Socioeconomic position and outdoor nitrogen dioxide (NO2) exposure in Western Europe: A multi-city analysis

DOI:10.1016/j.envint.2016.12.026

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Socioeconomic position and air pollution exposure in Western Europe:

A multi-city analysis

Sofia Temam[1,2,3*], Emilie Burte[1,2], Martin Adam[4,5], Josep M. Antó[6,7,8,9], Xavier Basagaña[6,8,9], Jean Bousquet[1,2,10], Anne-Elie Carsin[6,8,9], Bruna Galobardes[11], Dirk Keidel[4,5], Nino Künzli[4,5], Nicole Le Moual[1,2], Margaux Sanchez[1,2], Jordi Sunyer[6,8,9], Roberto Bono[12], Bert Brunekreef[13,14], Joachim Heinrich[15,16], Kees de Hoogh[4,5,17], Debbie Jarvis[17,18], Alessandro Marcon[19], Lars Modig[20], Rachel Nadif[1,2], Mark Nieuwenhuijsen[6,8,9], Isabelle Pin[21,22,23,24], Valérie Siroux[21,22,23], Morgane Stempfelet[25], Ming-Yi Tsai[4,5], Nicole Probst-Hensch[4,5], Bénédicte Jacquemin[1,2,6,8,9]

1. INSERM, U1168, VIMA: Aging and chronic diseases. Epidemiological and public health approaches, Villejuif, France
2. Université Versailles-St-Quentin-en-Yvelines, UMR-S 1168, Montigny-le-Bretonneux, France
3. Université Paris-Sud, Kremlin-Bicêtre, France
4. Swiss Tropical and Public Health Institute, Basel, Switzerland
5. University of Basel, Basel, Switzerland
6. Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
7. Hospital del Mar Medical Research Institute , Barcelona, Spain
8. Universitat Pompeu Fabra, Barcelona, Spain
9. CIBER Epidemiología y Salud Pública, Barcelona, Spain
10. Centre Hospitalo-Universitaire, Montpellier, France
11. School of Social and Community Medicine, University of Bristol, Bristol, United Kingdom

12. Department of Public Health and Pediatrics, University of Turin, Turin, Italy
13. Institute for Risk Assessment Sciences, University Utrecht, Utrecht, the Netherlands
14. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands
15. Institute of Epidemiology, German Research Center for Environmental Health (GmbH), Helmholtz Zentrum München, Neuherberg, Germany
16. Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine Ludwig Maximilians University, Munich, Germany
17. Faculty of Medicine, School of Public Health, Imperial College London, London, United Kingdom
18. MRC-PHE Centre for Environment and Health, Imperial College London, London, United Kingdom
19. Unit of Epidemiology and Medical Statistics, Department of Diagnostics and Public Health, University of Verona, Verona, Italy
20. Public Health and Clinical Medicine, Umea University, University Hospital, Umea, Sweden
21. IAB, Environmental Epidemiology Applied to Reproduction and Respiratory Health, INSERM, Grenoble, France
22. IAB, Environmental Epidemiology Applied to Reproduction and Respiratory Health, Université Grenoble-Alpes, Grenoble, France
23. IAB, Environmental Epidemiology Applied to Reproduction and Respiratory Health, CHU Grenoble, Grenoble, France
24. Pédiatrie. CHU Grenoble, Grenoble. France
25. InVS, French Institute for Public Health Surveillance, Saint-Maurice, France

Corresponding author:

Sofia Temam

INSERM UMR-S 1168

VIMA: Aging and chronic diseases. Epidemiological and public health approaches

16 Avenue Paul-Vaillant Couturier

F-94807 VILLEJUIF Cedex

Tel. +33145595012

sofia.temam@inserm.fr

ACKNOWLEDGMENTS

ESCAPE (FP7/2007-2011, Grant Nr.211250)

French National Institute for Statistics and Economic Studies

FUNDING

This work was supported by the French Agency for Food, Environmental and Occupational Health & Safety [Grand Nr.PNR-EST-12-166].

Sofia Temam benefited from a PhD scholarship of the Paris-Sud University, France.

Bruna Galobardes is funded by a Wellcome Trust fellowship (Grand Nr.089979)

SAPALDIA is funded by the Swiss National Science Foundation (Grand Nr.S33CSCO-134276/1)

COMPETING FINANCIAL INTEREST

None

ABSTRACT

Background: Inconsistent associations between socioeconomic position (SEP) and air pollution have been reported in Europe, but methodological differences prevent any direct between-study comparison.

Objectives: Assess and compare the association between SEP and air pollution exposure at residential address across 20 cities from eight European countries.

Methods: Three SEP indicators, defined at individual-level (education and occupation) and area-level (unemployment rate) were assessed in three European multicenter cohorts. NO_2 exposure was estimated at participants' addresses with land use regression models developed within the European Study of Cohorts for Air Pollution Effects (ESCAPE). Pooled and city-specific linear regressions were used to analyze associations between each SEP indicator and NO_2. Heterogeneity across cities was assessed using a random-effects meta-analysis.

Results: 8277 participants were included. Pooling the data, participants with lower individual-SEP indicators tended to be less exposed to NO_2. Conversely, participants living in neighborhood characterized by higher unemployment rate were more exposed. However, in both cases, city-specific results exhibited heterogeneity across areas (I^2>75%). When having individual- and area-SEP indicators in the same model, estimates were similar compared to the simple regression model (individual- and area-SEP in separate models), suggesting independent associations between individual-SEP and unemployment rate with NO_2.

Conclusions: At European level, associations between SEP and NO_2 were heterogeneous and no geographical or urban pattern could be identified. Our results showed that individual- and area-SEP indicators capture different aspects of the SEP distribution regarding exposure to air pollution, stressing the importance of considering both in air pollution epidemiological studies**.**

INTRODUCTION

Environmental inequality refers to a differential distribution of environmental hazards across socioeconomic or socio-demographic groups (1,2). Historically, research on environmental inequality has emerged in USA following the Environmental Justice Movement (3–8). Repeatedly, US studies reported that lower socioeconomic or minority groups were likely to be exposed to higher air pollution concentrations (7,9–12). However, results from US studies cannot be extended to European countries because of a very different socio-spatial organization, specifically in urban areas (9,13,14).

In Europe, a limited number of studies had investigated the relationship between SEP and air pollution, mainly in UK first and then in other European countries (15). These studies reported mixed results (9,16) according to the city considered (14,17–30). Mixed patterns were also reported within the same country, for instance in France or Spain (14,25,31,32). That being, these studies are difficult to compare because they used different methodologies to assess air pollution exposure or to define SEP (9,33). Most of these studies used ecological data that can raise methodological issues such as ecological fallacy, modifiable area unit problem (MAUP) or spatial autocorrelation (24,34–36). Few studies used individual-level data (i.e. air pollution exposure estimated at people's residential address and individual SEP) or multilevel data (i.e. SEP estimated at individual and area-level) and most of them considered one city at a time (14,18,22,26,37–40). Recent evidences showed the importance of accounting SEP at both levels because they are independently associated with health outcomes but this has rarely been investigated with air pollution exposure in Europe (9,41–44). Besides individual SEP and residential socioeconomic context, Soobader et al. underlined the importance of taking into account the macro-level (i.e. regional or national scale) as it could play a role in shaping environmental disparities (45). The macro-level may capture the broader social context (environmental policies, national economy, etc.) which could drive the pattern observed at local level.

Relationship between SEP and air pollution still need to be investigated in Europe (9,33) as SEP is one of the major potential determinant of variability of the association between air pollution and health outcomes (3,46,47). Within the framework of the multicenter European Study of Cohorts for Air Pollution Effects (ESCAPE) (48,49), we had the opportunity to fill this gap by comparing the relationship between SEP and air pollution across a large range of European cities using both homogenized individual pollutant exposure estimates and SEP indicators. The main objective of the present analysis was to assess the relationship between SEP (defined at both individual- and area-level) with outdoor air pollution exposure in Western European urban areas.

METHODS

Study population

This cross-sectional study included participants of three multicenter cohorts that had previously collaborated together (50) and were involved in the ESCAPE study: the European Community Respiratory Health Survey (ECRHS) (51), the Epidemiological study on Genetics and Environment of Asthma (EGEA) (52) and The Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA) (53). Details on each cohort are given elsewhere (51–53) and summarized in the supplementary file. Overall, 9556 are included in this study (4738, 1078, 2461 participants in ECRHSII, EGEA2 and SAPALDIA2 respectively; see Figure S1). The participants were from 20 different urban areas of eight Western European countries, geographically spread across the North (Umea (Sweden)), the middle (Norwich, Ipswich (United Kingdom); Erfurt (Germany); Antwerp (Belgium); Paris-

Region, Lyon, Grenoble, Marseille (France); Basel, Geneva, Lugano (Switzerland)) and the South of Europe (Verona, Pavia, Turin (Italy); Oviedo, Galdakao, Barcelona, Albacete, Huelva (Spain)).

Air pollution exposure

We considered nitrogen dioxide (NO_2) as a marker of near-road traffic-related air pollution, which is of particular interest in urban areas (54). In the framework of ESCAPE, a single harmonized exposure assessment protocol has been developed to estimate the NO_2 annual concentrations (48). ESCAPE only included a subset of the centers included in ECRHS, EGEA and SAPALDIA. Briefly, in each area covered, two-week integrated NO_2 measurements at approximately 40 sites were made in three different seasons over a one-year period between 2008 and 2011. Area-specific land use regression models (LUR) were developed to explain the spatial variation of NO_2 using a variety of geographical data including traffic, population and land use variables. These models were then used to assign estimates of NO_2 annual concentrations at each participant's geocoded residential address. Back-extrapolated exposure were also estimated because ESCAPE air pollution measurement campaigns took place after the health surveys for the three cohorts (48). However, correlations between back-extrapolated and non-back-extrapolated concentrations were high (r=0.95) so we considered for this analysis the non-back-extrapolated data (55). The areas included in the present analysis were of substantially different sizes (55). Most of these areas could be defined as metropolitan areas (large cities with surrounding smaller suburban communities) but some areas were restricted to a single city (municipality). For purposes of clarity, we refer to these different ESCAPE areas as "cities".

Markers of socioeconomic position

We used markers of SEP defined at two different scales:

Individual-level SEP: At individual-level, we used educational level and the occupational class. Both were assessed in the same way in the three cohorts. Educational level corresponded to the age at completion of full-time education. All participants were adults at the time of the survey and thus had completed their education. We categorized the continuous variable into country-specific tertiles (high, medium and low). Occupational class was based on the longest job held between baseline and follow-up and categorized in four classes according to the International Standard Classification of Occupation (ISCO-1988) (56): Manager and Professional (Occupational Class-I); Technician & associate (OC-II); Other non-manual (OC-III); Skilled, semi-skilled and unskilled manual (OC-IV). In SAPALDIA, occupation information between baseline and follow-up was missing for 659 participants therefore we used the longest job ever for 624 participants. These both individual-SEP indicators are related to income (57) and thus could influence individuals' economic capacities to live in less polluted areas.

Area-level SEP: To characterize the socioeconomic residential context of the participants, we used the unemployment rate (proportion of unemployed persons of the labor force). As NO_2 is a marker of intra-urban traffic pollution it was important to used intra-urban socioeconomic characteristics (42). The neighborhood level corresponded to the smallest geographical level unit with census-based data available in the different countries (see for specific characteristics Table S1). We obtained this indicator from 2001 national censuses (except for France: 2008 and Switzerland: 2006). Neighborhood unemployment rate has been associated to worse health outcomes in several studies in the European context (58–61). Moreover, this choice was also justified by the fact that among other neighborhood variables the unemployment rate was available for most cities (n=16) and had a relative comparable meaning across Europe. However, as the magnitude of the unemployment rate varied across Europe countries, we standardized it using country-specific z-scores to take into account this variability.

Macroeconomic data

In addition to individual and neighborhood SEP variables, we selected a range of regional statistics provided by the Organization for Economic Cooperation and Development (OECD). The Nomenclature of Territorial Units for Statistics (NUTS) geography was designed to provide units for statistical comparisons across Europe. We selected the level 3 of the 2002 version of this geography (NUTS3 regions hereafter) (62). To select the most relevant variables we used a principal components analysis (PCA) from a set of 22 variables covering different fields (demography, education, job market and housing; see Supplemental Materials for details). We kept 10 variables that contributed for 84% of the variability between the NUTS3 regions: density, employed persons Extra-European Union, Gross domestic product (GDP), Purchasing Power Standard, First and second stage of tertiary education, percentage of person living alone, percentage of household composed of non-family nucleus, percentage of one-person household, percentage of conventional dwellings occupied by the owner.

Strategy of analysis

Main analyses: We presented the general characteristics for all the cities (n=20) however the main analyses were performed including only cities with available data at both individual- and neighborhood-SEP (n=16). The strategy of analysis aimed at testing the hypothesis that the NO_2 annual concentration (dependent variable) differs according to the individual- and neighborhood-SEP of the participants. Given the high heterogeneity of the NO_2 distribution across the ESCAPE cities (63,64), we performed analyses considering first the pooled dataset and then each city separately (city-specific model).

First, we ran a standard linear regression model that ignored the nested structure of the observations (within cities/neighborhoods). Second, we ran a standard multilevel linear regression model with random effects that took into account the hierarchical structure of the data by disentangling the residual variability at the individual and neighborhood level (plus city level for the pooled data). As NO_2 concentrations were positively skewed in most cities, we transformed the variables using natural log transformation. For ease of interpretation, we converted the regression coefficients (βs) into percent increase (95% CI) per unit change in the explanatory factor using the formula [exp(β)-1]*100. For the categorical variable, we calculated the percent increase (95% CI) for each SEP indicator's subgroup (i.e. low, medium and high for educational level) and tested the statistical differences of the coefficients against the highest SEP group (reference group). We tested also the linear trend across the subgroups. In the analysis showing the association between NO_2 and occupational class, we deliberately did not show results for participants who were not in the labor force as this class was too heterogeneous to draw any kind of conclusion. For the unemployment rate, we calculated the percent increase (95% CI) for an increase of 1 SD of the unemployment rate.

All models were at least adjusted for the studies. Educational level and occupational class were not included in the same model because of collinearity. Separate analysis using different socioeconomic characteristics has been also recommended to evaluate the consistency of the associations potentially observed (65). We checked for potential interactions between SEP and sex, SEP and age and between each SEP indicator. Analyses were conducted using R statistical software (Version 3.0.3) and SAS 9.3.

Additional analyses: In the supplemental materials, we presented additional results including all the cities (n=20). To test for the robustness of our results, we ran logistic regression models using the proportion of participants with 'high' NO_2 exposure concentrations (above the 75th percentile of the distribution by cities) as the outcome because the linearity was not verified in all cities. To try to understand the heterogeneity of the associations between the cities, we conducted a meta-regression with variables at NUTS3 level as predictors of the variation (each variables was considered separately).

As pointed out above some areas included in this analysis were artefacts because they corresponded to metropolitan areas rather than cities. We ran a sensitivity analysis by examining more in detail the area labelled “Paris” which covered in reality the metropolitan area of “Paris-Region”. Instead of considering participants of Paris in only one area as it was done in the main analysis, we grouped the participants in three distinctive areas (i.e. City of Paris, the inner-suburbs and the outer-suburbs) which were characterized by particular sociodemographic and geographic situations that could influence the association between air pollution and SEP. The methods and results were presented in detail in the supplemental materials and discussed in the main article.

RESULTS

Description of the study population

Out of the 9556 participants with NO_2 estimates, we excluded participants with missing data on NO_2 (n=446), education (n=444) and occupation (n=389) (Figure S1). The neighborhood unemployment rate was not available for Umea, Erfurt, Basel and Lugano and was missing for 63 participants in the other cities for whom neighborhood could not be linked (Table 1a). The study population (Table 1b) was composed of 48% of males, with a mean age (±standard deviation; ±SD) of 46(±11). Regarding the NO_2 distribution, we found substantial variability between cities with a mean ranging from 5(±2.6) (Umea) to 57(±14) $\mu g/m^3$ (Barcelona) as well as within cities. Participants completed their education on average at age 20(±4) (Table 1a). The proportion of non-manual workers ranged from 7% (Paris) to 42% (Galdakao) and was generally higher in the Spanish cities (44% on average). The neighborhood unemployment rate varied from 3% (Pavia) to 22% (Huelva). In all cities, we observed that, on average, less educated participants were employed in less skilled occupations (p-value for trend <0.001) (see Table S2). Less educated participants or with less skilled occupations were also those who lived in neighborhoods with higher unemployment rate (see Table S3-S4).

Pooled results

Pooled results are shown in Table 2. In the model taking into account only clustering within cities (Model 1), low educational level and manual occupations were associated with a decrease of NO_2 exposure (Percent difference (95% CI) Low vs. High educational level= -6.9% (-9.1; -4.7); OC-I vs. OC-IV=-5.6% (-8.2; -3.0)). Conversely, higher unemployment rate at neighborhood level was associated with an increase in NO_2 exposure (7.3% (6.3; 8.4) per 1 SD increase in the unemployment rate). When both individual- and area-SEP markers were introduced simultaneously, we found similar effect size (Low vs. High educational level= -8.7% (-10.8; -6.5) and 7.8% (6.7; 8.9) per 1 SD increase in the unemployment rate). Accounting for both city and neighborhood clustering (Model 2) decreased the effect size of both the individual- and the neighborhood-SEP but associations remained significant for educational level and the unemployment rate, but no longer significant for occupational class.

City-specific results

In the city-specific analyses using standard linear regression models (Figures S2-S4), associations with NO_2 exposure exhibited strong between-city heterogeneity (I^2>76%, p<0.001) whatever the SEP indicator used. When accounting for neighborhood clustering (Table 3a for educational level and Table3b for occupational class), we found that individual-SEP was weakly or not associated with NO_2 exposure for most cities. Regarding educational level (Table 3a), significant associations were only found in Lyon (Low vs. High =-3.6 (-12.3; -5.9)) and Verona (-16.1 (-26.5; -4.3)). Regarding occupational class, significant associations were found for the middle class in Paris (OC-III vs. OC-I= -3.3 (-6.4; -0.1) and Oviedo (-8.7 (-15.7; -1.2). Regarding the area-SEP, in most cities, living in neighborhood with higher unemployment rate was associated with higher NO_2 exposure (regardless of the individual-

SEP marker included in the model) except in Oviedo, Barcelona where an inverse association was observed. No associations were found in Pavia, Turin and Albacete.

Additional analyses

In the pooled analysis, we did not find interactions between SEP and sex, SEP and age and between each SEP indicator (not shown). Results from the logistic regression models (high exposure) were consistent with the linear regression ones in both the pooled (Table 2) and city-specific analyses (see tables S5a for educational level and S5b for occupational class).

In the meta-regression, any of the regional variables explained the between cities heterogeneity of the associations between any of the three different SEP indicators and air pollution, except for the GDP variable with neighborhood unemployment rate; where we found that more the NUTS3 regions were wealthier more the people living in deprived neighborhood were exposed to NO_2 (Figure S5).

Finally, in Paris-Region (supplemental materials), we found similar results, thus was that participants with lower educational level or occupation class were less exposed to air pollution (not significant) but those living in more deprived areas were more exposed, whether pooling participants in one area (Paris-Region) than by more comprehensive sub-regions (i.e. city of Paris, inner suburbs and outer suburbs).

DISCUSSION

Main results

We investigated whether SEP evaluated at both individual- and area-level was associated with air pollution exposure across twenty cities of Western Europe. Pooled analyses masked important heterogeneity across the cities suggesting that environmental inequality in terms of air pollution cannot be generalized in Europe. Consistently with the few multi-city studies that used a comparable approach to ours (14,26,66), city appeared to be the major predictor for NO_2 exposure.

Associations between educational level on one part and occupational class on another part with NO_2 were in the same direction (lower exposure in lower individual-SEP) in the pooled data and usually in the same direction for the city-specific analyses showing that both indicators measured the same concept (67,68). Globally, associations between individual-SEP and NO_2 were generally weak and non-significant. We found opposite associations between neighborhood-SEP and NO_2 (higher exposure in lower area-SEP) compared to individual-SEP, in the pooled data and in most cities in the city-specific models. Opposite associations had also been reported in Europe (40) and in Montreal (35). One possible explanation for the difference in direction is that the area-SEP is capturing more than just SEP such as industrialization and could be more adapted to study environmental inequality than individual-SEP. Moreover, NO_2 variation was relatively small across the individual-SEP markers, and after adjusting for area-SEP marker there was little evidence of potential confounding by individual-SEP. Stronger associations with air pollution for area-level SEP compared to individual-level SES has been also reported in other studies in the European context (39,40,42). Place of residence is strongly patterned by social position (44) and outdoor air pollution is spatially located within cities, therefore the degree to which air pollution is socially patterned is likely to occur more at area-level as well. Area-SEP seemed a better predictor for air pollution exposure than the individual-SEP.

Accounting for both city and neighborhood clustering using a two level random intercept model drastically decreased the size effects of the associations for both individual- and area-SEP markers. This has been observed in others studies (40,47,69) showing the importance to accounting for clustering in analyses including spatially nested data. With the multilevel approach the effect of unemployment rate remained in all cities but the effect of the individual-SEP decreased and even became null for several cities showing that variability was mainly explained by the city first then by the neighborhoods and for a smaller part by the individual-SEP.

Strengths

To the best of our knowledge this is the first study including a large sample of cities geographically representative of Western Europe, with important within- and between-area variability of air pollution exposure. We used NO_2 a traffic related pollutant known to have a great intra-urban variability and thus was the most appropriate to study socioeconomic differences at individual-level. To date, no study had compared as many cities using standardized air pollution estimates at participant's residential address and homogenized SEP indicators at both individual- and area-level. As underlined in a recent review, studies including individual data (for both air pollution and SEP) are recommended because they allow producing more robust inferences at individual-level (9,33). We used two different individual-SEP indicators that allowed taking into account different components of the participants' SEP (57,67). Recent evidence showed the importance of accounting SEP at both levels because they were independently associated with health outcomes (43,44,46,66,70,71) but this had rarely been investigated with air pollution exposure (38,39,42). In our analysis, we used an area-based indicator defined at the smallest unit available in each country to avoid MAUP as recommended (35,72–74). To better understand the direction of the associations between SEP and NO_2 across the cities, we performed a meta-regression analysis following the recommendations of Thompson and Higgins (75). With the regional indicators we tried to capture a broader context that could encompass the spatial and historical urban patterning of the cities. We found that GDP explained in part the positive associations between unemployment rate and NO_2 suggesting that wealthiest cities were also those where environmental disparities were higher (13).

Limitations

Due to data confidentiality, we did not have access to participants' geographic coordinates and were not able to analyze their spatial distribution and check for potential spatial autocorrelation in the residuals within each city. However, Beelen et al. who developed the LUR models tested spatial autocorrelation of the NO_2 level using the Moran index and it was generally small and non-significant (48). We applied however an aspatial multilevel model that took into account the clustering of the participants within neighborhood. Some studies compared aspatial multilevel models to a spatial approach and found little difference both (65,66).

We considered only the unemployment rate, the sole indicator of neighborhood SEP uniformly available for most of the cities, but this single indicator might unlikely fully describe participants' neighborhood socioeconomic context (44). However, this indicator has also been used in studies that compared different countries regarding air pollution (59) and has been associated with adverse health outcomes at neighborhood level (58). We performed additional analyses with country-specific deprivation indices but available only for some cities (76–79) and found very similar results (data not shown).

Whilst we included an important number of cities, the sample in some cities was quite small and could explain the absence of associations and wide confidence intervals. Even if proportion of neighborhoods containing only one participant was relatively high in some cities, we performed a multilevel model, following Bell *et al.,* who showed that high proportion of singletons had little impact on either the point or interval estimates of model parameters when large numbers of level-2 units were included (generally more than 50, which is the case in our study) (80). This highlights however a common problem in studies that were not originally designed to study area-level determinants. Finally, we look only at NO_2, even if it was a good marker of traffic, we did not consider other sources of pollutants that could be potentially socially patterned (81). Likewise we did not have information on potential professional exposures or time-activity patterns (82) which could contribute to create or reinforce environmental inequalities. Further studies integrating different sources of exposition and time-activity patterns are needed to improve knowledge on environmental inequalities in Europe.

CONCLUSION

Differential distribution to air pollution exposure according to SEP groups in European cities is not a general phenomenon and not even a predictable one, but one that needs to be specifically assessed in each city. No clear geographical or urban pattern of associations between SEP and air pollution could be identified across Europe and the associations were not in the same direction even within the same country. Our results highlighted the importance of taking into account both individual- and area-SEP when studying air pollution effects on health in epidemiological studies**.**

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Table1a: Socioeconomic characteristics of the population (by city and data pooled)

City	Country	Number of participants	Age at end of school	Occupational Class[a], %					Neighborhood Unemployment Rate[b]
		N	Mean ±sd	Managers and Professionals (1-2)	Technicians & Associate Professionals (3)	Other non-manual (4-5)	Skilled Manual (6-9)	*Not in labor force*	Mean ±sd
Umea [c]	Sweden	451	22.4 ±6.3	16.0	19.7	31.0	31.5	*1.8*	NA
Norwich [c]	UK	242	17.6 ±3.1	25.6	19.4	27.3	24.0	*3.7*	11.1 ±7.2
Ipswich [c]	UK	338	17.1 ±2.6	22.5	16.6	30.8	22.2	*8.0*	10.4 ±6.6
Antwerp [c]	Belgium	539	20.2 ±3.1	33.0	18.6	31.0	16.8	*0.7*	8.2 ±5.9
Erfurt [c]	Germany	238	20.5 ±3.9	21.9	19.3	31.9	24.8	*2.1*	NA
Paris [c d]	France	785	21.3 ±3.6	41.7	23.6	18.5	6.2	*10.1*	10.6 ±4.0
Lyon [c]	France	210	19.5 ±3.7	20.5	24.8	26.2	21.0	*7.6*	9.1 ±3.8
Grenoble [c d]	France	690	20.8 ±3.8	37.5	20.1	17.4	13.9	*11.0*	9.8 ±4.5
Marseille [d]	France	119	20.6 ±3.4	46.2	20.2	14.3	9.3	*10.1*	12.1 ±5.5
Basel [e]	Switzerland	847	20.9 ±3.9	21.5	26.1	27.6	15	*7.6*	NA
Geneva [e]	Switzerland	612	20.5 ±4.3	32.4	20.4	24.8	11.4	*11.0*	4.3 ±1.4
Lugano [e]	Switzerland	1002	19.1 ±4.3	16.9	23.9	26.4	30.1	*2.9*	NA
Verona [e]	Italy	179	19.0 ±4.7	25.8	13.7	29.0	23.7	*7.9*	4.5 ±3.0
Pavia [c]	Italy	190	18.7 ±4.6	25.8	13.7	29.0	23.7	*7.9*	3.4 ±2.5
Turin [c]	Italy	176	19.5 ±5.2	21.6	13.1	36.4	22.1	*6.8*	7.4 ±4.1
Oviedo [c]	Spain	315	19.3 ±4.6	26.7	10.8	29.2	28.6	*4.8*	14.0 ±3.0
Galdakao [c]	Spain	408	18.2 ±4.1	17.9	8.6	25.3	37.7	*10.5*	10.7 ±3.5
Barcelona [c]	Spain	284	18.8 ±4.9	28.9	14.4	29.6	21.1	*6.0*	10.9 ±3.3
Albacete [c]	Spain	419	17.7 ±4.9	17.0	10.0	29.4	33.2	*10.5*	14.6 ±5.3
Huelva [c]	Spain	233	18.0 ±4.6	17.6	9.4	27.9	30.5	*14.6*	21.8 ±6.7
Pooled data		8277	19.8 ±4.4	25.9	20.0	26.4	21.2	*7.5*	10.0 ±6.0

NA: not available. Cities are sorted from north to south.

[a] Number in brackets refers to the ISCO code. Not in labor force participants (in italics) included retired, housewives and students.

[b] N=5692. The neighborhood unemployment rate has been assigned individually to participants using their residential addresses. The variable was not available in Umea, Erfurt, Basel and Lugano and was missing for some participants in Pavia (n=2), Antwerp (n=55) and Turin (n=6).

Participants were from [c] ECRHS, [d] EGEA, [e] SAPALDIA; Paris: ECRHS n=386, EGEA n=399, Grenoble: ECRHS n=350, EGEA n=340.

Table 1b: Characteristics of the population (by city and data pooled)

City	N	Sex	Age	NO_2 ($\mu g*m^{-3}$)	
		Men, %	mean ±sd	mean ±sd	Q1 – Q3
Umea[a]	451	48.6	42.6 ±7.0	5.3 ±2.6	3.7 – 5.7
Norwich[a]	242	43.0	43.6 ±6.5	25.6 ±5.7	22.8 – 28.7
Ipswich[a]	338	42.3	42.4 ±6.8	24.2 ±4.0	22.7 – 26.0
Antwerp[a]	539	49.9	42.7 ±6.9	39.4 ±9.0	32.7 – 45.6
Erfurt [a]	238	54.2	42.9 ±6.6	16.5 ±3.3	13.9 – 18.5
Paris [a b]	785	48.3	41.7 ±12.9	36.4 ±13.4	27.4 – 42.6
Lyon [a]	210	46.7	48.4 ±15.3	28.7 ±13.5	16.9 – 40.6
Grenoble [a b]	690	52.9	44.9 ±13.4	27.5 ±8.2	20.8 – 32.9
Marseille [b]	119	43.7	49.2 ±15.8	26.1 ±8.2	21.4 – 31.1
Basel [c]	847	48.4	52.0 ±11.9	28.1 ±5.1	25.7 – 31.2
Geneva [c]	612	49.4	52.1 ±11.3	26.5 ±7.0	21.1 – 31.3
Lugano [c]	1002	44.0	54.3 ±11.3	26.3 ±7.6	22.9 – 30.6
Verona [a]	179	44.1	42.6 ±7.1	30.7 ±13.8	22.6 – 40.2
Pavia [a]	190	53.7	44.2 ±6.6	20.5 ±4.8	17.6 – 21.8
Turin [a]	176	46.6	42.9 ±7.0	54.9 ±10.1	49.2 – 61.9
Oviedo [a]	315	49.8	42.9 ±7.1	36.6 ±12.5	29.3 – 43.9
Galdakao [a]	408	48.5	40.7 ±7.3	23.9 ±6.6	18.6 – 28.3
Barcelona [a]	284	44.4	41.9 ±7.1	57.4 ±14.1	49.6 – 62.4
Albacete [a]	419	46.8	40.8 ±7.3	28.6 ±14.8	19.5 – 38.1
Huelva [a]	233	50.2	41.1 ±7.2	25.2 ±6.4	20.6 – 29.8
Pooled data	**8277**	**47.9**	**45.9 ±11.3**	**28.2 ±13.4**	**21.0 – 35.6**

Participants were from [a]ECRHS, [b]EGEA, [c]SAPALDIA; Paris: ECRHS n=386, EGEA n=399, Grenoble: ECRHS n=350, EGEA n=340. Cities are sorted from north to south.

Table 2: Pooled results for the association between NO_2 concentration (µg*m-3) and SEP markers (n=5692)

			Percent increase/decrease (95%CI) in NO_2 and Odd ratios (OR) for high exposure (95%CI)								
				Model 1: City-level*			Model 2: City- + neighborhood-level[µ]				
			Crude [a]	Adjusted for individual factors [b]	Adjusted for individual factors plus unemployment rate[b]		Adjusted for Individual factors [b]	Adjusted for individual factors plus unemployment rate[b]			
					Educational level	Occupational class		Educational level		Occupation class	
		n		Percent increase/decrease (95%CI)	Percent increase/decrease (95%CI)	Percent increase/decrease (95%CI)	Percent increase/decrease (95%CI)	Percent increase/decrease (95%CI)	OR for high exposure (95% CI)	Percent increase/decrease (95%CI)	OR for high exposure (95% CI)
Individual-level markers											
Educational level	High (ref)	1917	0	0	0		0	0	0		
	Medium	2001	-4.3 (-6.4; -2.2)	-4.5 (-6.6; -2.3)	-5.1 (-7.1; -3.0)		-1.3 (-2.7; -0.2)	-1.3 (-2.7; 0.2)	0.82 (0.70; 0.96)		
	Low	1774	-6.3 (-8.5; -4.2)	-6.9 (-9.1; -4.7)	-8.7 (-10.8; -6.5)		-1.7 (-3.2; -0.1)	-1.8 (-3.3; -0.2)	0.65 (0.54; 0.78)		
p-value for trend [€]			*<0.0001*	*<0.0001*	*<0.0001*		*0.04*	*0.03*	*<0.0001*		
Occupational class	OC-I (ref)	1657	0	0		0	0			0	0
	OC-II	967	-2.6 (-5.3; 0.2)	-2.6 (-5.3; 0.2)		-2.7 (-5.4;0.01)	1.0 (-0.8; 2.9)			1.0 (-0.8; 2.9)	0.95 (0.78; 1.16)
	OC-III	1457	-0.7 (-3.2; 1.8)	-1.0 (-3.5 ; 1.6)		-2.0 (-4.1; 0.5)	-0.6 (-2.3;1.0)			-0.7 (-2.3; 1.0)	0.76 (0.63; 0.91)
	OC-IV	1118	-5.8 (-8.4; 3.2)	-5.6 (-8.2 ; -3.0)		-7.9 (-10.4; -5.3)	-0.6 (-2.5;1.2)			-0.8 (-2.6; 1.1)	0.63 (0.52; 0.78)
p-value for trend [€]			*0.001*	*0.001*		*<0.0001*	*0.03*			*0.03*	*<0.0001*
Neighborhood-level marker											
Unemployment∞		5692	7.3 (6.3; 8.4)	7.3 (6.2; 8.5)	7.8 (6.7; 8.9)	7.7 (6.6; 8.8)	3.33 (0.71; 6.01)	3.2 (1.5; 5.0)	1.38 (1.25; 1.51)	3.3 (1.5; 5.1)	1.37 (1.25; 1.52)

* A multilevel model was performed with city at level-2 (random intercept for city level). High exposure was defined as concentrations above the 75th percentile of the distribution by cities

[µ] A multilevel model was performed with neighborhood at level-2 and city at level-3 (random intercept for city and neighborhood levels)

[a] Adjusted for study

[b] Adjusted for study, age, sex

Occupational class (OC): OC-I: Manager and Professional, OC-II: Technician and associate professional, OC-III: other non-manual, OC-IV: skilled, semi-skilled and unskilled manual

Reference= High educational level or OC-I, p-value for trend were calculated by introducing the categorical variables in continuous. Negative value means a decrease in NO_2 (in percent) compared to the reference class.

[∞] Unemployment has been transformed in z-score, the increase/decrease in NO_2 is showed for 1 standard deviation

Table 3a: Percent increase in NO_2 (µg*m-3) concentration (95%CI) in relation to educational level with adjustment for neighborhood unemployment rate (n=5692)

City	n	Educational level (ref=high)			Neighborhood Unemployment t[∞]
		Medium	Low	P-value for trend	
Norwich	242	-0.9 (-5.7; 4.3)	-1.1 (-7.7; 6.0)	0.71	9.4 (5.1; 13.8)
Ipswich	338	2.0 (-0.6; 4.7)	0.5 (-2.8; 3.8)	0.69	4.9 (1.0; 8.9)
Antwerp	500	0.6 (-2.2; 3.4)	1.2 (-1.9; 4.3)	0.45	14.9 (11.8; 18.2)
Paris	785	0.1 (-2.6; 2.9)	-0.3 (-3.1; 2.6)	0.84	13.7 (9.7; 17.8)
Lyon	210	-9.4 (-17.0; -0.9)	-3.6 (-12.3; -5.9)	0.58	12.6 (2.2; 24.0)
Grenoble	690	0.5 (-2.1; 3.0)	0.8 (-1.9; 3.7)	0.56	9.3 (5.1; 13.7)
Marseille	119	-1.9 (-10.4; 7.3)	-7.1 (-16.1; 2.9)	0.13	12.1 (7.1; 17.4)
Geneva	612	-2.0 (-4.5; 0.6)	-1.8 (-4.4; 0.9)	0.18	9.5 (4.7; 14.6)
Verona	179	-0.9 (-15.8; 16.8)	-16.1 (-26.5; -4.3)	0.01	14.0 (3.6; 25.3)
Pavia	188	0.1 (-4.2; 4.6)	-1.4 (-5.4; 2.6)	0.48	2.6 (-1.0; 6.4)
Turin	170	2.8 (-5.9; 12.3)	5.9 (-3.9; 16.6)	0.22	2.3 (-1.4; 6.1)
Oviedo	315	-0.4 (-7.2; 7.0)	-5.0 (-12.3; 3.0)	0.25	-14.1 (-23.6; -3.3)
Galdakao	408	-1.3 (-5.1; 2.8)	-3.3 (-7.8; 1.5)	0.18	21.8 (14.1; 30.1)
Barcelona	284	3.3 (-2.7; 9.7)	3.7 (-3.3; 11.2)	0.28	-7.7 (-12.7; -2.4)
Albacete	419	-10.3 (-21.1; 1.9)	-8.4 (-18.4; 2.9)	0.11	-7.9 (-17.5; 2.9)
Huelva	233	-1.0 (-6.1; 4.3)	-2.6 (-8.5; 3.6)	0.39	1.9 (-2.3; 6.4)

Cities are sorted from north to south.
A multilevel linear regression model (PROC MIXED) was performed with neighborhood at level-2 (random intercept for neighborhood level); adjusted for study, age, sex
Reference= High educational level, p-value for trend were calculated by introducing the categorical variables in continuous.
Negative value means a decrease in NO_2 (in percent) compared to the reference class.
[∞] Unemployment has been transformed in z-score, the increase/decrease in NO_2 is showed for 1 standard deviation

Table 3b: Percent increase in NO_2 (µg*m-3) concentration (95%CI) in relation to occupational class with adjustment for neighborhood unemployment rate (n=5692)

City	n	Occupational class (ref=OC-I)				Neighborhood Unemployment t∞
		OC-II	OC-III	OC-IV	P-value for trend	
Norwich	242	-0.1 (-6.1; 6.2)	0.1 (-6.1; 6.7)	-5.8 (-16.1; 5.8)	0.45	9.7 (5.3; 14.3)
Ipswich	338	2.3 (-1.2; 5.8)	1.6 (-1.4; 4.7)	0.6 (-2.5; 3.7)	0.99	5.0 (1.2; 9.1)
Antwerp	500	0.9 (-2.5; 4.4)	1.6 (-1.4; 4.6)	-1.7 (-5.0; 1.7)	0.63	15.1 (11. 9; 8.3)
Paris	785	-2.3 (-5.0; 0.6)	-3.3 (-6.4; -0.01)	-4.8 (-9.5; 0.1)	0.03	13.7 (9.7; 17.8)
Lyon	210	3.2 (-5.7; 12.9)	-3.9 (-12.5; 5.5)	-2.1 (-11.7; 8.6)	0.78	13.0 (2.5; 24.6)
Grenoble	690	1.8 (-1.1; 4.8)	1.1 (-2.1; 4.3)	3.1 (-0.4; 6.7)	0.20	9.1 (4.9; 13.5)
Marseille	119	-8.6 (-16.6; 0.1)	-6.9 (-15.2; 2.2)	-4.8 (-15.8; 7.7)	0.07	12.1 (7.0; 17.3)
Geneva	612	1.7 (-1.3; 4.8)	-1.0 (-3.7; 1.9)	-0.7 (-4.1; 2.8)	0.72	9.3 (4.4; 14.3)
Verona	179	1.9 (-20.8; 31.0)	-2.7 (-18.3; 15.8)	-12.9 (-28.1; 5.4)	0.07	13.3 (2.9;4.7)
Pavia	188	-2.6 (-8.2; 3.4)	-3.7 (-7.8; 0.7)	-2.5 (-7.6; 2.8)	0.17	2.7 (-0.9; 6.4)
Turin	170	9.5 (-3.6; 24.4)	9.6 (-0.6; 20.8)	11.7 (-0.1; 25.0)	0.07	2.3 (-1.3; 6.1)
Oviedo	315	0.8 (-9.5; 12.3)	-8.7 (-15.7; -1.2)	-5.9 (-13.2; 2.1)	0.07	-13.7 (-23.6; -2.8)
Galdakao	408	3.9 (-3.1; 11.4)	3.6 (-1.6; 9.0)	3.3 (-1.8; 8.6)	0.67	21.4 (13.6; 29.6)
Barcelona	284	3.4 (-4.8; 12.2)	3.4 (-2.8; 10.1)	4.1 (-2.6; 11.2)	0.16	-7.7 (-12.7; -2.5)
Albacete	419	-3.7 (-18.2; 13.5)	-6.1 (-18.2; 7.8)	-4.6 (-16.5; 9.1)	0.34	-8.3 (-18.0; 2.6)
Huelva	233	8.5 (-0.1; 17.9)	4.1 (-2.1; 10.8)	6.8 (0.1; 13.8)	0.15	1.0 (-3.2; 5.3)

Cities are sorted from north to south.
A multilevel linear regression model (PROC MIXED) was performed with neighborhood at level-2 (random intercept for neighborhood level); adjusted for study, age, sex
Occupational class (OC): OC-I: Manager and Professional (ref), OC-II: Technician and associate professional, OC-III: other non-manual, OC-IV: skilled manual, semi-skilled and unskilled manual, p-value for trend were calculated by introducing the categorical variables in continuous.
Negative value means a decrease in NO_2 (in percent) compared to the reference class.
∞ Unemployment has been transformed in z-score, the increase/decrease in NO_2 is showed for 1 standard deviation