9,38}. Frequency of use was studied as a variable in three classes (reference, 1-3 days a week, 4-7 days a week) in the main analyses and as a binary variable (reference, ≥ 1 day a week) in stratified analyses.

The number of cleaning products used was calculated for irritants, sprays and scented products (composite variables). The number of irritants used per week was assessed in three classes (reference, 1 irritant per week, ≥ 2 irritants per week). The number of sprays and the number of scented products were defined in four classes (reference, 1 product per week, 2 products per week, ≥ 3 products per week).

2.4. Statistical analysis

Associations between household exposure to cleaning products, current asthma and the asthma symptom score were evaluated by logistic and negative binomial regression models, respectively. All analyses were adjusted for gender, age (continuous), smoking status (never smoker, ex-smoker, current smoker), Body Mass Index (BMI; <24.9 , $25-29.9$, >30 kg/m²) and educational level ($<$ high school diploma, high school to 1-level university, 2-level university to 4-level university, ≥ 5 -level university). As associations of household exposure to irritants⁹⁻¹³ and sprays^{9,14,16,18} with asthma were previously observed in the literature, we conducted a

125 sensitivity analysis to examine whether the potential associations observed for newly-studied
126 products (scented products, disinfecting wipes, green and home-made products) reflect the co-
127 exposure to irritants and/or sprays. For this analysis, we defined a three-class variable
128 (reference, exposed to a given product without being co-exposed to irritants and sprays, co-
129 exposed to irritants and/or sprays for a given product). In order to examine whether the six large
130 categories have an influence on the age of onset of asthma, we also studied the associations
131 between household exposure to cleaning products and the age of the onset of asthma (never
132 asthma, current asthma developed before 18 years, current asthma developed after 18 years) by
133 multinomial logistic regression models. In addition, analyses were stratified by sex, smoking
134 status, educational level and by household help (binary variable (yes/no) according to the
135 answer to the question “Are you getting help to do home cleaning, e.g., husband, household
136 employee, family members, friends,...?”) to evaluate the robustness of the results. Finally, we
137 performed another sensitivity analysis to consider occupational exposures to cleaning products,
138 which could be much more important than household exposures. Therefore, we repeated the
139 main analyses after exclusion of participants professionally exposed to cleaning products over
140 the last two years, estimated after a preliminary application of the OAsJEM (Occupational
141 Asthma specific Job-Exposure Matrix ³⁹) for jobs exposed to “high level chemicals
142 disinfectants”, “indoor cleaning” or “bleach” (49 job codes). A full transcoding (international
143 job codes to French job codes) of the OAsJEM by experts is still in progress for future finale
144 application in CONSTANCES.

145 The analyses were performed using the statistical analysis software SAS version 9.4 (SAS
146 Institute, Cary, NC, USA).

147 3. Results

148

149 Among the 68,168 participants included in the CONSTANCES cohort in 2017 and 2018,
150 47,643 had household exposure data available in 2019. Participants with missing data on
151 smoking status (n=1,443), BMI (n=1,332) or both on ever asthma status and asthma symptom
152 score (n=98) were excluded. Therefore, our study population consisted of 44,770 participants
153 (Figure 1). Participants non-included in 2017 or 2018, slightly differed from those included in
154 the present study: they were older, more often men and with a lower educational level, with less
155 current asthma and symptoms (Supplemental material, Table S1). Participants who did not
156 complete questionnaire for household exposure differed from the studied population: they were
157 younger, more often men, current smokers, obese, with a lower educational level, with more
158 current asthma and symptoms. The analyses related to current asthma were carried out on
159 41,570 participants without missing data on asthma status, including 4,144 with current asthma.
160 Analyses related to the asthma symptom score were conducted in 43,503 participants without
161 missing data on this outcome.

162

163 Participants were 46.8 years old on average (Table 1), 56% were women, 34% were ex-smokers
164 and 15% were current smokers, 30% were overweight (BMI > 25 kg/m²) and 28% had a high
165 educational level (≥5-level university). Regarding exposures to cleaning products, weekly use
166 of the six specific products/forms studied varied from 11% to 37% and 27% of participants
167 reported no weekly use at home. Around 50% reported having help to do home cleaning and
168 8% had a potential occupational exposure to cleaning products. Among participants not weekly
169 exposed to cleaning products at home, 4% reported never using any of the six categories of
170 cleaning products studied, whereas 96% used at least of one these products less than one day
171 per week (Supplemental material, Table S2). Participants with current asthma were more often
172 women, younger and current smokers, had a higher BMI and educational level, and were more
173 exposed to cleaning products than participants without asthma (Table 1). These characteristics
174 were also described according to the asthma symptom score (Supplemental material, Table S3).

175

176 3.1. Household use of cleaning products and asthma

177

178 Weekly use of cleaning products was significantly associated with current asthma, regardless
179 of the categories of products used (Table 2). Indeed, we observed a significant dose-response
180 association between the frequency of use of irritants, sprays, scented products, disinfecting

181 wipes, green products, home-made products and current asthma, before and after adjustment
182 for potential confounders. A dose-response association was also observed for the number of
183 irritants, sprays, scented products used and current asthma (Supplemental material, Figure S1).
184 These associations were slightly stronger for participants with an adult onset asthma,
185 especially for disinfecting wipes, compared to participants with asthma onset in childhood
186 (Supplementary material, Figure S2). The associations between weekly use of cleaning
187 products, studied in two classes, and current asthma were of similar magnitude after
188 stratification by gender, smoking status, educational level and household help, without
189 statistically significant interactions (Supplementary material, Table S4). In addition, after
190 exclusion of participants with potential occupational exposure in the last two years (n = 2,699),
191 the same associations remained significant (Supplementary material, Table S5).

192

193 Regarding the asthma symptom score, we observed a consistent dose-response association
194 with the frequency of use of the six large categories of cleaning products (Figure 2). A dose-
195 response association was also observed for the number of irritants (1 irritant: 1.19 [1.13-1.26];
196 ≥ 2 irritants: 1.27 [1.19-1.37]), sprays (1 spray: 1.17 [1.11-1.24]; 2 sprays: 1.22 [1.14-1.31]; ≥ 3
197 sprays: 1.27 [1.19-1.36]) and scented products used (1 perfume: 1.16 [1.09-1.22]; 2 perfumes:
198 1.30 [1.21-1.40]; ≥ 3 perfumes: 1.55 [1.42-1.69]). The associations appeared slightly stronger
199 than those previously noticed for current asthma. These results persisted after stratification by
200 several factors (gender, smoking status, educational level, household help and the asthma
201 status) and after exclusion of participants with potential occupational exposure in the last two
202 years (results not shown).

203

204 3.2. Co-exposure to irritants and sprays

205

206 The associations between a given cleaning product (disinfecting wipes, scented, green and
207 home-made products) used without irritants and sprays and current asthma were generally
208 weaker and not significant, compared to the co-use of these two products (Table 3), except for
209 disinfecting wipes which showed a significant association with current asthma whether used
210 alone (OR=1.16 [1.00-1.36]) or together with irritants or sprays (OR=1.21 [1.09-1.35]).

211 Furthermore, associations between these four cleaning products used at the highest frequency
212 (4-7 days a week), without co-exposure to irritants/sprays and current asthma remained not
213 significant (Supplementary material, Table S6).

214

215 Regarding the asthma symptom score, when the co-exposure was considered, the associations
216 for disinfecting wipes and scented products used without irritants or sprays were weaker, but
217 still significant (Figure 3). However, for the use of green and home-made products, the
218 associations were weaker and no longer significant.

219 4. Discussion

220

221 In this cross-sectional analysis of data from the CONSTANCES cohort, consistent significant
222 associations were found between weekly use of six large categories of cleaning products, both
223 for current asthma and the asthma symptom score, with a dose-response trend according to
224 frequency of use. Moreover, we found a dose-response association with the number of irritants,
225 sprays and scented products used. After considering the co-exposure to irritants or sprayed
226 products at home, well-established risk factors for asthma, significant associations persisted for
227 disinfecting wipes for both outcomes, whereas no association were observed for green and
228 home-made products.

229

230 Our findings are consistent with previous epidemiological studies on household exposure to
231 irritants, sprays and asthma. As in our study, a dose-response association was recently observed
232 between the frequency, the number of irritants used and current asthma in a large cohort of
233 elderly French women (Étude Épidémiologique de l'Éducation Nationale – E3N)¹⁰. Regarding
234 sprays, our results are consistent with those of ECRHS, the first study focusing on this issue¹⁸,
235 in which a dose-response association between the frequency of use of sprays and new-onset
236 asthma was identified. Regarding gender, borderline significant associations were observed
237 among men in ECRHS¹⁸. Given that we reported significant associations of the same
238 magnitude in both men and women, their finding can probably be explained by the smaller
239 number of men using at least two sprays per week. As in our study, in another French cohort
240 (Epidemiological study on the Genetics and Environment of Asthma – EGEA), weekly use of
241 at least two sprays was associated with current asthma and a high asthma symptom score (at
242 least two symptoms of asthma)¹⁶. Furthermore, current asthma was associated with the weekly
243 use of only one spray. Also in E3N, weekly use of at least one spray was significantly associated
244 with current asthma only among women without household help¹⁴, while in CONSTANCES
245 we found significant associations for both participants with and without household help. Since
246 the E3N cohort consists exclusively of elderly women, the help they benefit from is likely
247 provided by a household employee, so that they are likely to do less home cleaning themselves.
248 In the CONSTANCES cohort, as participants are younger, the household help could correspond
249 to a family member as well as a household employee, which the questionnaire does not allow
250 to determine. Our results for sprayed products add additional evidence on the negative impact
251 of this application mode on respiratory health. However, the sale of products in this form has
252 increased over the last decades and is still at high level^{18,40}.

253

254 To our knowledge, this is one of the first epidemiological studies testing the associations
255 between the household use of scented products and asthma and the first examining disinfecting
256 wipes, green, home-made products. For scented products, we first observed a dose-response
257 association between their frequency of use, current asthma and the asthma symptom score.
258 After considering co-exposures, the association with current asthma was no longer observed
259 but the one with the asthma symptom score persisted. Our results are consistent with those of
260 Lemire et al. in E3N ¹⁰ who found that weekly use of scented products identified using two
261 exposure assessment methods (self-questionnaire and a smartphone application linked to a
262 product compounds database) was significantly associated with at least one symptom of asthma.
263 Our results also suggest a deleterious effect of disinfecting wipes on asthma since we found a
264 dose-response association between the frequency of use of this product, current asthma and the
265 asthma symptom score. Moreover, this association is robust because it persisted in most
266 sensitivity analyses. For green products, our results are consistent with those of Garza et al. ²²
267 as we found less evidence for an association with asthma. Indeed, the associations observed
268 were lower than for other products and were no longer present after considering co-exposures,
269 nor among never smokers. Thus, in addition of being safer for the environment ⁸, green products
270 may be the category of cleaning products to be less harmful for respiratory health, compared to
271 the other products studied. For home-made products, the strength of the association with asthma
272 was close to those found in conventional products but this association disappeared after
273 considering co-exposures.

274

275 The underlying mechanisms involved in the respiratory effects of cleaning products are still
276 poorly understood ^{27,41}. The assumptions are that cleaning products can have two different
277 effects: some will have an irritating effect and others a sensitizing effect on the respiratory tract
278 ^{4,5,7}. However, some products may induce both effects, depending on whether exposure occurs
279 at a low or high concentration, as suspected for quaternary ammonium compounds, for example
280 ^{1,4,27}. Furthermore, products applied in a spray form contain perfumes and may therefore have
281 a sensitizing effect and induce asthma through allergic mechanisms ^{42,43}. In the scientific
282 literature, associations of the same magnitude for allergic and non-allergic asthma were once
283 reported with the use of sprays ¹⁶. In addition, another study reported strong association between
284 weekly use of at least one spray and current asthma among women without allergic rhinitis,
285 whereas no association was shown among women with allergic rhinitis ¹⁴. The other cleaning
286 products may rather operate by an irritating mechanism and would be more associated with

287 non-allergic asthma as previously shown ¹². The inhalation of irritating compounds may cause
288 epithelial damage, increase lung permeability and oxidative stress ^{4,7,8,42,44}.

289

290 The main strength of our study is that it is based on data from the large CONSTANCES cohort,
291 which allowed us to assess the effect of cleaning products in a large number of participants,
292 randomly selected among the general French population, and thus limits potential problems of
293 statistical power. Moreover, these data also allowed us to perform analyses on a mixed gender
294 population, with a wide range of age, whereas most epidemiological studies were only able to
295 study the impact of the household use of cleaning products on asthma among women ^{9,10,12,14,16}.
296 Secondly, we took into account the co-use of products for which associations with the
297 respiratory health were previously shown, including irritants ⁹⁻¹³ and sprays ^{9,14,16,18}. Another
298 strength of our study is the use of the asthma symptom score, which is an alternative method
299 recommended to assess asthma risk factors with greater statistical power ^{36,37}. By using this
300 definition, we showed more significant associations than with the traditional dichotomous
301 definition. Lastly, the results persisted after performing several sensitivity analyses, which
302 underlines their robustness. In addition, results for childhood and adult onset asthma are
303 consistent with other epidemiological studies in occupational context suggesting that the use of
304 cleaning products can induce asthma incidence but also exacerbate a pre-existing asthma ²¹.

305

306 Our study also has some limitations. First, household exposure to cleaning products was only
307 assessed by questionnaire, thus relying on participant statement, which could induce differential
308 and non-differential misclassification biases. Eight epidemiological studies have discussed this
309 type of bias, some of them estimated household exposure to cleaning products by different
310 methods (Principal Component Analysis – PCA ^{14,16}, composite score ¹⁴, scanning cleaning
311 products barcodes by a smartphone application linked to a product compounds database ¹¹, ...) and
312 observed similar results for irritants and sprays to those obtained by crude questionnaire-
313 based assessments. In addition, it was recently highlighted that almost all cleaning products
314 contain perfumes ¹¹. It is then possible that, when assessing exposure to scented products by
315 questionnaire, participants may not be aware that some contain perfumes and may
316 underestimate their exposure. In general, it would be important to develop more objective
317 methods to estimate household exposure to cleaning products. A recently developed
318 smartphone application ¹¹ may allow to identify the chemical compounds specifically causing
319 the health effect to better understand the mechanisms by which they can induce or exacerbate
320 asthma. Secondly, the use of green and home-made cleaning products could be influenced by

321 participants' lifestyle and socio-economic level. Indeed, participants with a healthier lifestyle
322 may perceive such products to cause the least adverse effects on the environment and the health
323 and rather use them than conventional ones. In addition, these products can be less affordable
324 than conventional ones. However, to consider this possibility, associations were adjusted on
325 major lifestyle risk factors known for asthma. Finally, because of the cross-sectional design of
326 our study and the assessment of respiratory health and household exposures 2 years apart, we
327 were not able to consider the temporal relationship between the use of cleaning products and
328 asthma. A possible reverse causation phenomenon, i.e. participants with current asthma using
329 more frequently cleaning products at home than non-asthmatic participants in order to eliminate
330 dust or molds which may cause symptoms, might partly explain our results. However,
331 significant associations were observed for sprays and irritants, but not for green and home-made
332 products when used alone, and it seems unlikely that participants with current asthma use
333 specifically more irritants and sprays than green and home-made products. In addition, our
334 results are consistent with literature in occupational settings^{45,46} where workers do not choose
335 the frequency of cleaning tasks, and with associations observed between household use of
336 sprays or disinfectants and new-onset asthma in longitudinal studies^{13,18}. Therefore, a reverse
337 causation phenomenon is unlikely to explain associations assessed in our manuscript.

338

339 5. Conclusions

340

341 In conclusion, household use of cleaning products with various application modes, was
342 associated with asthma among French adults. Based on our results, it seems less harmful to use
343 liquid products than sprays or ready-to-use disinfecting wipes and to use green products than
344 conventional ones. Further research is needed on this issue, in particular to clarify the impact
345 of green and home-made products on respiratory health. This will eventually allow the
346 development of preventive measures targeting the use of certain products with the final goal to
347 reduce the world's asthma-related morbidity.

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2

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5 participants were included and the CONSTANCES respiratory group.

6

7 Conflict of interest

8

9 The authors declare that they have no known competing financial interests or personal
10 relationships that could have appeared to influence the work reported in this paper.

11

12 Author contribution

13

14 E.P.D.S contributed to the analysis and interpretation of the data, and primary manuscript
15 preparation. M.G., C.R. and M.Z. contributed to acquisition and interpretation of the data and
16 critical revision of the manuscript. G.S, B.L., R.N., N.R., R.V. were involved in the data
17 interpretation and critical revision of the manuscript. N.L.M. and O.D. developed the study
18 hypotheses, and contributed to data interpretation, primary manuscript preparation and critical
19 revision of the manuscript. All authors approved the final version of the manuscript. All authors
20 have read and agreed to the published version of the manuscript.

21

22 Data availability

23

24 Data were obtained from the CONSTANCES group. It can be provided upon reasonable
25 request after approval by the CONSTANCES scientific committee.

26 The CONSTANCES cohort received ethical approval from the French National Data Protection
27 Authority (authorisation no. 910486) and the Institutional Review Board of the National
28 Institute for Medical Research (authorisation no.01-011). All participants gave informed
29 consent to participate.

30 The participants provided their written consent to participate in this study.

31

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33

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Table 1. Population characteristics according to current asthma status

	All n = 41,570	Never asthma n = 37,426	Current asthma n = 4,144	p-value
Gender, n (%)				
Male	18,348 (44.1)	16,577 (44.3)	1,771 (42.7)	0.056
Female	23,222 (55.9)	20,849 (55.7)	2,373 (57.3)	
Age (years), mean ± s.d	46.8 ± 13.2	47.1 ± 13.2	44.1 ± 13.2	< 0.0001
Smoking status, n (%)				
Never smoker	20,900 (50.3)	18,924 (50.6)	1,976 (47.7)	< 0.0001
Ex-smoker	14,258 (34.3)	12,891 (34.4)	1,367 (33.0)	
Current smoker	6,412 (15.4)	5,611 (15.0)	801 (19.3)	
BMI (Body Mass Index - kg/m²), n (%)				
< 24.9	24,422 (58.7)	22,196 (59.3)	2,226 (53.7)	< 0.0001
[25 – 29.9[12,345 (29.7)	11,048 (29.5)	1,297 (31.3)	
≥ 30	4,803 (11.6)	4,182 (11.2)	621 (15.0)	
Educational level, n (%)				
<high school diploma	8,142 (19.8)	7,413 (20.0)	729 (17.8)	0.0061
high school to 1-level university	6,113 (14.9)	5,513 (14.9)	600 (14.7)	
2-level university to 4-level university	15,398 (37.4)	13,836 (37.3)	1,562 (38.3)	
>5-level university	11,478 (27.9)	10,284 (27.8)	1,194 (29.2)	
Asthma symptom score, n (%)				
0 symptom	28,060 (69.5)	27,437 (75.4)	623 (15.7)	< 0.0001
1 symptom	7,736 (19.2)	6,322 (17.4)	1,411 (35.7)	
≥2 symptoms	4,567 (11.3)	2,645 (7.2)	1,922 (48.6)	
Weekly use of cleaning products, n (%)				
<1 day/week	10,760 (26.8)	9,790 (27.1)	970 (24.0)	< 0.0001
≥1 day/week	29,464 (73.2)	26,398 (72.9)	3,066 (76.0)	
Household help, n (%)	21,000 (51.2)	18,868 (51.1)	2,132 (52.1)	< 0.0001
Potential occupational exposure*, n (%)	2,699 (8.1)	2,394 (8.1)	305 (9.0)	0.0524

Results presented in bold are significant

*to cleaning products according to a preliminary transcoding for applying the OAsJEM (Occupational Asthma specific Job-Exposure Matrix ³⁹) to 49 job codes in CONSTANCES.

Table 2. Associations between the frequency of use of household cleaning products and current asthma

	All n = 41,570	Never asthma n = 37,426	Current asthma n = 4,144	Crude OR [95% CI]	Adjusted OR ^a [95% CI]	p trend
Not weekly exposed to any of the six large categories (ref)	n=10,760	n=9,790	n=970	1.00	1.00	
Irritants						
1-3 days/week	n=11,670	47.0%	51.5%	1.25 [1.15-1.37]	1.22 [1.11-1.34]	< 0.0001
4-7 days/week	n=2,172	8.7%	9.7%	1.27 [1.10-1.47]	1.30 [1.11-1.52]	
Sprays						
1-3 days/week	n=11,304	43.2%	44.6%	1.19 [1.09-1.30]	1.13 [1.02-1.24]	< 0.0001
4-7 days/week	n=4,005	14.9%	19.1%	1.47 [1.31-1.65]	1.37 [1.22-1.55]	
Scented products						
1-3 days/week	n=9,628	37.9%	40.6%	1.23 [1.12-1.35]	1.14 [1.03-1.25]	0.0018
4-7 days/week	n=4,847	18.9%	21.7%	1.32 [1.18-1.47]	1.19 [1.06-1.33]	
Disinfecting wipes						
1-3 days/week	n=6,442	33.3%	37.9%	1.32 [1.19-1.46]	1.18 [1.06-1.31]	< 0.0001
4-7 days/week	n=1,896	9.6%	12.7%	1.52 [1.31-1.76]	1.32 [1.13-1.55]	
Green products						
1-3 days/week	n=10,039	42.2%	43.4%	1.10 [1.00-1.21]	1.07 [0.97-1.18]	0.0182
4-7 days/week	n=2,939	12.2%	14.0%	1.22 [1.07-1.40]	1.18 [1.03-1.36]	
Home-made products						
1-3 days/week	n=3,429	21.8%	24.9%	1.24 [1.09-1.41]	1.15 [1.01-1.31]	0.0017
4-7 days/week	n=1,303	8.2%	10.6%	1.41 [1.18-1.69]	1.31 [1.08-1.58]	

^a Adjusted Odds Ratio (OR) for gender, age, smoking status, BMI and educational level of associations between the frequency of use of household cleaning products and current asthma, obtained by logistic regression models; results presented in bold are significant

Table 3. Associations between weekly use of cleaning products and current asthma according to the co-use of irritants and sprays at home

Adjusted OR ^a [95% CI]	Scented products	Disinfecting wipes	Green products	Home-made products
Not weekly exposed to any of the six large categories (ref)	1.00	1.00	1.00	1.00
Weekly exposed any of the six large categories	1.15 [1.06-1.26]	1.21 [1.09-1.34]	1.09 [1.00-1.20]	1.19 [1.06-1.34]
Co-exposure to risks previously identified ^b (irritants or sprays):				
Not co-exposed	0.97 [0.85-1.10]	1.16 [1.00-1.36]	0.94 [0.83-1.07]	0.99 [0.83-1.19]
Co-exposed	1.23 [1.12-1.35]	1.21 [1.09-1.35]	1.16 [1.05-1.29]	1.30 [1.14-1.49]

^a Adjusted Odds Ratio (OR) for gender, age, smoking status, BMI and educational level of associations between weekly use of cleaning products and current asthma according to the co-use of irritants and sprays at home, obtained by logistic regression models; results presented in bold are significant

^b exposure to irritants⁹⁻¹³ and sprayed^{14,16,18} cleaning products were associated to asthma in the literature

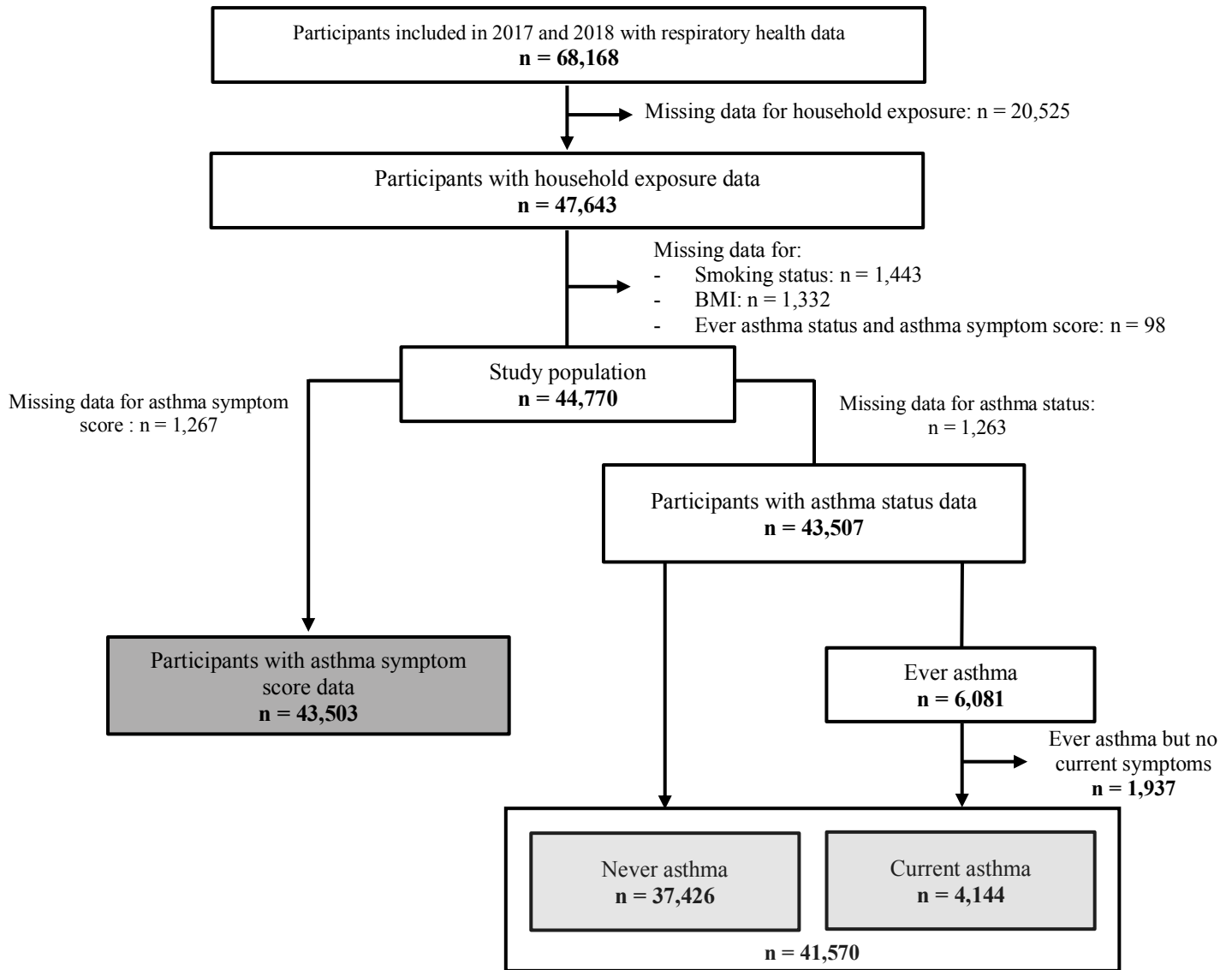


Figure 1. Flowchart of the study population

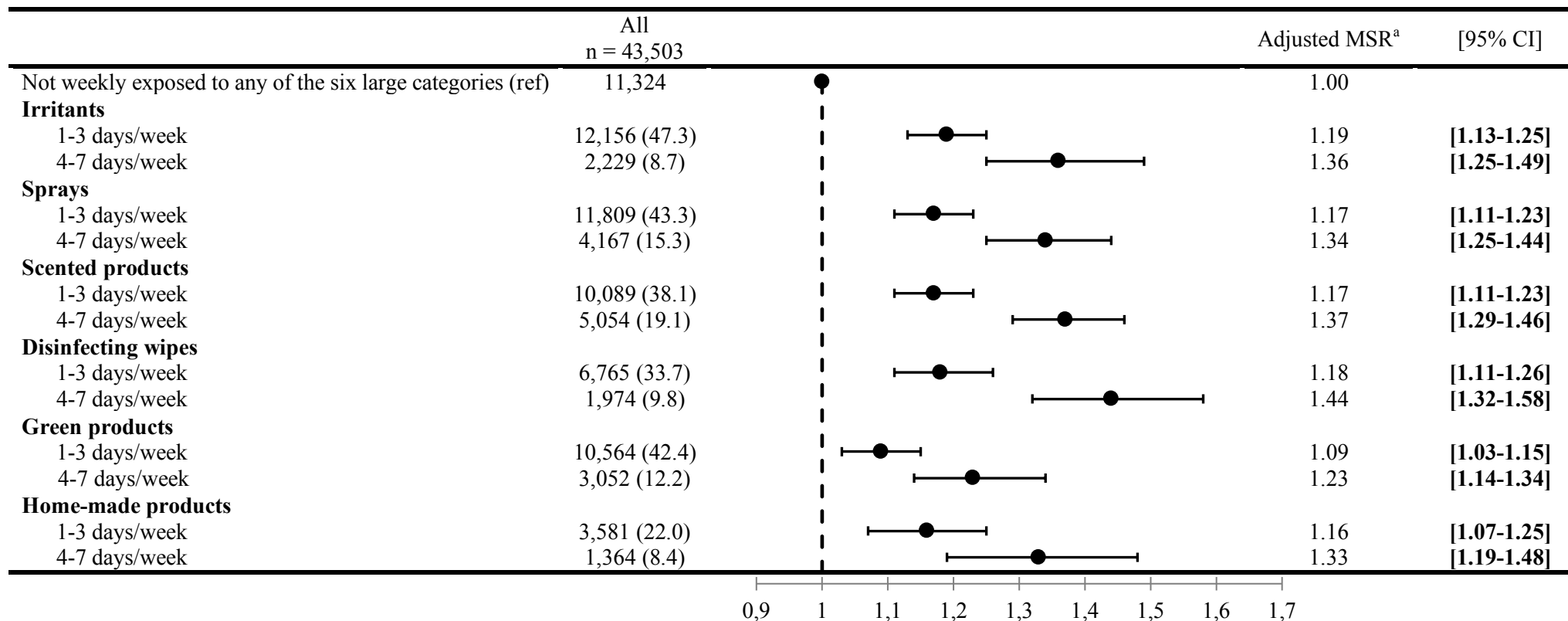


Figure 2. Associations between the frequency of use of cleaning products and the asthma symptom score
Mean Score Ratio (MSR) adjusted for gender, age, smoking status, BMI and educational level of associations between the frequency of use of cleaning products and the asthma symptom score, obtained by negative binomial regression model

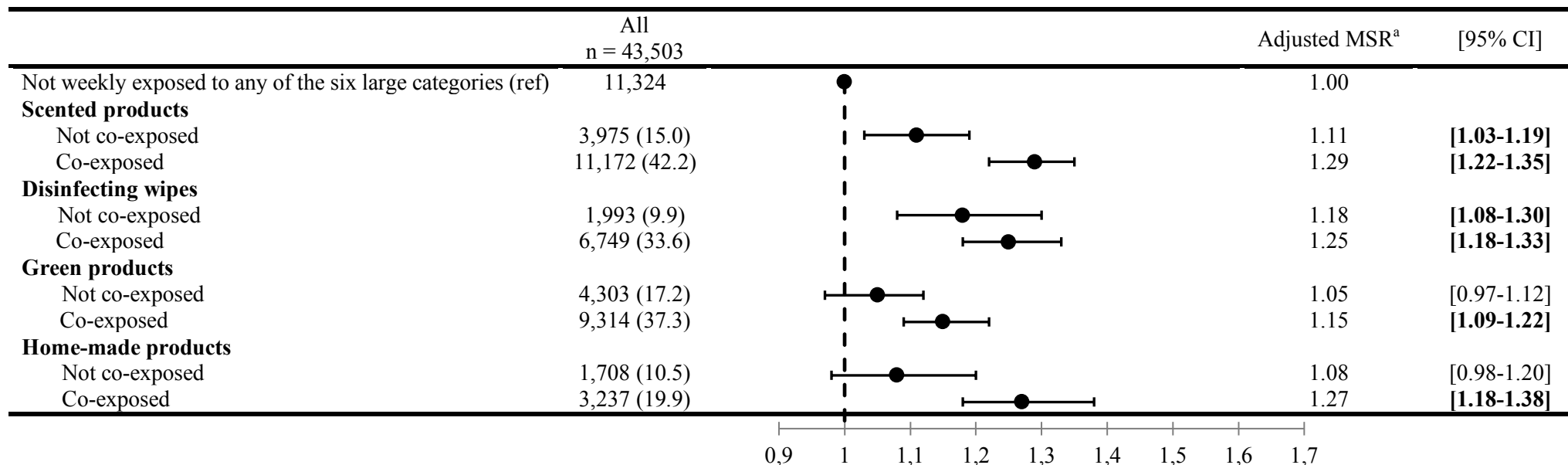


Figure 3. Associations between weekly use of cleaning products and the asthma symptom score, according to the co-use of irritants and sprays at home
Mean Score Ratio (MSR) adjusted for gender, age, smoking status, BMI and educational level of associations between weekly use of cleaning products and the asthma symptom score, according to the co-use of irritants and sprays at home, obtained by negative binomial regression models

Supplementary material

Household use of green and home-made cleaning products, wipe application mode and asthma among French adults from the CONSTANCES cohort

Emilie Pacheco Da Silva, Guillaume Sit, Marcel Goldberg, Bénédicte Leynaert, Rachel Nadif, Céline Ribet, Nicolas Roche, Marie Zins, Raphaëlle Varraso, Oriane Dumas, Nicole Le Moual

Table S1. Description of the study population and those excluded from the analysis

	Study population (n = 44,770)	Participants non-included in 2017 or 2018 (n = 69,915)	p-value	Missing data for household exposure (n = 20,525)	p-value
Gender, n (%)					
Male	19,943 (44.5)	32,231 (46.1)	< 0.0001	9,951 (48.5)	< 0.0001
Female	24,827 (55.5)	37,684 (53.9)		10,574 (51.5)	
Age (years), mean ± s.d	46.7 (13.2)	49.5 (13.2)	< 0.0001	44.2 (13.5)	< 0.0001
Smoking status, n (%)					
Never smoker	22,554 (50.4)	33,035 (49.1)	< 0.0001	8,608 (44.1)	< 0.0001
Ex-smoker	15,392 (34.4)	24,225 (36.0)		6,032 (30.9)	
Current smoker	6,824 (15.2)	10,014 (14.9)		4,875 (25.0)	
BMI (kg/m²), n (%)					
< 24.9	26,394 (58.9)	39,159 (57.5)	< 0.0001	10,427 (52.9)	0.0003
[25 – 29.9[13,277 (29.7)	21,225 (31.2)		6,218 (31.6)	
≥ 30	5,099 (11.4)	7,689 (11.3)		3,064 (15.5)	
Educational level, n (%)					
<high school diploma	8,690 (19.6)	15,816 (22.9)	< 0.0001	6,077 (30.4)	0.0005
high school to 1-level university	6,556 (14.8)	11,284 (16.4)		3,644 (18.2)	
2-level university to 4-level university	16,526 (37.4)	24,456 (35.5)		6,224 (31.2)	
>5-level university	12,476 (28.2)	17,382 (25.2)		4,031 (20.2)	
Asthma status, n (%)					
Never asthma	37,426 (90.0)	59,452 (91.3)	< 0.0001	16,798 (88.8)	0.0030
Current asthma	4,144 (10.0)	5,653 (8.7)		2,121 (11.2)	
Asthma symptom score, n (%)					
0 symptom	30,856 (70.9)	47,462 (70.8)	< 0.0001	12,502 (64.6)	< 0.0001
1 symptom	7,952 (18.3)	12,803 (19.1)		3,840 (19.8)	
2 symptoms	2,765 (6.4)	3,998 (6.0)		1,625 (8.4)	
3 symptoms	1,082 (2.5)	1,558 (2.3)		733 (3.8)	
4 symptoms	529 (1.2)	784 (1.2)		394 (2.0)	
5 symptoms	319 (0.7)	407 (0.6)		276 (1.4)	

BMI = Body Mass Index; results presented in bold are significant

Table S2. Description of participants non-weekly-exposed to any of the six large categories and participants weekly exposed

	Not weekly exposed n = 11,584		Weekly exposed	p-value
	No use n = 421	Use <1 day/week n = 11,163	Use ≥1 day/week n = 31,711	
Gender, n (%)				
Male	376 (89.3)	6,573 (58.9)	12,049 (38.0)	< 0.0001
Female	45 (10.7)	4,590 (41.1)	19,662 (62.0)	
Age (years), mean ± s.d	49.1 ± 13.9	47.2 ± 13.2	46.3 ± 13.2	< 0.0001
Smoking status, n (%)				
Never smoker	194 (46.1)	5,858 (52.5)	15,784 (49.8)	< 0.0001
Ex-smoker	181 (43.0)	3,766 (33.7)	10,893 (34.3)	
Current smoker	46 (10.9)	1,539 (13.8)	5,034 (15.9)	
BMI (Body Mass Index - kg/m²), n (%)				
< 24.9	215 (51.1)	6,884 (61.7)	18,568 (58.6)	< 0.0001
[25 – 29.9[160 (38.0)	3,265 (29.2)	9,306 (29.3)	
≥ 30	46 (10.9)	1,014 (9.1)	3,837 (12.1)	
Educational level, n (%)				
<high school diploma	89 (21.5)	1,671 (15.1)	6,394 (20.4)	0.0061
high school to 1-level university	52 (12.5)	1,338 (12.1)	4,960 (15.8)	
2-level university to 4-level university	101 (24.3)	3,900 (35.4)	12,115 (38.6)	
>5-level university	173 (41.7)	4,127 (37.4)	7,884 (25.2)	
Asthma status, n (%)				
Never asthma	341 (87.2)	9,449 (91.1)	26,398 (89.6)	< 0.0001
Current asthma	50 (12.8)	920 (8.9)	3,066 (10.4)	
Asthma symptom score, n (%)				
0 symptom	309 (74.6)	8,132 (74.5)	21,399 (69.5)	< 0.0001
1 symptom	66 (16.0)	1,863 (17.1)	5,783 (18.8)	
≥2 symptoms	39 (9.4)	915 (8.4)	3,589 (11.7)	
Household help, n (%)	332 (78.1)	5,952 (53.9)	15,754 (50.3)	< 0.0001

Results presented in bold are significant

Table S3. Population characteristics according to the asthma symptom score

	All n = 43,503	0 symptom n = 30,856	1 symptom n = 7,952	≥2 symptoms n = 4,695	p-value
Gender, n (%)					
Male	19,451 (44.7)	14,212 (46.1)	3,298 (41.5)	1,941 (41.3)	< 0.0001
Female	24,052 (55.3)	16,644 (53.9)	4,654 (58.5)	2,754 (58.7)	
Age (years), mean ± s.d	46.6 ± 13.2	46.8 ± 13.1	46.8 ± 13.5	45.2 ± 13.2	< 0.0001
Smoking status, n (%)					
Never smoker	21,936 (50.4)	16,448 (53.3)	3,531 (44.4)	1,957 (41.7)	< 0.0001
Ex-smoker	14,959 (34.4)	10,505 (34.1)	2,838 (35.7)	1,616 (34.4)	
Current smoker	6,608 (15.2)	3,903 (12.6)	1,583 (19.9)	1,122 (23.9)	
BMI (kg/m²), n (%)					
< 24.9	25,745 (59.1)	19,260 (62.4)	4,168 (52.4)	2,317 (49.3)	< 0.0001
[25 – 29.9[12,865 (29.6)	8,881 (28.8)	2,476 (31.1)	1,507 (32.1)	
≥ 30	4,893 (11.3)	2,711 (8.8)	1,308 (16.5)	871 (18.6)	
Educational level, n (%)					
<high school diploma	8,358 (19.5)	5,785 (19.0)	1,485 (18.9)	1,088 (23.4)	< 0.0001
high school to 1-level university	6,340 (14.7)	4,337 (14.2)	1,215 (15.5)	788 (17.0)	
2-level university to 4-level university	16,085 (37.4)	11,484 (37.6)	2,955 (37.7)	1,646 (35.5)	
>5-level university	12,232 (28.4)	8,930 (29.2)	2,186 (27.9)	1,116 (24.1)	
Weekly use of cleaning products, n (%)					
<1 day/week	11,324 (26.9)	8,441 (28.3)	1,929 (25.0)	954 (21.0)	< 0.0001
≥1 day/week	30,771 (73.1)	21,399 (71.7)	5,783 (75.0)	3,589 (79.0)	
Household help, n (%)	22,125 (51.5)	15,827 (51.9)	4,000 (51.0)	2,298 (49.7)	0.0098
Potential occupational exposure*, n (%)	2,816 (8.1)	1,945 (7.8)	515 (8.2)	356 (12.6)	0.0035

BMI = Body Mass Index; results presented in bold are significant

*to cleaning products according to a preliminary transcoding for applying the OAsJEM (Occupational Asthma specific Job-Exposure Matrix; Le Moual et al. 2018) to 49 job codes in CONSTANCES.

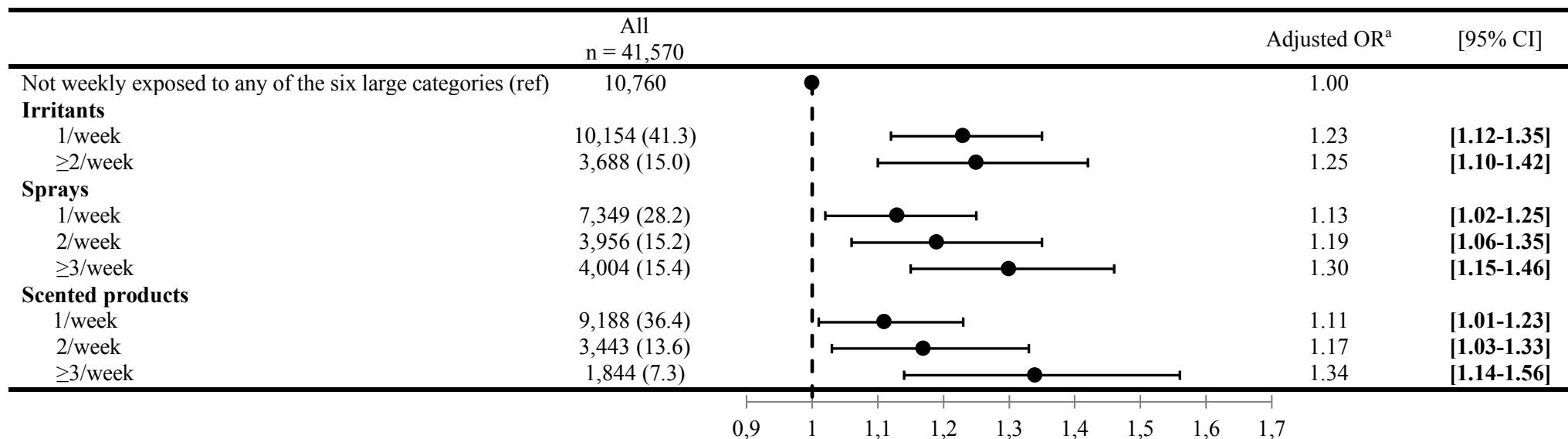


Figure S1. Associations between the number of products weekly used and current asthma

Adjusted Odds Ratio (OR) for gender, age, smoking status, BMI and educational level of associations between the number of products used and current asthma, obtained by logistic regression models

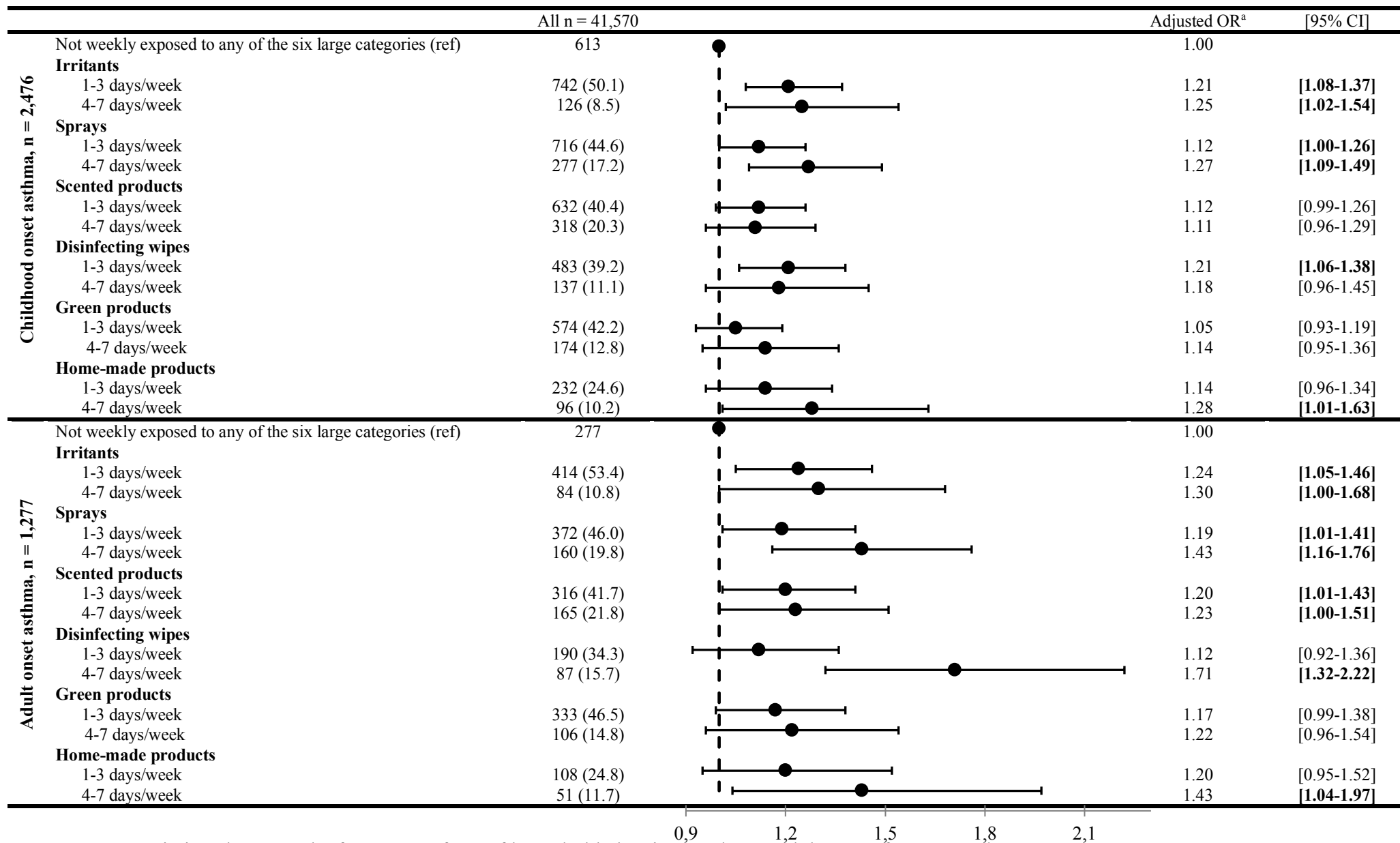


Figure S2. Associations between the frequency of use of household cleaning products and the age of current asthma onset

Adjusted Odds Ratio (OR) for gender, age, smoking status, BMI and educational level of associations between the frequency of use of household cleaning products and the age of onset of current asthma, obtained by multinomial logistic regression model

Table S4. Associations between weekly use of cleaning products and current asthma, stratified by gender, smoking status, educational level and household help

	Irritants	Sprays	Scented products	Disinfecting wipes	Green products	Home-made products
Not weekly exposed to any of the six large categories (ref)	1.00	1.00	1.00	1.00	1.00	1.00
Weekly exposed to any of the six large categories	1.23 [1.13-1.35]	1.18 [1.08- 1.29]	1.15 [1.06-1.26]	1.21 [1.09-1.34]	1.09 [1.00-1.20]	1.19 [1.06-1.34]
Gender ^a :						
Male, n = 18,348	1.27 [1.12-1.45]	1.16 [1.03-1.32]	1.16 [1.02-1.31]	1.16 [1.00-1.33]	1.04 [0.91-1.20]	1.23 [1.02-1.49]
Female, n = 23,222	1.20 [1.06-1.36]	1.20 [1.06-1.36]	1.15 [1.02-1.31]	1.26 [1.10-1.44]	1.14 [1.00-1.29]	1.16 [1.00-1.35]
Smoking status ^b :						
Never smoker, n = 20,900	1.23 [1.08-1.40]	1.22 [1.08-1.38]	1.23 [1.09-1.40]	1.22 [1.06-1.42]	1.07 [0.93-1.22]	1.06 [0.89-1.26]
Ex-smoker, n = 14,258	1.17 [1.00-1.36]	1.11 [0.96-1.29]	1.04 [0.89-1.21]	1.15 [0.97-1.37]	1.07 [0.92-1.25]	1.23 [1.00-1.51]
Current smokers, n = 6,412	1.35 [1.09-1.67]	1.19 [0.97-1.47]	1.15 [0.93-1.42]	1.23 [0.97-1.55]	1.20 [0.96-1.49]	1.49 [1.14-1.94]
Educational level ^c :						
≤1-level university, n = 14,255	1.18 [1.00-1.39]	1.16 [0.99-1.36]	1.12 [0.95-1.31]	1.26 [1.06-1.51]	0.99 [0.82-1.18]	1.01 [0.80-1.28]
≥2-level university, n = 26,876	1.25 [1.12-1.39]	1.19 [1.07-1.32]	1.16 [1.05-1.29]	1.17 [1.04-1.32]	1.13 [1.01-1.25]	1.26 [1.09-1.44]
Household help ^d :						
No, n = 20,044	1.27 [1.11-1.45]	1.20 [1.06-1.37]	1.19 [1.04-1.36]	1.32 [1.14-1.53]	1.11 [0.97-1.28]	1.22 [1.02-1.45]
Yes, n = 21,000	1.20 [1.06-1.36]	1.17 [1.04-1.32]	1.12 [1.00-1.26]	1.13 [0.98-1.29]	1.08 [0.95-1.22]	1.16 [0.99-1.36]

^a Adjusted Odds Ratio (OR) for age, smoking status, BMI and educational level of associations between weekly use of cleaning products and current asthma stratified by gender, obtained by logistic regression models; results presented in bold are significant

^b Adjusted Odds Ratio (OR) for gender, age, BMI and educational level of associations between weekly use of cleaning products and current asthma stratified by smoking status, obtained by logistic regression models; results presented in bold are significant

^c Adjusted Odds Ratio (OR) for gender, age, smoking status and BMI of associations between weekly use of cleaning products and current asthma stratified by educational level, obtained by logistic regression models; results presented in bold are significant

^d Adjusted Odds Ratio (OR) for gender, age, smoking status, BMI and educational level of associations between weekly use of cleaning products and current asthma stratified by household help, obtained by logistic regression models; results presented in bold are significant

Table S5. Associations between the frequency of use of household cleaning products and current asthma after exclusion of participants with potential occupational exposure

	All n = 38,871	Never asthma n = 35,032	Current asthma n = 3,839	Adjusted OR ^a [95% CI]	p trend
Not weekly exposed to any of the six large categories (ref)	n=10,308	n=9,383	n=925	1.00	
Irritants					
1-3 days/week	n=10,769	46.3%	50.8%	1.23 [1.11-1.35]	< 0.0001
4-7 days/week	n=1,935	8.3%	9.4%	1.35 [1.15-1.59]	
Sprays					
1-3 days/week	n=10,432	42.7%	44.4%	1.13 [1.03-1.25]	< 0.0001
4-7 days/week	n=3,590	14.4%	18.0%	1.36 [1.20-1.54]	
Scented products					
1-3 days/week	n=8,884	37.4%	40.1%	1.13 [1.03-1.25]	0.0034
4-7 days/week	n=4,395	18.4%	21.0%	1.18 [1.05-1.33]	
Disinfecting wipes					
1-3 days/week	n=5,959	32.7%	37.1%	1.17 [1.05-1.31]	< 0.0001
4-7 days/week	n=1,687	9.1%	12.4%	1.38 [1.17-1.63]	
Green products					
1-3 days/week	n=9,369	41.7%	43.4%	1.08 [0.98-1.20]	0.0400
4-7 days/week	n=2,686	11.9%	13.1%	1.15 [0.99-1.33]	
Home-made products					
1-3 days/week	n=3,166	21.4%	24.1%	1.13 [0.99-1.30]	0.0037
4-7 days/week	n=1,163	7.7%	10.1%	1.31 [1.07-1.59]	

^a Adjusted Odds Ratio (OR) for gender, age, smoking status, BMI and educational level of associations between the frequency of use of household cleaning products and current asthma after exclusion of participants with potential occupational exposure to cleaning products according to a preliminary transcoding for applying the OAsJEM (Occupational Asthma specific Job-Exposure Matrix; Le Moual et al. 2018) to 49 job codes in CONSTANCES, obtained by logistic regression models; results presented in bold are significant

Table S6. Associations between frequent use of cleaning products and current asthma according to the co-use of irritants and sprays at home

Adjusted OR ^a [95% IC]	Scented products	Disinfecting wipes	Green products	Home-made products
Not weekly exposed to any of the six large categories (ref)	1.00	1.00	1.00	1.00
Frequent use of cleaning products	1.19 [1.06-1.33]	1.32 [1.13-1.55]	1.18 [1.03-1.36]	1.31 [1.08-1.58]
Co-exposure to risks previously identified ^b (irritants or sprays):				
Not co-exposed ^c	0.92 [0.74-1.14]	1.13 [0.77-1.65]	1.09 [0.85-1.39]	1.22 [0.87-1.70]
Co-exposed ^d	1.26 [1.11-1.43]	1.35 [1.14-1.61]	1.24 [1.06-1.46]	1.34 [1.08-1.66]

^a Adjusted Odds Ratio (OR) for gender, age, smoking status, BMI and educational level of associations between frequent use of cleaning products (4-7 days/week) and current asthma according to the co-use of irritants and sprays at home, obtained by logistic regression models; results presented in bold are significant

^b exposure to irritants (Dumas et al. 2021; Lemire et al. 2020, 2021; Matulonga et al. 2016; Weinmann et al. 2017) and sprayed (Bédard et al. 2014; Dumas et al. 2021; Le Moual et al. 2012; Zock et al. 2007) cleaning products were associated to asthma in the literature

^c 1,008 never asthma/99 current asthma not co-exposed to scented products, 247 never asthma/31 current asthma not co-exposed to disinfecting wipes, 758 never asthma/83 current asthma not co-exposed to green products, 327 never asthma/42 current asthma not co-exposed to home-made products

^d 3,280 never asthma/460 current asthma co-exposed to scented products, 1,401 never asthma/217 current asthma co-exposed to disinfecting wipes, 1,863 never asthma/235 current asthma co-exposed to green products, 816 never asthma/118 current asthma co-exposed to home-made products