#### Respiratory Medicine (2013) 107, 1598–1607



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Received 4 April 2013; accepted 14 July 2013 Available online 3 August 2013

### KEYWORDS

Indoor air pollution; Aged; Respiratory disease; COPD; VOCs; Aldehydes; Glycol ethers

#### Summary

The purpose of this study was to explore respiratory health effects of indoor exposures to aldehydes and volatile organic compounds (VOCs) in elderly living in a population-based representative sample of French dwellings and to compare them to the rest of the occupants of the dwellings.

Twenty VOCs were objectively measured in 490 main dwellings. The respiratory conditions were assessed through a standardized questionnaire in 1012 inhabitants aged over 15 years, 144 of whom were aged over 65 years. Generalized estimating equations (GEE) were used to model the relationship between respiratory health outcomes and air pollutants concentrations using the median value of the distribution to define elevated exposure.

Similar levels of indoor air pollutants were found in elderly and others. However, associations between breathlessness and living in dwellings with elevated concentrations of toluene and *o*-xylene respectively were statistically significant in elderly but not in the rest of the population (adjusted odds ratios (AOR(95% confidence interval) = 3.36(1.13, 9.98) and 2.85(1.06, 7.68) in elderly vs. 0.91(0.59, 1.39) and 0.79( 0.47, 1.34) in the others respectively). A more

0954-6111/\$ - see front matter © 2013 Elsevier Ltd. All rights reserved. http://dx.doi.org/10.1016/j.rmed.2013.07.015

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pronounced effect of n-decane on past year breathlessness was observed in case of poor ventilation in the dwellings.

Our results showed a higher risk of breathlessness in elderly exposed to indoor air pollution than in the rest of the exposed population. Further investigations are needed to confirm whether this is related to frailty in elderly. © 2013 Elsevier Ltd. All rights reserved.

Second hand smoke

### Abbreviations

PM2.5 PM10 TSP SO <sub>2</sub> NO <sub>2</sub> NO <sub>2</sub> CO O <sub>3</sub> VOCs BS T ETS	Fine particles of $\leq$ 2.5 µm aerodiameter Particles of $\leq$ 10 µm aerodiameter Total suspended particles Suspension particles Sulfur dioxide Nitrogen dioxide Nitrogen oxides Carbon monoxide Ozone Volatile organic compounds Black smoke Temperature Environmental tobacco smoke	LD COPD FEV1 FVC GEE OQAI vol/h ECRHS OR AOR	Chronic obstructive pulmonary disease Forced expiratory volume in 1 s Forced vital capacity Generalized estimating equations Observatory for indoor air quality (Observatoire de la Qualité de l'Air Intérieur) Volume of air per hour European Community Respiratory Health Survey Odds ratios Adjusted odds ratios
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## Introduction

According to the United Nations (UN) estimations, the total number of people aged 65 years and older was 506 million in 2008; this is anticipated to double to 1.3 billion by 2040, accounting for 14 percent of the total global population. By 2050, Europe will continue to be the world's oldest region with its elder population increasing more than five-fold—from 40 million to 219 million (UN 2009) (http://www.un. org/esa/population/publications/WPA2009/WPA2009\_WorkingPaper.pdf).

Aging is associated with a decline in immune defences and respiratory function, and predisposition to respiratory infections [1]. Due to their fragility, elderly are more susceptible to the effects of air pollution and especially indoor air pollution than the rest of the population. Most people spend over 80% of their times in indoors and the elderly spend even more time at home [2,3].

Several studies have demonstrated that air pollutant concentrations are often much higher indoors due to the fact that many pollutants have an indoor source and the added effect of ambient air pollution that penetrates from outdoors [4]. Indoor air pollutants consist of chemical, biological and physical components. The most common chemical pollutants are environmental tobacco smoke (ETS), volatile organic compounds (VOCs) and aldehyde, Particulate Matters (PM), nitrogen dioxide (NO2), carbon monoxide (CO), biological contaminates are allergens, moulds, dust mites, cockroaches... and physical components include ventilation rate based on CO<sub>2</sub> measurement, dampness, temperature, radiation... [5].

VOCs or aldehydes significantly impact indoor air guality [6]. They have many sources, namely traffic and industrial emissions as outdoor sources, building and furnishing materials, and decoration products, cleaning agents, and personal care products as indoor sources [7]. The impact of VOCs or aldehydes consist of acute effects such as headaches and irritation of the nose and eyes [8] and adverse respiratory effects such asthma. Previous reports have demonstrated this association. Among French school children, an excess of asthma was observed in school children exposed to concentrations of formaldehyde higher than the preconized standards (according to the French Environmental Agency (ANSES)) in their classrooms [9] or dwellings [10]. In Swedish dwellings, the prevalence of asthma was higher among subjects living in newly painted dwellings compared to others [11]. In an adult population, a significant association was showed between asthma and personal exposure of VOCs, especially aromatic compounds [12].

Despite the fact that elderly are likely more exposed to indoors air pollution, because they spend more time at home than the rest of the population (World Health Organization http://www.euro.who.int/\_\_data/assets/pdf\_file/0009/128169/e94535.pdf), only few studies have considered the respiratory impact of VOCs in this age group. In one of the rare studies conducted in the elderly population, urinary levels of hippuric acid and methylhippuric acid, which are metabolites of toluene and xylene, respectively, were significantly associated with reduction of forced expiratory volume in 1 s (FEV<sub>1</sub>), FEV<sub>1</sub>/forced vital capacity (FVC), and forced expiratory flow at 25–75% of

FVC [13] thus confirming the potential adverse effect of VOCs on the elderly.

The purpose of this study was to determine the respiratory effects of exposures to aldehydes and VOCs, as objectively measured using passive samplers, in elderly living in a population-based representative sample of French dwellings.

## Materials and methods

### Study population

Data were drawn from the national-scale "housing" campaign of the French observatory for indoor air quality (Observatoire de la qualité de l'air intérieur (OQAI), www. air-interieur.org) conducted between October 1, 2003 and December 21, 2005 in Metropolitan France. The main objective of this campaign was to assess indoor air quality in French dwellings. The secondary objective was to relate air quality to respiratory health. Sampling took place in 55 French departments, 74 municipalities and 19 regions. 567 dwellings were randomly selected comprising 1612 individuals. 1012 eligible individuals accepted to respond to the health questionnaire, among them 144 subjects were aged over 65 years. The sampling method and the protocol were detailed previously [14,15].

### Environmental assessment

In the OQAI campaign, 30 indoor air pollutants were collected on the basis of a hierarchical classification designed by a panel of experts including one of the authors (IAM) (Mosqueron et al., 2003; http://www.air-interieur. org/) [14]. Among these 30 pollutants, 20 VOCs were

 Table 1
 Participants' social and health characteristics.

measured in dwellings selected during one week in bedroom of the reference person. In each household, the mean concentrations of VOCs were calculated for the week of observation.

Assessed air pollutants included:

- *Aldehydes*: formaldehyde, acetaldehyde, acroleine, hexaldehyde.
- Aromatic hydrocarbons: benzene, toluene, m/p-xylenes, o-xylene, 1.2.4-trimethylbenzene, ethylbenzene, styrene.
- *Aliphatic hydrocarbons: n*-decane, *n*-undecane; halogenated hydrocarbons: trichloroethylene, tetrachloroethylene, 1.4-dichlorobenzene; Glycol ethers: 1-metoxy-2-propanol, 2 butoxy ethanol, 2-butoxyethylacetate, 1-methoxy-2-propylacetate.

Measurements were performed by radial diffusive sampling onto 2,4-DNPH coated Florisil for aldehydes. Aldehyde-hydrazones formed in the cartridge were eluted by acetonitrile solvent and analyzed by liquid chromatography associated with a UV detector. Other VOCs were collected onto Carbograph four adsorbents (Radiello, Fondazione Salvatore Maugeri (FSM)). Adsorbed VOCs were extracted through thermodesorption and analyzed by gas phase chromatography equipped with flame ionization detector and/or mass spectrometry [14,16].

In addition to indoor air pollutants, in-home ventilation conditions were characterized using  $CO_2$  concentrations measured with built-in non-dispersive infrared sensor (Q-Track probe). Resulting from metabolic processes,  $CO_2$ concentrations express air stuffiness of the rooms and have been used to build an air change rate indicator. The daytime and night-time air-exchange rates were calculated based on  $CO_2$  average levels and the metabolic output of

	All ( $N = 1012$ )	<65 Years ( $N = 868$ )	$\geq$ 65 Years (N = 144)
Demographic			
Women N (%)	527 (52)	452(52)	75 (52)
Age (years) ( $m \pm$ STD)	44 ± 17	$39 \pm 14$	71 ± 4.8
Ethnic origin (French) N (%)	967 (96)	828(95)	139 (97)
Education			
No studies or primary studies N (%)	83(8)	34(3.95)	49(35)
Until college N (%)	323(32)	287(33)	36(25)
High school N (%)	252(25)	221(25)	31(22)
Graduate study N (%)	344(34)	318(37)	26(18)
Smoking status			
Never smoked N (%)	442(44)	371(42)	71(49)
Ex smoker N (%)	301(30)	245(28)	56(39)
Smoke actually N (%)	268(27)	251(29)	17(12)
Presence indoor mean (%)	67	66	80
Ventilation mean (vol/h)	0.761	0.743	0.768
Respiratory health status N [%(CI)]			
Chronic bronchitis	71 [8(0.06, 0.09)]	57 [7(0.05, 0.09)]	14 [10(0.05, 0.15)]
Past year breathlessness at night	160 [16(0.13, 0.18)]	139 [16(0.14, 0.19)]	21 [15(0.09, 0.21)]



**Figure 1** Distribution of aldehydes and VOCs in the elderly compared to the rest of population. Air pollution levels (in  $\mu$ g/m<sup>3</sup>) measured in dwellings during one week. Box plots (fifth percentile, first quartile, mean, median, third quartile, 95th percentile). Formaldehyde, acetaldehyde, acroleine, hexaldehyde, benzene, toluene, *m*/*p*-xylenes, *o*-xylene, 1.2.4-trimethylbenzene, ethylbenzene, styrene, *n*-decane, *n*-undecane, trichloroethylene, tetrachloroethylene, 1,4-dichlorobenzene, 1-metoxy-2-propanol, 2 butoxy ethanol.

the full household according to occupancy density, and then re-calculated relative to the volume considered as affected under the  $CO_2$  measurement [15]. Ventilation was defined by the air-exchange rate at home in the week of the survey expressed in terms of air change per hour (ach measured by volume per hour) and presented as a continuous variable. Based on the air-exchange rate distribution, poor ventilation was defined by an air-exchange rate value less than the median of the distribution in the dwellings and satisfactory ventilation by an air-exchange rate value above the median.

### Respiratory health assessment

Individuals were interviewed about the usual status of their respiratory health and their respiratory symptoms in the preceding year by completing a standardized selfadministered questionnaire derived from the European Community Respiratory Health Survey (ECRHS) (http:// www.ecrhs.org/). Outcomes considered in the analysis included past year breathlessness at night as defined by "woken in the night by breathlessness during the past 12 months" and chronic bronchitis defined on the basis of the question "Do you have cough or phlegm on most days during periods of at least 3 months each year?" as disease.

Factors considered as potential confounders included age, sex, tobacco smoking habit (classed as: never, ex or current smoking according to the ECRHS definition), educational level, season and moulds at home according to the questionnaire.

### Statistical analysis

Classical statistical methods were used to estimate means, frequencies (percentages), correlation and  $\chi^2$ . Week averages of the VOCs concentrations were provided in  $\mu g/m^3$ . The correlations between the VOCs concentrations were estimated using Spearman correlation coefficient. The prevalence of respiratory health conditions was expressed as a frequency (percentage) of positive responses to the corresponding questions with 95% of Cl. Potential confounders of the relationships between air pollution exposure and health outcomes were described in terms of mean

 Table 2
 Correlation between aldehydes and VOCs.

(quantitative variables) or percentages (qualitative variables). As a first step, to assess the associations between exposure to each VOC and health outcomes, exposure was initially classified as a categorical variable, namely 'low' vs. 'high' exposure, the latter being defined with respect to median value in the distribution of the measured concentration for each pollutant. This categorization of the exposure variable allowed taking into account the nonlinearity in the association between VOCs concentrations and health outcomes. The prevalence of health outcomes was then calculated in each category of exposure, and corresponding unadjusted odds ratios (OR) with 95% confidence intervals (95% CI) were calculated and the associated probability estimated using contingence table for  $\chi^2$  test.

In order to adjust for correlations within people belonging to the same dwelling, to estimate the OR with 95% CI for the relation of exposure to each pollutant to each respiratory outcome, a generalized estimating equation approach (GEE) with exchangeable covariance matrix was performed. This was adjusted for potential confounders (aOR) using the categorical variable. To select adjustment variable for the model relating exposure to air pollutants to health outcomes, bivariate analyses between potential confounders and breathlessness and chronic bronchitis respectively were performed. Variables significantly associated with breathlessness or chronic bronchitis with a p < 0.20 were considered as confounders in the association analysis. Confounders taken into account were gender, age, smoking habit, season of the study, presence of pets, presence of mould, the highest educational level among individuals of the dwelling and the % of the time spent indoors. As a second step, to avoid the use of cut-points for the air pollution exposure variables, statistically significant associations were also explored taking for the exposure to the air pollutant the logarithm of the concentration as a continuous variable in the model into account.

	Acetaldehyde	Acroleine	Hexaldehyde	n-	n-	Benzene	Toluene	1,2,4-
				Decane	Undecane			Trimethylbenzene
Ventilation	-0.17*	-0.34*	-0.25*	-0.26*	-0.09	-0.13	-0.14*	-0.09
Formaldehyde	0.38*	0.50*	0.57*	0.28*	0.25*	0.13*	0.31*	0.33*
Acetaldehyde	1	0.72*	0.53*	0.31*	0.31*	0.35*	0.40*	0.39*
Acroleine		1	0.52*	0.31*	0.29*	0.37*	0.34*	0.34*
Hexaldehyde			1	0.35*	0.34*	0.01	0.3*	0.40*
<i>n</i> -Decane				1	0.84*	0.16*	0.29*	0.61*
n-Undecane					1	0.14*	0.25*	0.56*
Benzene						1	0.65*	0.39*
Toluene							1	0.57*
1,2,4-Trimethylbenzene								1
Ethylbenzene								
m,p-Xylene								
o-Xylene								
Styrene								
1,4-Dichlorobenzene								
Trichloroethylene								
Tetrachloroethylene								
2-Butoxy ethanol								
1-Methoxyl-2-propanol								

In order to guantify the effects of indoor air pollution in elderly compared to the rest of population, analyses were stratified by age. A mean comparison between pollutants concentrations in each group was done by using ANOVA test. In addition, ANOVA test was conducted to compare the distribution of the pollutants in each group. Interaction terms between VOCs and respiratory outcomes were also tested in these models.

Lastly, in case of significant relationships between indoor air pollution and respiratory symptom in the elderly, stratification on poor vs. satisfactory ventilation as previously defined was done.

Analyses were performed with SAS software version 9.2 (PROC ANOVA, PROC GENMOD).

# Results

# Participants and characteristics of population

The population study comprised the 1012 eligible (>15 years) individuals living in 490 dwellings and who completed the health questionnaire [14]. Among the respondents, 14.2% were aged over 65 years with an average age of 71 years, 52% were female. In terms of educational level, among elderly 35% had no formal education or had a primary school level, 25% have been to middle school/college level, 22% to high school level and 18% to higher education. A total of 49% reported that they had never smoked, 39% were ex-smokers and 12% still smoked. Subjects aged over than 65 years spent 80% of their time indoor against 66% in the rest of population. Ten percent of the elderly reported that they had chronic bronchitis and 15% breathlessness. The corresponding percentages in the rest of the study population were respectively: 7%, and 16%. Participants' social and health characteristics comparing the elderly to the rest of population are shown in Table 1.

### VOCs, aldehydes and ventilation

The distribution of VOCs and aldehydes in elderly compared to the rest of population is shown in Fig. 1. Among the 20 air pollutants measured in the French national-scale "housing" campaign, we deliberately excluded 2-butoxyethylacetate and 1-metoxy-2-propylacetate for which very low concentrations were observed, as the median values of their concentrations were 0.3  $\mu g/m^3$  and 0.7  $\mu g/m^3,$  respectively, both being below the limit of detection (LD). For various pollutants, very low and sometimes below LD concentrations were observed in some dwellings. As expected, various air pollutants were strongly correlated each other (Table 2). There was no significant difference in the distribution of air pollutants in the dwellings of the elderly compared to those of the others, according to the ANOVA test (p > 0.05). Ventilation rate within the household did not vary significantly between the elderly and the others in terms of means (0.77 vol/h in elderly vs. 0.74 vol/h in the rest of the population) and medians (0.57 vol/h vs. 0.54 vol/h). Ventilation rate was inversely correlated to several air pollutants, significantly in the case of acetaldehyde, acrolein, hexaldehyde, N-decane, toluene, ethylbenzne and 1,4-dichlorobenzene (Table 2).

# Associations between respiratory health status and VOCs indoor air pollution

The adjusted associations between exposure to VOCs indoor air pollution (categorical variable) and respiratory health outcomes are outlined in Table 3. In the elderly, high levels of toluene and o-xylene were related to breathlessness with AOR = 3.36(1.13, 9.98) and 2.85(1.06, 7.68)respectively. This relationship did not exist in the rest of the population (AOR = 0.91(0.59, 1.39) and 0.84(0.55,1.30) respectively). Reversely, an inverse relationship

Ethylbenzene	m/,p- Xylene	<i>o</i> -Xylene	Styrene	1,4-Dichlorobenzene	Trichloroethylene	Tetrachloroethylene	2-Butoxy ethanol	1-Methoxyl- 2-propanol
-0.18*	-0.07	-0.05	-0.09	-0.18*	-0.03	-0.01	0.04	-0.11
0.29*	0.30*	0.27*	0.37*	0.11	0.09	0.08	0.37*	0.23*
0.36*	0.32*	0.31*	0.44*	0.26*	0.12*	0.08	0.28*	0.28*
0.33*	0.30*	0.27*	0.43*	0.16*	0.13*	0.08	0.32*	0.25*
0.27*	0.26*	0.26*	0.38*	0.13*	0.10*	0.15*	0.42*	0.34*
0.43*	0.40*	0.45*	0.35*	0.30*	0.18*	0.15*	0.20*	0.17*
0.38*	0.35*	0.40*	0.35*	0.25*	0.11	0.08	0.16*	0.15*
0.65*	0.63*	0.56*	0.38*	0.05	0.16*	0.12*	0.13*	0.07
0.78*	0.78*	0.73*	0.45*	0.14*	0.14*	0.12*	0.26*	0.14*
0.66*	0.66*	0.67*	0.43*	0.16*	0.12*	0.09*	0.21*	0.21*
1	0.95*	0.91*	0.53*	0.16*	0.20*	0.17*	0.21*	0.11
	1	0.91*	0.46*	0.13*	0.17*	0.16*	0.19*	0.10
		1	0.49*	0.15*	0.17*	0.15*	0.21*	0.12*
			1	0.21*	0.30*	0.30*	0.35*	0.24*
				1	0.21*	0.28*	0.19*	0.14*
					1	0.49*	0.16*	0.04
						1	0.22*	0.07
							1	0.26*
								1
*P < 0.0001								

between styrene and breathlessness was observed in the entire population and in individuals aged less than 65 years (AOR = 0.64(0.43, 0.95) and 0.58(0.38, 0.89), respectively). The same inverse relationship was found in the elderly between 1-metoxy-2-propanol and chronic bronchitis AOR = 0.10(0.01, 0.82). No other significant relationships were observed. Out of the interactions between VOCs and aldehydes and respiratory symptoms, only those between toluene, o-xylene on one side and past year breathlessness symptoms at night on the other side were statistically significant (p < 0.05). Taking into account the air pollutant concentration as a continuous variable confirmed the results in elderly with odds ratio higher than 1 between past year breathlessness symptoms and toluene (AOR = 1.36(0.96, 1.95)) and o-xylene (AOR = 1.51(0.95, 1.95))2.40)) respectively. In addition, a new significant relationship was observed in the elderly between styrene and past year breathlessness symptoms (AOR = 1.48(1.03, 2.11)).

Stratification according to ventilation conditions in the dwellings showed that *N*-decane was significantly related to past year breathlessness in the case of poor ventilation as defined by an ach value less than the median but not in the case of normal ventilation as defined by an ach value above the median (AOR = 3.66(1.16, 11.53)) (Table 4). Borderline significance associations were observed in the case of poor ventilation between past year breathlessness and toluene and trichloroethylene AOR = 2.76(0.88, 8.63) and 3.27(0.94, 11.41), respectively.

# Discussion

This study explored the relationship between exposure to VOCs and aldehydes and respiratory health outcomes. To our knowledge, this is the first epidemiological study conducted in a representative sample of dwellings focusing on respiratory health effects of indoor VOCs and aldehydes air pollution among elderly compared to the rest of the population in the same sample.

Most of the investigations on health effects of air pollution in elderly have been conducted for outdoor air pollutants, such as particulate matter ( $PM_{10}$ ), nitrogen dioxide ( $NO_2$ ), ozone ( $O_3$ ),  $SO_2$  [17–21]. Major pollutants investigated indoors are ETS and  $PM_{10}$  [22–27]. VOCs have indoor and outdoor sources and concentrations indoors are two- to five-fold higher than outdoors [28,29]. Elderly are more exposed to indoor air pollutants than the rest of the population due to reduced outdoor activities and time spent indoors [8]. In our study population, those aged over 65 years spent 80% of their time at home compared to 66% for the rest of the population (Table 1).

Our results revealed a significant relationship between air pollutants of the VOCs family and breathlessness among the elderly. Toluene and *o*-xylene were associated with an increased prevalence of breathlessness in elderly compared to the rest of the population in spite of the fact that exposure to such pollutants did no differ in the two age groups. These results are in agreement with those from a study conducted by Yoon et al. having showed that exposure to toluene and xylene had a harmful effect on pulmonary function in 154 subjects aged over 65 years [13], under the hypothesis that breathlessness and

dyspnoea are a proxy of lung function deterioration. However, no pulmonary function was available in our study to confirm this hypothesis. In another population of elderly, we had already found that exposure to air pollution was also related to breathlessness in the case of exposure to SO<sub>2</sub> (AOR (95% CI: 1.64 (0.91, 2.96))) [18]. In that population, we also had found a significant link between air pollution and bronchitis-like symptoms, namely a 10% and a 23% increase in usual cough for a 10  $\mu$ g/m<sup>3</sup> increment in  $PM_{10}$  and a 1  $\mu g/m^3$  increment in  $SO_2$ respectively, and a 23% increase in usual phlegm for a  $1 \ \mu g/m^3$  increase in SO<sub>2</sub>, thus confirming health impact of air pollution in the elderly population. In regard to ventilation, previous study had showed that increases rates should result in reduced prevalence of negative respiratory and health outcomes [31]. Our study is in agreement with this result, as stratification on ventilation showed a pronounced effect of n-decane, toluene and trichloroethylene on past year breathlessness in case of poor ventilation in dwellings of the elderly (Table 4).

In order to take strong correlations between pollutants (Table 2) into account, we analyzed the relationship between health outcomes and all pollutants in the same model by using a global VOCs score employed previously in the same population [14]. To obtain the global VOCs score. VOCs including aldehydes concentrations were categorized as 0 if less than the median value and 1 if greater. The global VOCs score was then defined as the sum of the categorized VOCs. As a result, the global VOCs score is the number of air pollutants in the dwellings for which elevated (>median value) concentrations were found. In the present study, the global VOCs score, which ranged 0-20, was fitted as a continuous variable. However, no significant relationship was observed between the global VOCs score and past year breathlessness and chronic bronchitis in both elderly and the rest of population. This supports the proper role of the considered air pollutants.

The observed relationships of VOCs and aldehydes to chronic respiratory symptoms need to be further investigated as these air pollutants are known not to be very reactive [30,31] and moreover were found in low concentrations in our survey except for aldehydes. However, an increasing number of data show that between air pollution and health effects the exposure-response relation is near linear with no evidence of a threshold and it can be hypothesized that the effect is greater in the elderly due to their frailty [32–36]. This is supported by Yoon et al.' study in which exposure to VOCs was also low, indoor levels of benzene, toluene, ethylbenzene and xylene being 5.96  $\pm$  4.08, 11.18  $\pm$  10.49, 4.55  $\pm$  1.78 and 5.24  $\pm$  1.35  $\mu g/$ m<sup>3</sup>, respectively and the outdoor levels 4.31  $\pm$  3.00, 6.20  $\pm$  8.71, 3.10  $\pm$  1.56 and 2.84  $\pm$  1.49  $\mu g/m^3,$  respectively. The underlying mechanisms could consist of oxidative stress and irritation damaging the airways mucosa. It has been shown that aldehydes and VOCs could also influence immune system.

Other explanations for the relationships between breathlessness and living in dwellings with elevated concentrations of toluene and *o*-xylene and for the more pronounced effect of *n*-decane on past year breathlessness observed in cases of poor ventilation in the dwellings found in elderly but not in the rest of the population can be

Table 3         Association betw	een respiratory health	outcomes and concentrati	ons of indoor aldehydes a	nd VOCs in the elder	ly compared to the rest o	f population.		
	Past year breathless	ness at night		Chronic bronchitis				
	All ( <i>N</i> = 1012)	<65 years ( $N = 868$ )	$\geq$ 65 years (N = 144)	All ( <i>N</i> = 1012)	<65 years ( $N = 868$ )	$\geq$ 65 years (N = 144)		
Aldehydes								
Formaldehyde	0.85(0.58, 1.23)	0.71(0.47, 1.07)	2.32(0.91, 5.93)	1.25(0.75, 2.11)	1.16(0.64,2.07)	1.77(0.56, 5.54)		
Acetaldehyde	1.04(0.71, 1.52)	0.94(0.62, 1.41)	2.01(0.77, 5.25)	1.03(0.61, 1.75)	1.15(0.64, 2.08)	0.66(0.21, 2.06)		
Acroleine	1.07(0.73, 1.58)	1.03(0.68, 1.55)	1.43(0.53, 3.87)	1.53(0.90, 2.63)	1.80(0.97, 3.35)	0.82(0.26, 2.58)		
Hexaldehyde	0.83(0.57, 1.20)	0.71(0.47, 1.08)	2.04(0.80, 5.22)	0.81(0.48, 1.34)	0.81(0.46, 1.44)	0.79(0.26, 2.34)		
Aliphatic hydrocarbons								
<i>n</i> -Decane	1.11(0.76, 1.64)	0.99(0.65, 1.52)	2.38(0.90, 6.27)	1.05(0.61, 1.78)	0.87(0.48, 1.57)	2.33(0.72, 7.50)		
n-Undecane	0.95(0.65, 1.37)	0.88(0.58, 1.34)	1.39(0.53, 3.65)	0.92(0.53, 1.56)	0.91(0.50, 1.69)	0.90(0.28, 2.87)		
Aromatic hydrocarbons								
Benzene	0.93(0.63, 1.37)	0.90(0.59, 1.38)	1.10(0.40, 3.00)	1.40(0.83, 2.38)	1.73(0.92, 3.26)	0.59(0.16, 2.11)		
Toluene	1.08(0.74, 1.58)	0.91(0.59, 1.39)	3.36(1.13, 9.98)***	1.11(0.65, 1.91)	1.20(0.64, 2.27)	0.85(0.26, 2.74)		
1,2,4-trimethylbenzene	0.99(0.67, 1.44)	0.87(0.57, 1.32)	2.23(0.84, 5.94)	1.24(0.74, 2.11)	1.58(0.86, 2.89)	0.47(0.13, 1.63)		
Ethylbenzene	0.93(0.63, 1.37)	0.84(0.54, 1.30)	1.70(0.64, 4.51)	1.29(0.75, 2.22)	1.16(0.62, 2.14)	2.00(0.59, 6.71)		
m,p-Xylene	0.95(0.64, 1.37)	0.86(0.56, 1.32)	1.61(0.60, 4.31)	1.36(0.74, 2.50)	1.34(0.73, 2.45)	1.66(0.49, 5.58)		
o-Xylene	1.00(0.68, 1.47)	0.84(0.55, 1.30)	2.85(1.06, 7.68)*,**	1.46(0.86, 2.48)	1.57(0.86, 2.87)	1.09(0.33, 3.58)		
Styrene	0.64(0.43, 0.94)*	0.79(0.47, 1.34)	1.08(0.40, 2.90)	0.99(0.58, 1.64)	1.16(0.63, 2.10)	0.50(0.15, 1.65)		
Halogenated hydrocarbons								
1,4-dichlorobenzene	0.91(0.62, 1.32)	0.84(0.55, 1.28)	1.46(0.55, 3.87)	0.92(0.54, 1.53)	0.85(0.48, 1.53)	1.20(0.34, 4.19)		
Trichloroethylene	1.24(0.85, 1.82)	1.10(0.72, 1.67)	2.81(1.02, 7.76)*	1.50(0.90, 2.53)	1.47(0.83, 2.61)	1.67(0.52, 5.34)		
Tetrachloroethylene	1.23(0.85, 1.82)	1.12(0.73, 1.68)	2.48(0.89, 6.85)	1.27(0.76, 2.13)	1.24(0.70, 2.21)	1.39(0.42, 4.55)		
Glycol ethers								
2 Butoxy ethanol	0.91(0.61, 1.34)	0.81(0.53, 1.25)	1.80(0.67, 4.81)	0.92(0.54, 1.55)	1.03(0.57, 1.87)	0.54(0.15, 1.87)		
1-Metoxy-2-propanol	0.81(0.54, 1.17)	0.80(0.53, 1.22)	0.76(0.26, 2.22)	0.75(0.45, 1.24)	1.01(0.57, 1.80)	0.10(0.01, 0.82)*		

Values are odds ratios (OR) and 95% confidence interval (95% CI) obtained the generalized estimating equation approach adjusted for age, sex, tobacco smoking habit, education status, season, presence of pets, moulds and % of the time spent indoors. Exposure was defined with respect to the median value of the distribution of the evaluated concentrations at home. \*P < 0.05.

\*\*Interaction: *P* < 0.05.

Table 4	Relationship	between	past y	/ear	breathl	essness
and aldehy	des and VOCs	accordin	g to ve	ntila	tion in e	elderly.

	Past year breathlessness			
	Poor ventilation	Satisfactory ventilation		
Formaldehyde	2.43(0.78, 7.55)	1.50(0.23, 9.77)		
N-decane	3.66(1.16, 11.53)*	5.89(0.70, 49.41)		
Toluene	2.76(0.88, 8.63)**	4.22(0.60, 29.37)		
o-Xylene	2.37(0.76, 7.40)	2.91(0.47, 17.95)		
Trichloroethylene	3.27(0.94, 11.41)**	5.76(0.65, 50.51)		

Values are odds ratios (aOR) and 95% confidence interval (95% CI) obtained through the generalized estimating equation approach adjusted for age, sex, tobacco smoking habit, education status, season, presence of pets, moulds and % of the time spent indoors.

Exposure to air pollution was defined with respect to the median value of the distribution of the measured concentrations at home.

Based on the air-exchange rate distribution, a poor ventilation was defined by an air-exchange rate value less than the median and a satisfactory ventilation by a value above the median. \*P < 0.05.

\*\*P < 0.10.

evoked. These include dampness, biologicals such as moulds and or bacteria or other air pollutant partly due to low ventilation that could not be assessed in detail in our survey (data not shown). However, adjustment for dampness and moulds assessed by the technicians during the survey did not modify the results. Recently, Sarigiannis reported that the concentrations of benzene and other VOCs are somewhat higher in southern Europe, something that can be attributed to the higher temperatures that lead to higher volatilization [37]. On the other hand, during spring and summer, the frequent opening of windows results in higher air-exchange rates and therefore decrease of the concentration of VOCs indoors. The type of ventilation may also differ, e.g. in northern Europe, mechanical ventilation is common, whereas in southern parts of Europe natural ventilation is used. The air flow rates may differ significantly among the different ventilation types resulting in consequent differences in concentration levels.

The principal strength of this study is the selection process of our population through a random populationbased sample of dwellings drawn from the entire sample of all principal residences in mainland France (24 million) [15,16]. The other strong point of our study consists in the objective assessments of air quality. Indoor air concentrations of aldehydes and VOCs were objectively measured by using passive samplers in the bedroom of the reference person in the household. In addition, our analyses were adjusted on several risk factors such as gender, age, smoking habit, season, presence of pets, presence of mould, the highest educational level among individuals of the dwelling and the percentage of the time spent indoors. Lastly, taking the multi-pollution mixture into account did not modify the findings.

Our study presents certain limitations. Measurements of aldehydes and VOCs exposure were conducted for one week only. This may be not representative of long-lasting exposure and in particular of past year exposure. Outdoor air pollution was not considered in this study so that the exact role of indoor exposure could not be identified. Symptoms and respiratory disease were assessed by questionnaire and not confirmed by a physician although our questionnaire is standardized and validated. In addition, our sample contained only 144 subjects aged more than 65 years old compared to the rest of population (868 subjects); such a sample size does not allow us to generalize the obtained results.

### Conclusion

A comparison between elderly and the rest of population regarding respiratory health effects of indoor air pollution by aldehydes and VOCs exposure shows a higher prevalence of breathlessness in the former compared to the latter in spite of similar levels of air pollutants in their dwellings. This could be due to the fact that elderly spend more times indoors and are thus more exposed than the others. This could also be an effect of normal or pathological ageing in the response to air pollution aggressions. Further investigations are needed to investigate whether the elderly are frailer than the rest of population regarding adverse effects of indoor air pollution.

# **Conflicts of interest**

None.

### References

- Boita F, et al. Evaluation of pulmonary function in the elderly. Intergroupe Pneumo Geriatrie SPLF-SFGG. Rev Mal Respir 2006;23(6):619-28.
- [2] Simoni M, et al. Indoor air pollution and respiratory health in the elderly. Eur Respir J Suppl 2003;40:15s-20s.
- [3] Zeghnoun ADF. Description du budget espace-temps et estimation de l'exposition de la population française dans son logement. Rapport. OQAI-InVS, D.d.b.e.-t.e.e.d.l.e.d.l.p.f.d.s. logement; 2010. p. 1–37.
- [4] Payne-Sturges DC, et al. Personal exposure meets risk assessment: a comparison of measured and modeled exposures and risks in an urban community. Environ Health Perspect 2004;112(5):589–98.
- [5] Bakke JV, et al. Symptoms, complaints, ocular and nasal physiological signs in university staff in relation to indoor environment – temperature and gender interactions. Indoor Air 2008;18(2):131–43.
- [6] Viegi G, et al. Indoor air pollution and airway disease. Int J Tuberc Lung Dis 2004;8(12):1401-15.
- [7] Sexton K, et al. Estimating volatile organic compound concentrations in selected microenvironments using timeactivity and personal exposure data. J Toxicol Environ Health A 2007;70(5):465–76.
- [8] Hulin M, Simoni M, Viegi G, Annesi-Maesano I. Respiratory health and indoor air pollutants based on quantitative exposure assessments. Eur Respir J 2012;40(4):1033-45.
- [9] Annesi-Maesano I, et al. Poor air quality in classrooms related to asthma and rhinitis in primary schoolchildren of the French 6 cities study. Thorax 2012;67(8):682–8.
- [10] Hulin M, Caillaud D, Annesi-Maesano I. Indoor air pollution and childhood asthma: variations between urban and rural areas. Indoor Air 2010;20(6):502–14.

- [11] Wieslander G, et al. Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces. Int Arch Occup Environ Health 1997;69(2):115-24.
- [12] Arif AA, Shah SM. Association between personal exposure to volatile organic compounds and asthma among US adult population. Int Arch Occup Environ Health 2007;80(8):711-9.
- [13] Yoon HI, et al. Exposure to volatile organic compounds and loss of pulmonary function in the elderly. Eur Respir J 2010; 36(6):1270-6.
- [14] Billionnet C, et al. Quantitative assessments of indoor air pollution and respiratory health in a population-based sample of French dwellings. Environ Res 2011;111(3):425–34.
- [15] Kirchner S, et al. Air quality in French homes. Environnement, Risques et Sante 2007;6:259–69.
- [16] Ramalho ODM, Grégoire A, Garrigue J, Kirchner S. French permanent survey on indoor air quality. Part 1: measurement protocols and quality control. In: Healthy buildings. Lisboa: PRT; 2006. p. 327–31.
- [17] Anderson HR, et al. Particulate air pollution and hospital admissions for cardiorespiratory diseases: are the elderly at greater risk? Eur Respir J Suppl 2003;40:39s-46s.
- [18] Bentayeb M, et al. Bronchitis-like symptoms and proximity air pollution in French elderly. Respir Med 2010;104:880-8.
- [19] Filleul L, et al. Difference in the relation between daily mortality and air pollution among elderly and all-ages populations in southwestern France. Environ Res 2004;94:249-53.
- [20] Lee JT, Son JY, Cho YS. The adverse effects of fine particle air pollution on respiratory function in the elderly. Sci Total Environ 2007;385:28–36.
- [21] Medina-Ramon M, Zanobetti A, Schwartz J. The effect of ozone and PM10 on hospital admissions for pneumonia and chronic obstructive pulmonary disease: a national multicity study. Am J Epidemiol 2006;163:579–88.
- [22] Hussein T, et al. Particle size characterization and emission rates during indoor activities in a house. Atmos Environ 2006; 40(23):4285–307.
- [23] Jaakkola MS. Environmental tobacco smoke and health in the elderly. Eur Respir J 2002;19(1):172-81.
- [24] Janson C, et al. Effect of passive smoking on respiratory symptoms, bronchial responsiveness, lung function, and total serum IgE in the European Community Respiratory Health

Survey: a cross-sectional study. Lancet 2001;358(9299): 2103-9.

- [25] Lanki T, et al. Determinants of personal and indoor PM2.5 and absorbance among elderly subjects with coronary heart disease. J Expo Sci Environ Epidemiol 2007;17(2):124–33.
- [26] Downs SH, et al. Reduced exposure to PM10 and attenuated age-related decline in lung function. N Engl J Med 2007; 357(23):2338-47.
- [27] Yin P, et al. Passive smoking exposure and risk of COPD among adults in China: the Guangzhou Biobank Cohort Study. Lancet 2007;370(9589):751-7.
- [28] Sexton K, et al. Comparison of personal, indoor, and outdoor exposures to hazardous air pollutants in three urban communities. Environ Sci Technol 2004;38(2):423–30.
- [29] Wallace LA. Personal exposure to 25 volatile organic compounds. EPA's 1987 team study in Los Angeles, California. Toxicol Ind Health 1991;7(5–6):203–8.
- [30] Wolkoff P, Wilkins CK, Clausen PA, Nielsen GD. Organic compounds in office environments – sensory irritation, odor, measurements and the role of reactive chemistry. Indoor Air 2006 Feb;16(1):7–19.
- [31] Mohave L. Organic compounds as indicators of air pollution. Indoor Air 2003;13(Suppl. 6):12-9.
- [32] Sundell J, et al. Ventilation rates and health: multidisciplinary review of the scientific literature. Indoor Air 2011;21(3): 191–204.
- [33] Delfino RJ, et al. Effects of air pollution on emergency room visits for respiratory illnesses in Montreal, Quebec. Am J Respir Crit Care Med 1997;155(2):568-76.
- [34] Morgan G, Corbett S, Wlodarczyk J. Air pollution and hospital admissions in Sydney, Australia, 1990 to 1994. Am J Public Health 1998;88(12):1761–6.
- [35] Prescott GJ, et al. Urban air pollution and cardiopulmonary ill health: a 14.5 year time series study. Occup Environ Med 1998; 55(10):697–704.
- [36] Bentayeb M, Simoni M, Norback D, Baldacci S, Maio S, Viegi G, et al. Indoor air pollution and respiratory health in elderly. J Environ Sci Health Part A 2013 [in press].
- [37] Sarigiannis DA, Karakitsios SP, Gotti A, Liakos IL, Katsoyiannis A. Exposure to major volatile organic compounds and carbonyls in European indoor environments and associated health risk. Environ Int 2011 May; 37(4):743–65.