

Cleaning at home and at work in relation to lung function decline and airway obstruction

Ø Svanes^{1,2}, RJ Bertelsen¹, SHL Lygre², AE Carsin^{3,4,5}, JM Antó³, B Forsberg⁶, JM García-García⁷, JA Gullón⁷, J Heinrich⁸, M Holm⁹, M Kogevinas³, I Urrutia¹², B Leynaert^{13,14}, JM Moratalla¹⁵, N Le Moual^{16,17}, T Lytras^{3,18}, D Norbäck¹⁹, D Nowak⁸, M Olivieri²⁰, I Pin²¹, N Probst-Hensch^{22,23}, V Schlünssen^{24,25}, T Sigsgaard²⁴, TD Skorge², S Villani²⁶, *D Jarvis¹⁰, *JP Zock³ and *C Svanes^{2,27}

1. Department of Clinical Science, University of Bergen, Bergen, Norway
2. Department of Occupational Medicine, Haukeland University Hospital, Bergen, Norway
3. ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain;
4. Universitat Pompeu Fabra (UPF), Barcelona, Spain;
5. CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain
6. Division of Occupational and Environmental Medicine, Umeå University, Umeå, Sweden
7. Pneumology Department, University Hospital San Agustín, Avilés, Spain
8. Institute and Outpatient Clinic for Occupational and Environmental Medicine, Clinic Center, Ludwig Maximilian University, Comprehensive Pneumology Centre Munich, German Centre for Lung Research, Muenchen, Germany
9. Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden
10. National Heart and Lung Institute, Imperial College, London, UK
12. Pulmonology Department, Galdakao Hospital, Spain
13. Inserm U1152, Pathophysiology and Epidemiology of Respiratory Diseases, Paris, France
14. UMR 1152, Univ Paris Diderot Paris7, Paris, France
15. Servicio de Neumología, Complejo Hospitalario Universitario de Albacete, Spain
16. Inserm, U1168, Aging and chronic diseases. Epidemiological and Public health approaches, F-94807 Villejuif, France
17. Univ Versailles St-Quentin-en-Yvelines, UMR-S 1168, France
18. Department of Experimental and Health Sciences, Universitat Pompeu Fabra (UPF), Barcelona, Spain
19. Department of Medical Sciences, Occupational and Environmental Medicine, Uppsala University, Uppsala, Sweden
20. University Hospital of Verona, Verona, Italy
21. Pneumologie Pédiatrique, Antenne Pédiatrique du CIC, Grenoble, France
22. Swiss Tropical and Public Health Institute, Basel, Switzerland
23. Department Public Health, University of Basel, Switzerland
24. Department of Public Health, Danish Ramazzini Center, Aarhus University, Denmark
25. National Research Center for the Working Environment, Copenhagen, Denmark
26. Unit of Biostatistics and Clinical Epidemiology, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Italy
27. Centre for International Health, University of Bergen, Bergen, Norway

*Contributed equally

Corresponding author: Øistein Svanes; oistein.svanes@uib.no; telephone: +47 95758248; Department of Clinical Science, University of Bergen, Bergen, Norway

Contributorship statement: Ø Svanes wrote the plan of analysis, analysed the data, and drafted and revised the manuscript. C Svanes and JP Zock contributed with the plan of analysis, participated in coordination and collection of data, contributed with interpretation of analyses and revised the manuscript. D Jarvis contributed as above and in addition quality controlled the lung function tests. Ø Svanes, JP Zock and C Svanes are guarantors. RJ Bertelsen, SHL Lygre, JM Antó, AE Carsin, B Forsberg, JM García-García, JA Gullón, J Heinrich, M Holm, D Jarvis, M Kogevinas, I Urrutia, B Leynaert, JM Moratalla, N Le Moual, T Lytras, D Norbäck, D Nowak, M Olivieri, I Pin, N Probst-Hensch, V Schlünssen, T Sigsgaard, TD Skorge and S Villani participated in coordination and collection of data and revised the manuscript. All authors read and approved the final manuscript.

Funding: None of the study sponsors/funders had any role on study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all the data in the study and had full responsibility for the decision to submit for publication.

The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 633212. The co-ordination of ECRHS I and ECRHS II was supported by the European Commission. The co-ordination of ECRHS III was supported by the Medical Research Council (Grant Number 92091). The funding sources for the local ECRHS studies are provided in the online data supplement.

Running head: Long-term respiratory health effects of cleaning

Descriptor number: 1.25 Occupational and Environmental Airways Disease

Word count: 3036

At a Glance Commentary:

Scientific Knowledge on the Subject: It is known that cleaning tasks may imply exposure to chemical agents with potential harmful effects to the respiratory system. Further, increased risk of asthma and respiratory symptoms among professional cleaners and in persons cleaning at home is reasonably well documented.

What This Study Adds to the Field: This study suggests that also long-term respiratory health is impaired 10-20 years after cleaning activities. We found accelerated lung function decline in women both following occupational cleaning and cleaning at home. The effect size was comparable to the effect size related to 10-20 pack-years of tobacco smoking.

This article has an online supplement, which is accessible from this issue's table of content online at www.atsjournals.org

1 ABSTRACT

2 *Rationale* Cleaning tasks may imply exposure to chemical agents with potential harmful
3 effects to the respiratory system, and increased risk of asthma and respiratory symptoms
4 among professional cleaners and in persons cleaning at home has been reported. Long-term
5 consequences of cleaning agents on respiratory health are, however, not well described.

6 *Objectives* This study aims to investigate long-term effects of occupational cleaning and
7 cleaning at home on lung function decline and airway obstruction.

8 *Methods* The European Community Respiratory Health Survey (ECRHS) investigated a multi-
9 centre population based cohort at three time points over twenty years. 6230 participants
10 with at least one lung function measurement from 22 study centres, who in ECRHS II
11 responded to questionnaire modules concerning cleaning activities between ECRHS I and
12 ECRHS II were included. The data were analysed with mixed linear models adjusting for
13 potential confounders.

14 *Main results* As compared to women not engaged in cleaning ($\Delta FEV_1 = -18.5$ ml/year), FEV_1
15 declined more rapidly in women responsible for cleaning at home (-22.1 , $p=0.01$) and
16 occupational cleaners (-22.4 , $p=0.03$). The same was found for decline in FVC ($\Delta FVC = 8.8$
17 ml/year; -13.1 , $p=0.02$ and -15.9 , $p=0.002$, respectively). Both cleaning sprays and other
18 cleaning agents were associated with accelerated FEV_1 decline (-22.0 , $p=0.04$ and -22.9 ,
19 $p=0.004$, respectively). Cleaning was not significantly associated with lung function decline in
20 men, or with FEV_1/FVC -decline or airway obstruction.

21 *Conclusions* Women cleaning at home or working as occupational cleaners had accelerated
22 decline in lung function, suggesting that exposures related to cleaning activities may
23 constitute a risk to long-term respiratory health.

24 *Word count:* 250

25 *Key words:* Occupational Medicine, Spirometry, Lung Diseases

26

27 INTRODUCTION

28 Cleaning tasks are associated with exposure to several chemical agents with potential
29 harmful effects to the respiratory system [1] as well as on cardiovascular markers [2].
30 Excess risk of asthma and respiratory symptoms among professional cleaners [3] [4], as well
31 as asthma and respiratory symptoms in persons cleaning their own home [5] [6] [7] [8], has
32 been reported in several studies. Both specific immunological mechanisms and non-specific
33 inflammatory responses have been suggested [9].

34 The long-term consequences of cleaning agents on respiratory health are, however, not well
35 described and there is a need for further studies [10]. It seems biologically plausible that
36 exposure to cleaning chemicals could result in accelerated lung function (LF) decline and
37 chronic airway obstruction; low-grade inflammation over many years could possibly lead to
38 persistent damage to the airways, alternatively, persistent damage could result from
39 continued exposure after onset of cleaning-related asthma. To our knowledge there is no
40 previous investigation of long-term effects of cleaning at home on lung function decline and
41 respiratory health. A previous study has shown increased risk of self-reported COPD among
42 occupational cleaners [11] and a newly published large population-based cohort-study from
43 the UK showed cleaners to be among the occupations with the highest risk of spirometric
44 defined COPD [12].

45 The European Community Respiratory Health Survey (ECRHS) provided an opportunity for
46 longitudinal assessment of cleaning exposure in a large population-based cohort that
47 included information about occupational cleaning and cleaning at home as well as
48 spirometry performed at three time-points. The aim of this paper was to investigate
49 associations of both professional cleaning and cleaning at home with lung function decline
50 and chronic airway obstruction. In addition, the type and frequency of applied cleaning
51 agents were analyzed.

52 Some of the results of this study have been previously reported in the form of an abstract
53 [13].

54 METHODS

55 Study design and population

56 ECRHS is an international multi-centre population-based cohort, established from random
57 population samples of men and women aged 20-44 years in 1992-94 (ECRHS I),
58 reinvestigated 1998-2002 (ECRHS II) and 2010-12 (ECRHS III). Each survey included
59 interviews, spirometry, anthropometric measurements a.o. Written consent were obtained
60 from all participants in each survey, ethical approval was obtained from the regional ethic
61 committee of each centre.

62 In ECRHS II, 22 study centres included questionnaire modules for selected occupations. This
63 paper presents data from participants who answered entrance questions to questionnaire
64 modules assessing cleaning activities between ECRHS I and II, and had lung function
65 measured at least once (figure E1, online data supplement).

66 **Cleaning exposure**

67 Based on the entrance questions (wording at <http://www.ecrhs.org>), participants were
68 categorised as “not cleaning”, “cleaning at home” and “occupational cleaning”. Participants
69 responding “yes” to at least one module entrance question, answered a questionnaire
70 concerning use of cleaning agents (sprays, other cleaning agents); defining the exposure
71 categories “not cleaning”, “ ≥ 1 cleaning spray ≥ 1 /week”, and “ ≥ 1 other cleaning product
72 ≥ 1 /week”.

73 **Lung function**

74 Maximum Forced Vital Capacity (FVC) and maximum Forced Expired Volume in one second
75 (FEV_1) were determined by spirometry; in ECRHS III bronchodilator test was performed.
76 Decline in pre-bronchodilator FEV_1 and FVC was defined as the slope of change between
77 each measurement in millilitres. Post-bronchodilator airway obstruction at ECRHS III was
78 defined as $FEV_1/FVC < \text{Lower Limit of Normal (LLN)}$ predicted using the NHANES equations
79 [14]. Persons with any airway obstruction at ECRHS I were excluded from analyses with
80 airway obstruction as outcome variable (n=314).

81 **Covariates**

82 Pack-years were calculated from cigarettes per day x years smoked/20, body mass index
83 (BMI) from weight per square height. Age at attained education was used as proxy for
84 socioeconomic status [15] [16]. Father’s and mother’s educational background and an

85 occupational based socio-economic variable [17] were used as proxies for socioeconomic
86 status in sensitivity analyses.

87 **Statistical analyses**

88 Possible effect on decline in lung function from cleaning exposure was analysed with mixed
89 effect models adjusting for age at baseline and its square, number of years from baseline to
90 each follow-up, height, BMI, lifetime pack-years at each time-point, age at completed
91 education, spirometer type, and centre. Absolute lung function (FEV₁ or FVC) was the
92 outcome variable in all models. Effects of exposures on longitudinal lung function decline
93 were estimated by including interaction terms of exposure with time since baseline. Study
94 participants with only one observation were included in the analyses; although not
95 contributing direct information about the effect of the exposures, they informed the effect
96 of the other fixed covariates on lung function, thereby raising the overall statistical power of
97 the analysis. Change in FEV₁ and FVC was expressed as ml/year; a negative value
98 represented a decline.

99 Associations between cleaning exposure and airway obstruction were analysed with multiple
100 logistic regression adjusting for BMI, height, age at completed education, pack-years,
101 spirometer and centre. Associations were reported as odd ratios with 95% confidence
102 intervals.

103 A more detailed description of methods can be found in the online data supplement.

104 **RESULTS**

105 The study population included 6,230 participants with a mean age of 34 years at baseline
106 and 54 years at the second follow-up (ECRHS III). Fifty-three percent of the participants were
107 women, 44% were lifelong non-smokers and ever-smokers had smoked mean 7.0 pack-years
108 at baseline (table 1). The prevalence of asthma confirmed by a doctor increased from the
109 first to the second study wave, and the prevalence of spirometric defined any airway
110 obstruction (based on pre-bronchodilator spirometry), increased from the second to the
111 third study wave. The mean FEV₁ and FVC at baseline were 3.8 and 4.5 litres respectively
112 (table 1).

113 Of 6235 participants, 2693 (43.2%) and 2740 (44.0%) respectively, performed satisfactory
114 FEV₁ and FVC manoeuvres in two study waves (table 2). 2717 (43.6%) and 2597 (41.7%),
115 respectively, performed FEV₁ and FVC manoeuvres in all three study waves while 825
116 (13.2%) and 898 (14.4%) respectively, performed spirometry manoeuvres in one study wave
117 (table 2).

118 Among 3,298 female participants, the majority reported to be the person cleaning at home
119 (85.1%), as compared to 46.5% of 2932 male participants (table 3). There were 293 (8.9%)
120 women and 57 (1.9%) men that reported working with occupational cleaning. Persons
121 cleaning at home were more often never-smokers and had smoked less pack-years than the
122 other two exposure groups. The occupational cleaners had a lower age at attained education
123 compared to others, independent of sex. Women cleaning at home and female occupational
124 cleaners had more doctor diagnosed asthma than women not cleaning. Further, men
125 cleaning at home had more doctor diagnosed asthma as compared to men not cleaning and
126 male occupational cleaners. There was not substantially higher prevalence of spirometric
127 defined chronic airway obstruction in either of the exposure groups as compared to the
128 unexposed group (table 3).

129 Women not working as cleaners and not involved in cleaning at home showed the lowest
130 decline in FEV₁ and FVC (table 4). Female occupational cleaners, including those who in
131 addition also cleaned at home, had the highest mean decline in FEV₁ and FVC. The
132 differences between each of the two exposed groups and the reference group were
133 statistically significant (table 4). In relation to exposure, the increase in decline was similar
134 for FEV₁ and FVC, and therefore no apparent difference in the decline of the FEV₁/FVC ratio
135 was seen. The average annual decline was 0.5% in all three exposure groups. Male
136 occupational cleaners and men cleaning at home did not have accelerated lung function
137 decline as compared to men who reported no cleaning activities between ECRHS I and
138 ECRHS II (table E1 in the online data supplement).

139 Among women, the use of sprays or other cleaning products (i.e. non-sprays) at least one
140 once per week was associated with accelerated decline in FEV₁ as compared to not
141 performing cleaning activities (table 4). Use of other cleaning products at least once per
142 week was also associated with accelerated decline in FVC (table 4). Among male cleaners,

143 not either sprays or other cleaning products were significantly associated with lung function
144 decline (table E1 in the online data supplement).

145 There was no apparent increased risk of chronic airway obstruction in neither of the cleaning
146 exposure groups and likewise, there was no apparent increased risk of chronic airway
147 obstruction with regard to either use of cleaning sprays or other cleaning products (table 5).

148 **DISCUSSION**

149 This longitudinal analysis observed that women who had either cleaned at home or worked
150 as professional cleaners had accelerated decline in FEV₁ and FVC as compared to women not
151 regularly engaged in cleaning activities. Furthermore, compared to women not engaged in
152 cleaning activities, women who used sprays or other cleaning agents at least one time per
153 week had significantly accelerated decline in FEV₁ while women who used other cleaning
154 products at least one time per week had increased decline in FVC. No association between
155 lung function and cleaning was seen for males.

156 To the best of our knowledge, this analysis is the first to address lung function decline in
157 relation to cleaning exposure in occupational life or at home. In general, our findings of
158 poorer respiratory health outcomes in relation to cleaning exposures are supported in the
159 literature on cleaning-related asthma [4] [18]. Previous longitudinal studies on occupational
160 cleaning have shown increased risk of COPD [11] [12]. In the present study, there were
161 relatively few cases of incident COPD and associations with cleaning activities did not reach
162 statistical significance. Our study suggested a steeper decline in FVC than in FEV₁ in relation
163 to cleaning. FVC is an outcome of particular interest as survival in asymptomatic adults
164 without a chronic respiratory diagnosis or persistent respiratory symptoms has been shown
165 to be associated with FVC rather than airway obstruction as defined by the lower than
166 normal FEV₁/FVC ratio [19]. Brodtkin et al. showed that increased decline in the FEV₁/FVC
167 ratio might signify accelerated obstructive changes even when the ratio was not below the
168 fixed ratio or LLN [20]. However, in our study there was no difference in yearly FEV₁/FVC
169 decline between the three exposure groups. This might in part be due to our studying a
170 relatively young population where airway obstruction has not yet manifested as spirometric
171 changes.

172 The excess decline in the exposed groups amounted to 3.6 ml/year (cleaning at home) and
173 3.9 ml/year (occupational cleaning) for FEV₁, and 4.3 and 7.1 ml/year, respectively, for
174 decline in FVC. The absolute decline in lung function over time may possibly be
175 underestimated [21], due to the multi-centre design of our study with 22 participating
176 centres, with different spirometers and technical personnel. This could possibly attenuate
177 true differences between groups, and our study could also be less sensitive to small changes.
178 For comparison within our study population, similar models with similar adjustments
179 showed that heavy smokers (>20 pack-years) had excess decline of 6.1 ml/year in FEV₁ and
180 8.9 ml/year in FVC (as compared to the excess decline in occupational cleaners of 4.3 and 7.1
181 ml/year). The effect of occupational cleaning was thus comparable to smoking somewhat
182 less than 20 pack-years.

183 Most cleaning agents have an irritative effect on the mucous membranes of the airways [22]
184 [9]. One possible mechanism for the accelerated decline in cleaners is the repetitive
185 exposure to low-grade irritative cleaning agents over time, thereby causing persistent
186 changes in the airways. Also, some cleaning agents may have sensitizing properties through
187 specific immunological mechanism; quaternary ammonium compounds are known to have
188 sensitizing effects in the airways, as well as also having an irritative effect [22]. Repeated
189 exposure could lead to remodelling of the airways, thereby over time causing an accelerated
190 decline in FVC and FEV₁. Also, one could hypothesize that long-term exposure to airway
191 irritants such as ammonia and bleach used when cleaning at home could cause fibrotic or
192 other interstitial changes in the lung tissue, thereby leading to accelerated decline of FVC
193 [23].

194 Earlier studies have shown that people with asthma, regardless of sex and smoking status,
195 show greater decline in FEV₁ than people without [24]. In the present analysis, asthma was
196 more prevalent in the exposed groups (12.3 and 13.7% versus 9.6%, respectively for women
197 (table 3)); however, adjusting for ever had asthma in either of the three study waves in a
198 sensitivity analysis did not change the associations (table E2 in the online data supplement).
199 Furthermore, the effects were similar when excluding asthmatics (table E3 in the online data
200 supplement), suggesting that the observed accelerated lung function decline is generally not
201 mediated by cleaning-related asthma. This sensitivity analysis also suggests that the

202 associations with cleaning exposure was not limited to, mediated by or confounded by
203 asthma treatment.

204 Spirometric chronic airway obstruction is according to the Global Initiative for Chronic
205 Obstructive Disease [25] defined as individuals with a fixed FEV₁/FVC ratio < 0.70. However,
206 there is concern that using the fixed cut-off as definition of airway obstruction can
207 misdiagnose cases of obstruction as the FEV₁/FVC ratio varies with age, height and gender
208 [26]. Therefore, using the fixed ratio may result in over-diagnosis of elderly patients whose
209 lung volumes may be reduced as a result of the normal aging process, hence, any airway
210 obstruction was defined as an FEV₁/FVC ratio less than LLN.

211 The major strengths of this study include the long-time follow-up with spirometry
212 measurements at three time-points in a large number of participants with extensive data.
213 The population-based design and the multicentre structure make the results applicable to a
214 general population rather than to specific groups. Furthermore, the data from the
215 participants were extensive, ensuring that each participant was well characterised, with
216 ample possibilities to adjust for potential confounders. Post-bronchodilator spirometry
217 values in ECRHS III provided the preferred measure for diagnosing chronic airway
218 obstruction [27] [28]. Cleaning activities were recorded in the ECRHS II, thereby making it
219 possible to establish a temporal relationship between cleaning activities and long-term
220 outcomes. Our data did not allow for a detailed exploration between years in or onset of
221 cleaning activities in relation to lung function decline.

222 This analysis has some methodological challenges. Firstly, cleaning at home or work by social
223 class may have differential associations across centres, for example it stands to reason that
224 the customs of having someone to clean at home varies between countries. To account for
225 this, centre has been used as an adjustment variable to take into account social-cultural
226 differences. Thus, the multicultural structure of the study makes it possible to take into
227 account heterogeneous cultural differences between centres. Secondly, occupational
228 cleaning may be related to an unhealthy lifestyle where smoking might be one factor even
229 though this was not apparent in this study population. To account for possible confounding,
230 smoking, in terms of pack-years, has been adjusted for in the analyses. Further, age at
231 attained education was used to further adjust for confounding by socio-economic status.

232 Thirdly, the reference group with women not cleaning at home or working as occupational
233 cleaners was small (n=197) and one could suspect that this group would constitute a
234 selected socioeconomic group. However, adjusting for SES (age at attained education) in the
235 main analysis did not alter the associations, and SES itself was not a significant predictor
236 ($p=0.17$) of decline in lung function. Furthermore, sensitivity analysis with adjustment for
237 mother's and father's educational level (each in three categories) did not influence the
238 associations of cleaning exposure with lung function decline, and these markers did not have
239 significant effects on lung function decline. Additional sensitivity analysis with adjustment
240 for the occupational based socio-economic variable (based on "uksc") did not either alter
241 the associations, and this social class variable was not a significant independent predictor for
242 accelerated lung function decline.

243 Smoking in terms of pack-years was included as a time-varying variable in the model in order
244 to account for the effect of smoking over time on lung function decline. To account for
245 possible residual confounding of smoking on accelerated FEV₁ decline, we performed a
246 sensitivity analysis including an interaction term between pack-years and time in the model.
247 This did not alter the estimates of annual decline in FEV₁ or the confidence intervals in the
248 two exposure groups. Differential misclassification bias with regard to occupational cleaning
249 is possible and could cause positive or negative confounding. However, a reporting error in
250 cleaning exposure assessment is more likely to give non-differential bias. The exposure
251 assessment in the present paper is crude ("person doing the cleaning and/or washing at
252 home"; "having worked as a cleaner"), but overall, while the analyses have several
253 methodological challenges, these are likely to have attenuated the associations and cannot
254 easily explain the accelerated fall in lung function in women cleaning at home or working as
255 occupational cleaners.

256 There was no apparent accelerated decline in lung function in men, but it seems likely that
257 the exposures in men who work as cleaners may be different from those in women. Also, the
258 low number of male occupational cleaners (n=57) gave little power to discover accelerated
259 decline in lung function as compared to men not cleaning. Our entrance questions might
260 possibly not have picked up i.e. male industrial cleaners. Further, it is possible that
261 occupational groups with other, but equally or more, harmful exposures such as industrial
262 cleaners and other industrial workers, were included in the reference category, thereby

263 leading to an underestimation of the excess loss in lung function due to cleaning activities.
264 Finally, the greater impact seen in women (both cleaning at home and occupational
265 cleaners) could be mediated by a different susceptibility according to sex, as is reported for
266 other mixed chemical exposures such as tobacco smoke and other occupational exposures
267 as wood dust, where studies have indicated that less exposure in women is need to develop
268 illness [29] [30] [31].

269

270 In conclusion, this longitudinal analysis of a cohort followed over twenty years found that
271 women cleaning at home or working as occupational cleaners had accelerated decline in FVC
272 and FEV₁, but no apparent accelerated decline in the FEV₁/FVC ratio. A causal effect might
273 be biological plausible, since cleaning agents have known irritative effects and potential for
274 causing inflammatory changes in the airways [9]. The effect of treatment for asthma was not
275 investigated in this study. The findings suggest that cleaning activities in women, whether at
276 home or as an occupation, may constitute a risk to respiratory health, not only in terms of
277 asthma as previously shows, but also in terms of long-term impact on lung function decline.
278 Our findings advocate a need for further focus on preventing harmful exposure to the
279 airways from exposure in cleaning activities.

American Journal of Respiratory and Critical Care Medicine
Copyright © 2018 American Thoracic Society

Table 1. Characteristics of the study population at each survey

	ECRHS I (n=6,235)*	ECRHS II (n=6,235)*	ECRHS III (n=3,804)*
Sex (% women)	52.9	52.9	53.2
Age (years Mean \pm SD [†])	33.8 \pm 7.2	42.7 \pm 7.2	54.1 \pm 7.2
Height (meters, Mean \pm SD [†])	1.7 \pm 0.10	1.7 \pm 0.10	1.7 \pm 0.10
BMI (Mean \pm SD [†])	23.8 \pm 3.7	25.4 \pm 4.3	26.9 \pm 4.8
Never-smokers (%)	44	41	40
Pack-years (Mean \pm SD [†])	7.0 \pm 11.0	9.9 \pm 16.1	11.1 \pm 19.4
Age at completed education (years Mean \pm SD [†])	19.7 \pm 4.5	20.8 \pm 5.4	-
FVC (litres, Mean \pm SD)	4.5 \pm 1.0	4.4 \pm 1.0	4.0 \pm 1.0
FVC % predicted based on NHANES (Mean \pm SD [†])	100.4 \pm 11.9	99.9 \pm 12.4	97.3 \pm 13.2
FVC < LLN (%)	5.6	6.3	8.9
FEV ₁ (litres, Mean \pm SD [†])	3.8 \pm 0.8	3.5 \pm 0.8	3.1 \pm 0.8
FEV ₁ % predicted based on NHANES (Mean \pm SD [†])	101.2 \pm 12.8	99.8 \pm 13.6	95.4 \pm 14.4
Asthma (%) ("Asthma confirmed by a doctor?")	6.1	9.5	7.0
Airway obstruction (%) (defined by LLN [‡])	5.0	5.3	9.8
Chronic airway obstruction (%) (defined by LLN [§])			5.6
Cleaning at home		4,486 (72%)	
Occupational cleaning		350 (6%)	

* Study participants in each study wave who gave information on cleaning activities in ECRHS II and had at least one acceptable measurement of lung function at either of the three study waves.

[†]SD – Standard Deviation

[‡]LLN – Lower Limit of Normal, pre-bronchodilator

[§]LLN – Lower Limit of Normal, post-bronchodilator

^{||}Cleaning activities between ECRHS I and ECRHS II

Table 2 Number of spirometry test

	FEV ₁	FVC
Spirometry in one study wave	825 (13.2)	898 (14.4)
Spirometry in two study waves	2693 (43.2)	2740 (44.0)
Spirometry in three study waves	2717 (43.6)	2597 (41.7)

American Journal of Respiratory and Critical Care Medicine
Copyright © 2018 American Thoracic Society

Table 3. Covariates at ECRHS II according to exposure to cleaning (from module entrance questions in ECRHS II)

	Not cleaning (reference)		Cleaning at home		Occupational cleaner	
	Men (n=1,512)	Women (n=197)	Men (n=1,363)	Women (n=2,808)	Men (n=57)	Women (n=293)
Age (years) Mean \pm SD*	43.4 \pm 7.2	40.3 \pm 7.5	42.1 \pm 7.3	42.9 \pm 7.1	41.3 \pm 6.8	42.8 \pm 7.0
Height (meters) Mean \pm SD*	1.8 \pm 0.07	1.6 \pm 0.07	1.8 \pm 0.07	1.6 \pm 0.07	1.7 \pm 0.07	1.6 \pm 0.07
BMI Mean \pm SD*	26.4 \pm 3.6	24.6 \pm 4.9	25.6 \pm 3.5	24.7 \pm 4.6	26.6 \pm 3.8	25.9 \pm 5.4
Never-smokers (%)	32	41	43	45	28	44
Pack-years Mean \pm SD*	15.8 \pm 22.0	9.1 \pm 14.2	9.6 \pm 15.1	6.9 \pm 11.7	15.3 \pm 17.1	8.9 \pm 13.7
Age at completed education (years) Mean \pm SD*	20.0 \pm 4.7	22.2 \pm 4.3	21.6 \pm 5.2	21.0 \pm 5.6	19.9 \pm 5.1	18.1 \pm 6.0
FVC (litres) Mean \pm SD*	5.0 \pm 0.8	3.7 \pm 0.7	5.2 \pm 0.8	3.7 \pm 0.6	5.1 \pm 0.8	3.6 \pm 0.6
FVC % predicted, NHANES (Mean \pm SD*)	99.2 \pm 12.1	99.8 \pm 13.7	99.1 \pm 12.3	100.6 \pm 12.5	101.1 \pm 10.2	100.2 \pm 12.6
FVC < LLN [†] (%)	6.8	8.1	7.6	5.2	2.0	7.0
FEV ₁ (litres) Mean \pm SD*	4.0 \pm 0.7	3.1 \pm 0.5	4.1 \pm 0.7	3.0 \pm 0.5	4.1 \pm 0.7	2.9 \pm 0.5
FEV ₁ % predicted, NHANES (Mean \pm SD*)	100.7 \pm 13.7	100.3 \pm 14.2	99.3 \pm 13.9	99.7 \pm 13.3	102.1 \pm 11.0	98.3 \pm 13.4
Asthma (%) ("Asthma confirmed by a doctor?")	7.0	9.6	10.3	12.3	7.0	13.7
Airway obstruction (%) (defined by LLN [†])	5.0	3.1	6.1	5.1	5.3	6.1

*SD – Standard Deviation

[†]LLN – Lower Limit of Normal pre-bronchodilator values

American Journal of Respiratory and Critical Care Medicine
Copyright © 2018 American Thoracic Society

Table 4. Associations of decline in FEV₁ and FVC with cleaning at home and occupational cleaning in women. Association between smoking and decline in FEV₁ and FVC given for comparison.

	Adjusted* decline in FEV ₁ and FVC					
	ΔFEV ₁ (ml/year) (95% CI)	p [†]	ΔFVC (ml/year) (95% CI)	p [†]	ΔFEV ₁ /FVC (%/year) (95% CI)	p [†]
No cleaning activities between EC I and EC II (reference) (n=197)	-18.5 (-21.3, -15.7)		-8.8 (-12.4, -5.1)		-0.5 (-0.58, -0.45)	
Cleaning at home (n=2,808)	-22.1 (-23.2, -21.0)	0.01	-13.1 (-14.6, -11.7)	0.02	-0.5 (-0.57, -0.52)	0.39
Occupational cleaner (n=293)	-22.4 (-24.8, -20.0)	0.03	-15.9 (-19.0, -12.7)	0.002	-0.5 (-0.59, -0.48)	0.60
No cleaning activities between EC I and EC II (reference) (n=197)	-18.7 (-21.6, -15.7)		-9.5 (-13.3, -5.7)			
≥1 spray ≥1 time/week (n=569)	-22.0 (-23.9, -20.1)	0.04	-13.3 (-15.8, -10.9)	0.07		
≥1 other cleaning product ≥1 time/week (n=1,567)	-22.9 (-24.4, -21.5)	0.004	-14.3 (-16.2, -12.5)	0.01		
Never-smoker (reference) (n=1,670)	-21.1 (-22.4, -19.9)		-11.8 (-13.4, -10.2)			
<10 pack-years (n=769)	-21.8 (-23.3, -20.3)	0.4	-12.2 (-14.2, -10.2)	0.7		
10-20 pack-years (n=442)	-23.3 (-25.2, -21.4)	0.03	-12.8 (-15.3, -10.3)	0.4		
>20 pack-years (n=411)	-27.2 (-29.3, -25.2)	<.001	-20.7 (-23.3, -18.0)	<0.001		

*Adjustments: Age at ECRHS II (centered), age at ECRHS II squared, number of years since baseline, height at baseline, BMI at each study wave, life-time pack-years, age at completed education, spirometer model used at each study wave, and study centre

†p-value from mixed effect models for difference in lung function decline between reference group and exposed groups

Table 5. Associations between different cleaning exposures and incident airway obstruction in women and men. Association between smoking and incident chronic airway obstruction given for comparison.

	Chronic airway obstruction*			
	Women		Men	
	OR [†] (95% CI)	p [‡]	OR [†] (95% CI)	p [‡]
Cleaning at home	5.20 (0.67 – 40.71) (n [§] =86)	0.1	0.89 (0.38 – 2.13) (n [§] =32)	0.8
Occupational cleaner	1.93 (0.14 – 20.89) (n [§] =7)	0.6	1.45 (0.17 – 12.49) (n [§] =2)	0.7
≥1 spray ≥1 time/week	5.87 (0.68 – 51.04) (n [§] =16)	0.1	0.68 (0.79 – 5.76) (n [§] =2)	0.7
≥1 other cleaning product ≥1 time/week	4.78 (0.56 – 40.10) (n [§] =51)	0.2	1.05 (0.38 – 2.87) (n [§] =22)	0.9
<10 pack-years	1.16 (0.54 – 2.47) (n [§] =22)	0.7	2.07 (0.67 – 6.38) (n [§] =10)	0.2
10-20 pack-years	1.51 (0.63 – 3.61) (n [§] =11)	0.4	1.79 (0.55 – 5.84) (n [§] =11)	0.3
>20 pack-years	3.31 (1.56 – 7.03) (n [§] =28)	0.002	7.16 (2.91 – 17.64) (n [§] =36)	<0.001

*Participants with obstructive spirometry in ECRHS I (n=314) excluded from the analysis.

†Adjustments: BMI and height at baseline, age at attained education, life-time pack-years, spirometer model and centre. In the analyses on smoking adjustment is made for cleaning.

‡p-value for the association between different exposures groups and OR of chronic airway obstruction

§n signifies the number of persons with spirometric defined chronic airway obstruction in each exposure group

References

1. Zock JP, Kogevinas M, Sunyer J, Jarvis D, Toren K, Anto JM. Asthma characteristics in cleaning workers, workers in other risk jobs and office workers. *European Respiratory Journal* 2002;20:679-685.
2. Mehta AJ, Adam M, Schaffner E, Barthélémy JC, Carballo D, Gaspoz JM, Rochat T, Schindler C, Schwartz J, Zock JP, Künzli N, Probst-Hensch N, SAPALDIA T. Heart rate variability in association with frequent use of household sprays and scented products in SAPALDIA. *Environ Health Perspect* 2012;120:958-964.
3. Medina-Ramón M, Zock JP, Kogevinas M, Sunyer J, Antó JM. Asthma symptoms in women employed in domestic cleaning: a community based study. *Thorax* 2003;58:950-954.
4. Kogevinas M, Anto JM, Sunyer J, Tobias A, Kromhout H, Burney P. Occupational asthma in Europe and other industrialised areas: a population-based study. *European Community Respiratory Health Survey Study Group. Lancet* 1999;353:1750-1754.
5. Zock JP, Vizcaya D, Le Moual N. Update on asthma and cleaners. *Curr Opin Allergy Clin Immunol* 2010;10:114-120.
6. Zock JP, Plana E, Jarvis D, Antó JM, Kromhout H, Kennedy SM, Künzli N, Villani S, Olivieri M, Torén K, Radon K, Sunyer J, Dahlman-Hoglund A, Norbäck D, Kogevinas M. The use of household cleaning sprays and adult asthma: an international longitudinal study. *Am J Respir Crit Care Med* 2007;176:735-741.
7. Le Moual N, Varraso R, Siroux V, Dumas O, Nadif R, Pin I, Zock JP, Kauffmann F, Epidemiological, Study on the Genetics and Environment of Asthma. Domestic use of cleaning sprays and asthma activity in females. *Eur Respir J* 2012;40:1381-1389.
8. Bédard A, Varraso R, Sanchez M, Clavel-Chapelon F, Zock JP, Kauffmann F, Le Moual N. Cleaning sprays, household help and asthma among elderly women. *Respir Med* 2014;108:171-180.
9. Siracusa A, De Blay F, Folletti I, Moscato G, Olivieri M, Quirce S, Raulf-Heimsoth M, Sastre J, Tarlo SM, Walusiak-Skorupa J, Zock JP. Asthma and exposure to cleaning products - a European Academy of Allergy and Clinical Immunology task force consensus statement. *Allergy* 2013;68:1532-1545.
10. Mirabelli MC, London SJ, Charles LE, Pompeii LA, Wagenknecht LE. Occupation and three-year incidence of respiratory symptoms and lung function decline: the ARIC Study. *Respir Res* 2012;13:24.
11. Svanes Ø, Skorge TD, Johannessen A, Bertelsen RJ, Bråtveit M, Forsberg B, Gislason T, Holm M, Janson C, Jögi R, Macsali F, Norbäck D, Omenaas ER, Real FG, Schläunssen V, Sigsgaard T, Wieslander G, Zock JP, Aasen T, Dratva J, Svanes C. Respiratory Health in Cleaners in Northern Europe: Is Susceptibility Established in Early Life. *PLoS One* 2015;10:e0131959.
12. De Matteis S, Jarvis D, Hutchings S, Darnton A, Fishwick D, Sadhra S, Rushton L, Cullinan P. Occupations associated with COPD risk in the large population-based UK Biobank cohort study. *Occup Environ Med* 2016;73:378-384.
13. Svanes Ø; Bertelsen RJ; Lygre SHL; Antó, JM; Carsin, AE; Kogevinas, M; Leynaert, B; Lytras, T; Mirabelli, M; Moratalla, J; Moual, N Le; Norbäck, D; Olivieri, O; Schläunssen, V; Skorge, TD; Zock, JP, Svanes, C. Long term effect of cleaning on lung function decline in the ECRHS study.
14. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 1999;159:179-187.
15. Liberatos P, Link BG, Kelsey JL. The measurement of social class in epidemiology. *Epidemiol Rev* 1988;10:87-121.

16. Basagaña X, Sunyer J, Kogevinas M, Zock JP, Duran-Tauleria E, Jarvis D, Burney P, Anto JM, European CRHS. Socioeconomic status and asthma prevalence in young adults: the European Community Respiratory Health Survey. *Am J Epidemiol* 2004;160:178-188.
17. Rose M. Official social classifications in the UK. Guildford: University of Surrey 1998
18. Kogevinas M, Zock JP, Jarvis D, Kromhout H, Lillienberg L, Plana E, Radon K, Toren K, Alliksoo A, Benke G, Blanc PD, Dahlman-Hoglund A, D'Errico A, Hery M, Kennedy S, Kunzli N, Leynaert B, Mirabelli MC, Muniozguren N, Norback D, Olivieri M, Payo F, Villani S, van Sprundel M, Urrutia I, Wieslander G, Sunyer J, Anto JM. Exposure to substances in the workplace and new-onset asthma: an international prospective population-based study (ECRHS-II). *Lancet* 2007;370:336-341.
19. Burney PG, Hooper R. Forced vital capacity, airway obstruction and survival in a general population sample from the USA. *Thorax* 2011;66:49-54.
20. Brodtkin CA, Barnhart S, Checkoway H, Balmes J, Omenn GS, Rosenstock L. Longitudinal pattern of reported respiratory symptoms and accelerated ventilatory loss in asbestos-exposed workers. *Chest* 1996;109:120-126.
21. Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. *Clin Interv Aging* 2006;1:253-260.
22. Quirce S, Barranco P. Cleaning agents and asthma. *J Investig Allergol Clin Immunol* 2010;20:542-50; quiz 2p following 550.
23. Arif AA, Hughes PC, Delclos GL. Occupational exposures among domestic and industrial professional cleaners. *Occup Med (Lond)* 2008;58:458-463.
24. Lange P, Parner J, Vestbo J, Schnohr P, Jensen G. A 15-year follow-up study of ventilatory function in adults with asthma. *N Engl J Med* 1998;339:1194-1200.
25. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. 2016
26. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, Enright PL, Hankinson JL, Ip MS, Zheng J, Stocks J, ERS GLFI. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012;40:1324-1343.
27. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J* 2006;28:523-532.
28. van den Boom G, van Schayck CP, van Mollen MP, Tirimanna PR, den Otter JJ, van Grunsven PM, Buitendijk MJ, van Herwaarden CL, van Weel C. Active detection of chronic obstructive pulmonary disease and asthma in the general population. Results and economic consequences of the DIMCA program. *Am J Respir Crit Care Med* 1998;158:1730-1738.
29. Silverman EK, Weiss ST, Drazen JM, Chapman HA, Carey V, Campbell EJ, Denish P, Silverman RA, Celedon JC, Reilly JJ, Ginns LC, Speizer FE. Gender-related differences in severe, early-onset chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;162:2152-2158.
30. Foreman MG, Zhang L, Murphy J, Hansel NN, Make B, Hokanson JE, Washko G, Regan EA, Crapo JD, Silverman EK, DeMeo DL, COPDGene I. Early-onset chronic obstructive pulmonary disease is associated with female sex, maternal factors, and African American race in the COPDGene Study. *Am J Respir Crit Care Med* 2011;184:414-420.
31. Jacobsen G, Schlünssen V, Schaumburg I, Taudorf E, Sigsgaard T. Longitudinal lung function decline and wood dust exposure in the furniture industry. *Eur Respir J* 2008;31:334-342.