

Socioeconomic position and outdoor nitrogen dioxide (NO 2) exposure in Western Europe: A multi-city analysis

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 multi-city analysis

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74 <u>COMPETING FINANCIAL INTEREST</u>

75 The authors declare no conflict of interest.

76

78 <u>ABSTRACT</u>

Background: Inconsistent associations between socioeconomic position (SEP) and outdoor 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 outdoor nitrogen dioxide
(NO₂) exposure as a marker of traffic exhaust, in 16 cities from eight Western European
countries.

85 Methods: Three SEP indicators, two defined at individual-level (education and occupation) and one at neighborhood-level (unemployment rate) were assessed in three European 86 multicenter cohorts. NO2 annual concentration exposure was estimated at participants' 87 addresses with land use regression models developed within the European Study of Cohorts 88 for Air Pollution Effects (ESCAPE; http://www.escapeproject.eu/). Pooled and city-specific 89 linear regressions were used to analyze associations between each SEP indicator and NO₂. 90 91 Heterogeneity across cities was assessed using the Higgins' I-squared test (I²). Results: The study population included 5692 participants. Pooled analysis showed that 92 participants with lower individual-SEP were less exposed to NO₂. Conversely, participants 93 living in neighborhoods with higher unemployment rate were more exposed. City-specific 94 results exhibited strong heterogeneity (I²>76% for the three SEP indicators) resulting in 95 variation of the individual- and neighborhood-SEP patterns of NO₂ exposure across cities. 96 97 The coefficients from a model that included both individual- and neighborhood-SEP indicators were similar to the unadjusted coefficients, suggesting independent associations. 98 99 Conclusions: Our study showed for the first time using homogenized measures of outcome and exposure across 16 cities the important heterogeneity regarding the association between 100 SEP and NO₂ in Western Europe. Importantly, our results showed that individual- and 101 102 neighborhood-SEP indicators capture different aspects of the association between SEP and

- 103 exposure to air pollution, stressing the importance of considering both in air pollution health
- 104 effects studies.
- 105
- 106 Keywords: Europe, socioeconomic position, air pollution, environmental inequality
- 107

108 <u>ABREVIATIONS</u>

- 109 ECRHS: European Community Respiratory Health Survey
- 110 EGEA: French Epidemiological family-based study of the Genetics and Environment of
- 111 Asthma
- 112 ESCAPE: European Study of Cohorts for Air Pollution Effects
- 113 LUR: land use regression
- 114 MAUP: modifiable area unit problem
- 115 NO₂: Nitrogen dioxide
- 116 OC: occupational class
- 117 PM: Particulate matter
- 118 SAPALDIA: Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults
- 119 SEP: socioeconomic position

120 1. INTRODUCTION

Environmental inequality refers to a differential distribution of environmental hazards across 121 socioeconomic or socio-demographic groups (1). Historically, research on environmental 122 inequality has emerged in the United States (US) following the Environmental Justice 123 124 Movement (2–5). Repeatedly, US studies reported that lower socioeconomic or minority groups were more likely to be exposed to higher traffic-related air pollution exposure such as 125 nitrogen dioxide (NO₂) or particulate matter (PM) (6). However, results from US studies 126 127 cannot be extended to European countries because of very different socio-spatial characteristics, specifically in urban areas (7). For example, one of the main differences is that 128 in general in most US cities, lower socioeconomic groups tend to live downtown when upper 129 socioeconomic groups reside in the suburbs. In European cities, compared to US, social 130 segregation is lower and lower socioeconomic groups rather live on the outskirts of the city 131 132 (7).

In Europe, a rather limited number of studies compared to US had investigated the association 133 134 between socioeconomic position (SEP) and air pollution, mainly in the UK first and then in 135 other European countries (6,8). Inconsistent results have been reported in the European literature (9). Some studies reported that populations with low SEP are more exposed to 136 outdoor air pollution (10–14) while other studies reported an inverse association (15–18). 137 Nonlinear association (higher exposure in middle class) (19) and no association (20) were 138 also reported. Inconsistent results were also reported within the same country, for instance in 139 140 France or Spain (20–23). However, these studies were difficult to compare with each other because they used different methodologies to assess air pollution exposure or to define SEP 141 (6,24). Moreover, most studies relied on ecological data that can raise methodological issues 142 such as ecological fallacy, modifiable area unit problem (MAUP) or spatial autocorrelation 143 (19,25). Few studies used individual-level data (i.e. air pollution exposure at residential 144

address and individual-level SEP) or multilevel data (i.e. SEP estimated at individual- and
area-level) (15,17,26–30). Recent evidence showed the importance of considering SEP at both
individual and area levels because they are independently associated with health outcomes

148 (6,10,31–33).

149 More generally, the association between SEP and air pollution still needs to be investigated in

150 Europe (6,24) as SEP is one of the major potential determinants of variability in the

association between air pollution and health (2,34,35).

Within the framework of the multicenter European Study of Cohorts for Air Pollution Effects (ESCAPE) (36), we had the opportunity to tackle this research gap using outdoor NO₂ annual concentrations at participants' home addresses estimated from standardized procedures across a large range of European cities (36). The main objective of the present analysis was to test the environmental justice hypothesis that people with lower SEP (defined at both individual and neighborhood level) were more exposed to traffic related air pollution exposure than people with higher SEP in Western Europe.

159

160 2. MATERIALS AND METHODS

161 2.1. Study population

162 This cross-sectional study included participants of three multicenter epidemiological

163 European cohorts that had previously collaborated together (37) and were involved in the

164 ESCAPE study: the French Epidemiological family-based study of the Genetics and

165 Environment of Asthma (EGEA2) (2003–2007) (38), and two population-based studies: the

166 European Community Respiratory Health Survey (ECRHSII) (1999–2002) (39) and The

167 Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA2)

168 (2001-2003) (40). Details on each cohort are given elsewhere (38–40) and summarized in the

supplementary materials. For the three cohorts, information on participants were collected
from detailed, standardized and validated questionnaires completed by face-to-face
interviews.

Initially, the ESCAPE study included a subsample of the three cohorts (n=9556 participants, 172 Figure 1) from 20 urban areas of eight Western European countries. Of these 20 areas, we 173 were able to recover homogenized SEP data at individual and neighborhood level for 16 174 (n=5692 participants: 4002, 1078 and 612 in ECRHS, EGEA and SAPALDIA respectively; 175 Figure 1) including Norwich, Ipswich (Great Britain; GB); Antwerp (Belgium; BE); Paris, 176 Lyon, Grenoble, Marseille (France; FR); Geneva, (Switzerland; CH); Verona, Pavia, Turin 177 (Italy; IT); Oviedo, Galdakao, Barcelona, Albacete, Huelva (Spain; SP) (Figure S1). The 178 179 areas covered by ESCAPE were of substantially different sizes (Table S1) with a range of density population from 152 to 21154 inhabitants/km² (41). Most of them could be defined as 180 metropolitan areas (large cities with surrounding smaller suburban communities) but some 181 182 areas were restricted to a single city (municipality). For purposes of clarity, we refer to these different areas as "cities". 183

184

185 2.2. NO₂ exposure assessment

We considered nitrogen dioxide (NO₂) as a marker of near-road traffic-related air pollution 186 (42). The major sources of NO2 are motorized road traffic, industry, shipping and heating 187 (41). In the framework of ESCAPE, a single harmonized exposure assessment protocol has 188 been developed to estimate the NO₂ annual concentrations. A common protocol described in 189 detail in Beelen et al. was used to ensure high standardization of all procedures (i.e. 190 measurement and estimation model) across the study areas (36). Briefly, in each city covered, 191 two-week integrated NO₂ measurements at approximately 40 urban sites were made in three 192 different seasons over a one-year period between 2008 and 2011. City-specific land use 193

194	regression (LUR) models (see supplementary materials) were developed to explain the spatial
195	variation of NO ₂ using a variety of geographical data including traffic, population and land
196	use variables. The model explained variances (R^2) of the LUR models ranged from 55% in
197	Huelva to 92% in Pavia, 10 out of the 16 cities have a R^2 above 75% (36). These LUR models
198	were used to assign estimates of NO2 annual average concentrations at each participant's
199	geocoded residential address. Back-extrapolated estimates were also derived because
200	ESCAPE measurement campaigns took place after the health surveys for the three cohorts
201	(43). Correlations between back-extrapolated and non-back-extrapolated concentrations were
202	high (Pearson correlation coefficient=0.95) so we only considered the non-back-extrapolated
203	data in the present analysis.

204

205 2.3. Markers of socioeconomic position

206 We indexed SEP defined at two different levels:

207 2.3.1. Individual-level SEP

We characterized individual-level SEP based on educational level and occupational class. For 208 209 the three cohorts, educational level corresponded to the age at completion of full-time education. We categorized the continuous educational variable into country-specific tertiles 210 (high, medium and low). Occupational class was based on the longest job held between 211 baseline and follow-up (in average 10-12 years), and categorized in five classes according to 212 the International Standard Classification of Occupation (ISCO-1988) (44): Manager and 213 214 Professional (Occupational Class-I); Technician & associate (OC-II); Other non-manual (OC-III); Skilled, semi-skilled and unskilled manual (OC-IV) and "not in labor force". 215

216 2.3.2. Neighborhood-level SEP

To characterize the socioeconomic residential environment of the participants, we used the 217 218 neighborhood unemployment rate (i.e. proportion of unemployed persons of the labor force). The neighborhood level corresponded to the smallest geographical level unit (with a 219 220 population size ranging from 169 to 2000 inhabitants) with census-based data available in the different countries (see Table S2 for neighborhood specific characteristics). We obtained the 221 222 unemployment rate variable from 2001 national censuses (except for France: 2008 and 223 Switzerland: 2006). As the magnitude of the unemployment rate varied across European 224 countries, we standardized it using country-specific z-scores to take this variability into 225 account.

226

227 2.4. Strategy of analysis

228 2.4.1. Main analyses

The strategy of analysis aimed to test the hypothesis that the NO₂ annual concentration
(dependent variable) differs according to the individual- and neighborhood- SEP of the
participants (explanatory variables).

232 We performed analyses considering first the pooled dataset and then each city separately, due to the heterogeneity of the associations between SEP and air pollution among the cities 233 (assessed with the Higgins' I-squared test (I^2) (45)) We ran several multilevel linear 234 regression models (Table S3) with neighborhood random effects (plus city random effects for 235 the pooled dataset) including one individual SEP indicator (education or occupation) mutually 236 237 adjusted for neighborhood unemployment rate. In the supplementary materials, we present the results for the single-level linear regression models that ignore the nested structure of the 238 239 observations.

We transformed NO₂ using a natural log transformation to obtain a normally distributed 240 241 variable. For ease of interpretation, we converted the regression coefficients (β s) into percent change (and 95% Confidence Interval (CI)) per one unit increase in the explanatory factor 242 243 using the formula $[exp(\beta)-1]*100$ (a 95% CI which does not include zero indicates the presence of significant differences). The considered unit for unemployment rate was 1 244 standard deviation (SD). For the individual-level SEP variables, we considered each subgroup 245 246 and tested the statistical differences of the coefficients against the highest group (thus 247 reference group were high educational level and OC-I for occupational class). We deliberately did not show results for participants who were not in the labor force as this class was too 248 249 heterogeneous to draw any kind of conclusion (i.e. housepersons, unemployed, not working because of poor health, full-time student and retired). This category was excluded to assess 250 the trend across the occupational groups. 251

252 2.4.2. Additional analyses

We ran a sensitivity analysis using logistic regression models considering high vs. low
exposure (high exposure was defined as an exposure above the 75th percentile of the
distribution for each city). All models were adjusted for cohort, age and sex. We checked for
potential interactions between SEP and sex, SEP and age and between individual- and
neighborhood-level SEP (supplementary materials). Analyses were conducted using R
statistical software (Version 3.0.3) and SAS 9.3.

As pointed out above some "cities" included in this analysis had a wide geographic coverage.

260 For example, the city labelled "Paris" (FR) covered actually the metropolitan area of Paris-

Region (*i.e.* 12,000 km²). Therefore, we ran a sensitivity analysis by examining more in detail

this area: instead of considering participants of Paris in only one area, we considered three

- distinctive areas (i.e. City of Paris, the inner-suburbs and the outer-suburbs) defined by
- 264 particular sociodemographic and geographic situations that could influence the association

between SEP and air pollution. The methods and results are presented in detail in thesupplementary materials and discussed in the main article.

267

268 3. RESULTS

269 *3.1. Study population characteristics*

The study population (Table 1a) was composed of 48% males, with a mean age (±standard 270 271 deviation; \pm SD) of 44 (\pm 11) years. Regarding the NO₂ distribution, we found substantial variability between cities with a mean ranging from 21 (\pm 5) (Pavia; IT) to 57 (\pm 14) µg m⁻³ 272 (Barcelona; ES). Substantial variability was also found within cities. The average range for 273 NO₂ (difference between the highest and the lowest annual average) within each area was 274 $50.3 \mu \text{g m}^{-3}$. The largest variation for NO₂ was found in the two largest cities Paris (FR) 275 276 (85.0) and Barcelona (SP) (92.8). Regarding the socioeconomic characteristics of the population (Table 1b), participants 277 278 completed their education on average at age 20 (± 4) years. The proportion of manual workers 279 ranged from 6% (Paris; FR) to 38% (Galdakao; SP) and was generally higher in the Spanish cities. On average, participants with lower educational attainment were employed in less 280 skilled occupations (p-value for trend <0.001) (Table S4). The neighborhood unemployment 281 rate varied from 3% (Pavia; IT) to 22% (Huelva; SP). Participants with lower educational 282 attainment or less skilled occupations were more likely to live in neighborhoods with higher 283 unemployment rate. However, the associations did not reach the level of significance in 7 and 284

6 out of the 16 cities for education and occupation respectively (Tables S5a-S5b).

286

287 *3.2. Pooled results*

288 Pooled results are shown in Table 2. In the model taking into account only clustering within

cities, low educational level and manual occupations were associated with a lower NO₂

exposure (Percent difference (95% CI) Low vs. high educational level= -6.9% (-9.1; -4.7); 290 291 OC-IV vs. OC-I=-5.6% (-8.2; -3.0)). Conversely, higher neighborhood unemployment rate was associated with higher NO₂ exposure (7.3% (6.2; 8.5) per 1 SD increase in the 292 293 unemployment rate). The introduction of individual- and neighborhood-SEP in the same model did not substantially alter effect estimates (Low vs. High educational level= -8.7% (-294 10.8; -6.5) and 7.8% (6.7; 8.9) per 1 SD increase in the unemployment rate). Accounting for 295 both city and neighborhood clustering decreased the effect size of both the individual- and 296 297 neighborhood-SEP. Associations remained significant for educational level and the unemployment rate. 298

299

300 *3.3. City-specific results*

In the city-specific analyses using standard linear regression models (Table S4), associations 301 with NO₂ were highly heterogeneous for all SEP indicators ($I^2 > 76\%$, p<0.001). Using 302 multilevel linear regression models, individual-SEP was weakly or not associated with NO₂ 303 exposure for most cities (14 out of 16 cities). For educational level (Table 3a), significant 304 associations were only found in Lyon (FR) (Low vs. High =-3.6 (-12.3; -5.9)) and Verona 305 (IT) (-16.1 (-26.5; -4.3)). For occupational class (Table 3b), significant associations were 306 found for the middle class in Paris (FR) (OC-III vs. OC-I= -3.3 (-6.4; -0.1) and Oviedo (-8.7 307 308 (-15.7; -1.2). Living in a neighborhood with higher unemployment rate was associated with higher NO₂ exposure (regardless of the individual-SEP marker included in the model) in 11 309 out of 16 cities. In Oviedo (ES) and Barcelona (ES) an inverse association was observed. 310

311 *3.4. Additional analyses*

Results from the logistic regression models (high vs. low exposure) were consistent with the
linear regression ones for the educational level (Table S6a) as well for occupational class
(Table S6b).

In Paris-Region (FR), when considering participants in three distinctive areas (i.e. city of Paris, inner suburbs and outer suburbs; supplementary materials), participants with lower educational level or occupational class were less exposed to air pollution (not significant) but those living in neighborhood with higher unemployment rate were more exposed. These results are consistent with those observed when considering participants in one area.

320

321 4. DISCUSSION

We investigated, in three European cohorts, whether SEP evaluated at both individual- and neighborhood-level was associated with traffic related air pollution exposure across sixteen Western European cities. The pooled analyses masked important heterogeneity across the cities showing that city appeared to be the major predictor of the association between SEP and NO₂ exposure.

The associations between individual-SEP and NO₂ were generally weak and inconsistent 327 across the cities. This is in accordance with those of the three studies that used a comparable 328 approach to ours (17,20,46). Education and occupation showed the same pattern with NO₂ in 329 the pooled data and in most cities, in the city specific analyses, showing that both indicators 330 331 measured the same concept (47,48). The associations between neighborhood-SEP and NO₂ were in the opposite direction (higher exposure in lower neighborhood-SEP) compared to the 332 individual-SEP variables, both in the pooled data and in most cities in the city-specific 333 models. This has also been observed in other studies in Europe (30) and in Montreal, Canada 334 (49). 335

One possible explanation for the difference in direction is that the neighborhood-SEP is 336 337 capturing aspects beyond the SEP of the population living in that area, such as how industrialized the neighborhood may be. Moreover, NO2 variability was relatively small 338 339 across the individual-SEP groups, and after adjusting for neighborhood-SEP there was little evidence of potential confounding by individual-SEP. Place of residence is strongly patterned 340 by social position and outdoor air pollution is spatially located within cities, therefore the 341 342 degree to which air pollution is socially patterned is likely to occur more at area-level as well 343 (33).

Accounting for both city and neighborhood clustering using a two level random intercept 344 345 model drastically decreased the size effects of the associations for both individual- and area-SEP markers compared to the single level linear regression model (Table S7). This has been 346 observed in other studies (30,35,50) showing the importance to accounting for clustering in 347 348 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 349 350 even became null for several cities showing that variability was mainly explained by the city 351 first then by the neighborhoods and for a smaller part by the individual-SEP. We looked at some socioeconomic variables at city level (e.g. population density, gross domestic product, 352 353 etc.) to try to explain the heterogeneity of the association between SEP and NO_2 among the cities using a meta-regression. However, none of the tested variables explained this 354 heterogeneity (not shown). 355

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 NO₂ as 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 (10,41,51). The NO₂ annual concentrations have been

361	estimated at participant's residential address with a single harmonized exposure assessment
362	protocol across the cities. The measurement time of NO ₂ does not overlap with the
363	questionnaire data from the cohorts. However, we assume that spatial contrasts in outdoor
364	NO ₂ pollution were stable over time; an assumption supported from observations in different
365	settings in European countries (52,53). We used homogenized SEP indicators at both
366	individual- and neighborhood-level. Recent evidence showed the importance of accounting
367	SEP at both levels because they were independently associated with health outcomes (32–
368	34,46,54,55) but this had rarely been investigated with air pollution exposure (10,28,29). We
369	used an area-based indicator defined at the smallest geographical unit available in each
370	country to avoid MAUP as recommended (49,56–58).
371	Our study has some limitations. Due to data confidentiality, we did not have access to
372	participants' geographical coordinates for the present analysis and we were not able to analyze
373	their spatial distribution. We applied an aspatial multilevel model to take into account the
374	clustering of the participants within neighborhoods (46,59) but the proportion of
375	neighborhoods containing only one participant was relatively high in some cities (60). This
376	highlights a common problem in studies that were not originally designed to study area-level
377	determinants. We compared a large number of European cities, but the sample in some cities
378	was quite small and could explain the absence of associations and large confidence intervals.
379	The different areas were also of different sizes and with different population density.
380	However, the additional analysis performed for the Paris-Region suggested that the results
381	were not sensitive to this aspect.
382	We considered he unemployment rate, the sole indicator of neighborhood SEP uniformly

available for most of the cities with ESCAPE NO₂ estimates. This single indicator does not

fully describe participants' neighborhood-SEP (33) but has been used in other studies that

385 compared different countries regarding air pollution (61) and has been associated with

adverse health outcomes neighborhood level (61–64). We performed additional analyses with
country-specific deprivation indices that were available at neighborhood level only for 12 out
of the 16 cities (65–68) and we found consistent results compared to the ones with the
neighborhood unemployment rate (Table S8).

Finally, we did not have information on other type of exposures such as occupational and
indoor exposures or time-activity patterns (69) which could contribute to create or reinforce
environmental inequalities.

393

394 5. CONCLUSIONS

Unequal distribution to air pollution exposure according to SEP groups is complex in European cities and no general pattern exists across cities, but rather inequalities need to be specifically assessed in each city. Importantly, our results highlighted the importance of taking into account both individual- and neighborhood-SEP in order to fully describe and understand the complexity of current patterns of social inequalities relating to air pollution.

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604 Figure 1: Flow chart of the study population



606 Dotted frame: missing data

- 607 ESCAPE: European Study of Cohorts for Air Pollution Effects
- 608 ECRHS: European Community Respiratory Health Survey (1999-2002)
- 609 EGEA: Epidemiological study on Genetics and Environment of Asthma (2003-2007)
- 610 SAPALDIA: Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (2001-2003)

City	Country	n	Sex	Age	NO ₂ (μg*m ⁻³)
			Men, %	mean ±sd	mean ±sd	Q1 – Q3
Norwich ^a	UK	242	43.0	43.6 ± 6.5	25.6 ± 5.7	22.8 - 28.7
Ipswich ^a	UK	338	42.3	42.4 ± 6.8	24.2 ± 4.0	22.7 - 26.0
Antwerp ^a	Belgium	500	49.9	42.7 ± 6.9	39.4 ±9.0	32.7 - 45.6
Paris ^{ab}	France	785	48.3	41.7 ± 12.9	36.4 ± 13.4	27.4 - 42.6
Lyon ^a	France	210	46.7	48.4 ± 15.3	28.7 ± 13.5	16.9 - 40.6
Grenoble ^{a b}	France	690	52.9	44.9 ± 13.4	27.5 ± 8.2	20.8 - 32.9
Marseille ^b	France	119	43.7	49.2 ± 15.8	26.1 ± 8.2	21.4 - 31.1
Geneva ^c	Switzerland	612	49.4	52.1 ± 11.3	26.5 ± 7.0	21.1 - 31.3
Verona ^a	Italy	179	44.1	42.6 ± 7.1	30.7 ± 13.8	22.6 - 40.2
Pavia ^a	Italy	188	53.7	44.2 ± 6.6	20.5 ± 4.8	17.6 - 21.8
Turin ^a	Italy	170	46.6	42.9 ± 7.0	54.9 ± 10.1	49.2 - 61.9
Oviedo ^a	Spain	315	49.8	42.9 ± 7.1	36.6 ± 12.5	29.3 - 43.9
Galdakao ^a	Spain	408	48.5	40.7 ± 7.3	23.9 ± 6.6	18.6 - 28.3
Barcelona ^a	Spain	284	44.4	41.9 ± 7.1	57.4 ± 14.1	49.6 - 62.4
Albacete ^a	Spain	419	46.8	40.8 ± 7.3	28.6 ± 14.8	19.5 - 38.1
Huelva ^a	Spain	233	50.2	41.1 ± 7.2	25.2 ± 6.4	20.6 - 29.8
Pooled data		5692	48.2	43.9 ±10.6	31.8 ±13.6	22.4 - 38.6

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

Cities are sorted from north to south.

Participants were from aECRHS, bEGEA, cSAPALDIA; Paris: ECRHS n=386, EGEA n=399, Grenoble: ECRHS n=350, EGEA n=340. 615

City	n	Individual-level SEP Neighborhoo						Neighborhood-level SEP
		Age at end of school		Occupational Class, %				Unemployment rate*
		mean ±SD	Managers and Professionals (OC-I)	Technicians & Associate Professionals (OC-II)	Other non-manuals (OC-III)	Manuals (OC-IV)	Not in labor force	mean ±SD (min-max)
Norwich ^a	242	17.6 ± 3.1	25.6	19.4	27.3	24.0	3.7	11.1 ±7.2 (2.1-34.1)
Ipswich ^a	338	17.1 ± 2.6	22.5	16.6	30.8	22.2	8.0	10.4 ±6.6 (2.4-32.0)
Antwerp ^a	500	20.2 ± 3.1	33.0	18.6	31.0	16.8	0.7	8.2 ±5.9 (0.8-31.2)
Paris ^{ab}	785	21.3 ± 3.6	41.7	23.6	18.5	6.2	10.1	10.6 ±4.0 (3.0-28.0)
Lyon ^a	210	19.5 ± 3.7	20.5	24.8	26.2	21.0	7.6	9.1 ±3.8 (3.4-25.1)
Grenoble ^{a b}	690	20.8 ± 3.8	37.5	20.1	17.4	13.9	11.0	9.8 ±4.5 (3.4-31.3)
Marseille ^b	119	20.6 ± 3.4	46.2	20.2	14.3	9.3	10.1	12.1 ±5.5 (4.9-35.0)
Geneva ^c	612	20.5 ± 4.3	32.4	20.4	24.8	11.4	11.0	4.3 ±1.4 (0.7-9.1)
Verona ^a	179	19.0 ± 4.7	25.8	13.7	29.0	23.7	7.9	4.5 ±3.0 (1.0-15.4)
Pavia ^a	188	18.7 ±4.6	25.8	13.7	29.0	23.7	7.9	$3.4 \pm 2.5 (0.7 - 14.3)$
Turin ^a	170	19.5 ± 5.2	21.6	13.1	36.4	22.1	6.8	7.4 ±4.1 (1.4-21.7)
Oviedo ^a	315	19.3 ±4.6	26.7	10.8	29.2	28.6	4.8	14.0 ±3.0 (7.5-33.3)
Galdakao ^a	408	18.2 ± 4.1	17.9	8.6	25.3	37.7	10.5	$10.7 \pm 3.5 (3.1 - 21.9)$
Barcelona ^a	284	18.8 ± 4.9	28.9	14.4	29.6	21.1	6.0	10.9 ±3.3 (4.1-26.4)
Albacete ^a	419	17.7 ± 4.9	17.0	10.0	29.4	33.2	10.5	14.6 ±5.3 (7.7-60.4)
Huelva ^a	233	18.0 ± 4.6	17.6	9.4	27.9	30.5	14.6	21.8 ±6.7 (10.7-41.4)
Pooled data	5692	19.5 ±4.3	29.1	17.0	25.6	19.6	8.7	10.0 ±6.0 (0.7-60.4)

616 Table1b: Socioeconomic characteristics of the population (by city and data pooled)

617 Cities are sorted from north to south

618 SD=standard deviation

619 Participants were from ^{*a*} ECRHS, ^{*b*}EGEA, ^{*c*}SAPALDIA; Paris: ECRHS n=386, EGEA n=399, Grenoble: ECRHS n=350, EGEA n=340

620 OC= Occupational class. Not in labor force participants (in italics) included unemployed, retired, housepersons and students

621 * The neighborhood unemployment rate has been assigned individually to participants using their residential addresses.

622 Table 2: Pooled results for the association between NO₂ concentration (μg*m-3) and SEP markers (n=5692) in percent change (95%CI)

			Multilevel model with			Multilevel model with neighborhood (level 2) and city (level 3) ^{\dagger}			
		n	Adjusted for individual factors	Adjusted for Mutually adjusted for individual individual factors and neighborhood SEP		Adjusted for individual factors	Mutually adjusted for individual and neighborhood SEP		
Individual-level SEP	II : 1 ()	1017							
Educational level	High (ref) Medium Low	1917 2001 1774	- -4.5 (-6.6; -2.3) -6.9 (-9.1; -4.7) <0.0001	- -5.1 (-7.1; -3.0) -8.7 (-10.8; -6.5) <0.0001		- -1.3 (-2.7; -0.2) -1.7 (-3.2; -0.1) 0.04	- -1.3 (-2.7; 0.2) -1.8 (-3.3; -0.2) 0.03		
Occupational class	OC-I (ref) OC-II OC-III OC-IV	1657 967 1457 1118	- -2.6 (-5.3; 0.2) -1.0 (-3.5 ; 1.6) -5.6 (-8.2 ; -3.0) 0.001		- -2.7 (-5.4;0.01) -2.0 (-4.1; 0.5) -7.9 (-10.4; -5.3) <0.0001	- 1.0 (-0.8; 2.9) -0.6 (-2.3;1.0) -0.6 (-2.5;1.2) 0.03		- 1.0 (-0.8; 2.9) -0.7 (-2.3; 1.0) -0.8 (-2.6; 1.1) 0.03	
Neighborhood-level SE Unemployment rate	P §	5692	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) [¶]	3.3 (1.5; 5.1)#	

* A multilevel model was performed with city at level-2 (random intercept for city level).

624 † A multilevel model was performed with neighborhood at level-2 and city at level-3 (random intercept for city and neighborhood levels).

the unemployment rate has been transformed in z-score, the change in NO₂ is showed for 1 standard deviation.

626 ¶ Mutually adjusted for educational level and neighborhood unemployment rate.

627 # Mutually adjusted for occupational class and neighborhood unemployment rate.

628 All models are adjusted for cohort, age and sex.

629 Results are expressed in percent change in NO₂ (µg*m-3) concentration adjusted for cohort, age, sex. Negative value means a decrease in NO₂ (in percent) compared to the

630 reference class for categorical variable and for 1SD increase for the continuous variable; p-value for trend were calculated by introducing the categorical variables in 631 continuous.

632 Occupational class (OC): OC-I: Managers and Professionals, OC-II: Technician and associate professionals, OC-III: other non-manuals, OC-IV: skilled, semi-skilled and

633 unskilled manuals.

634	Table 3a: Percent change (95%CI) in NO ₂ concentration (µg*m-3) in association to educational level mutually adjusted for neighborhood
635	unemployment rate (n=5692)

City	n	Educa	Neighborhood		
					Unemployment rate [*]
		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)

636 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 cohort, age and
 sex.

Results are expressed in percent change in NO₂ (μ g*m-3) concentration. Negative value means a decrease in NO₂ (in percent) compared to the reference class for the

640 categorical variable; p-value for trend were calculated by introducing the categorical variables in continuous. The unemployment rate has been transformed in z-score, the

641 change in NO_2 is showed for 1 standard deviation.

City	n		Occupational class (ref=O	C-I)		Neighborhood
		OC-II	OC-III	OC-IV	P-value for trend	Chemployment fate
Norwich	242	-0.1 (-6.1; 6.2)	0.1 (-6.1; 6.7)	4.9 (-1.5; 11.8)	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)
Ântwerp	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)

Table 3b: Percent change (95%CI) in NO₂ concentration (μ g*m-3) in association to occupational class mutually adjusted for neighborhood unemployment rate (n=5692)

644 Cities are sorted from north to south.

645 A multilevel linear regression model (PROC MIXED) was performed with neighborhood at level-2 (random intercept for neighborhood level); adjusted for cohort, age and

sex. Results are expressed in percent change in NO₂ (μ g*m-3) concentration. Negative value means a decrease in NO₂ (in percent) compared to the reference class for the

647 categorical variable; p-value for trend were calculated by introducing the categorical variables in continuous. The unemployment rate has been transformed in z-score, the

 $648 \qquad \text{change in NO}_2 \text{ is showed for 1 standard deviation.}$

649 Occupational class (OC): OC-I: Managers and Professionals (ref), OC-II: Technicians and associate professionals, OC-III: other non-manuals, OC-IV: skilled, semi-skilled

and unskilled manuals. P-value for trend were calculated by introducing the categorical variables in continuous.

Supplementary materials

Socioeconomic position and outdoor nitrogen dioxide (NO2) exposure in Western Europe: a

multi-city analysis

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Methods

Study population

ECRHSis a population-based cohort study. About 18,000 young adults aged 20-44 were recruited mainly across Europe in 1991 – 1993 (ECRHS I) and 10,364 participated to the first follow-up (ECRHS II) between 1999 – 2002. 4738 follow-up participants were included in the ESCAPE project from Umea (Sweden), Norwich, Ipswich (United Kingdom; Erfurt (Germany); Antwerp (Belgium); Paris-Region, Grenoble (France); Verona, Pavia, Turin (Italy); Oviedo, Galdakao, Barcelona, Albacete, Huelva (Spain) (Jarvis & ECRHS 2002).

EGEA is a French case-control and family-based study including 2047 participants aged 7-65 recruited between 1991 – 1995 (EGEA1). At the first follow-up (EGEA2), 1922 participants provided a questionnaire between 2003 – 2007. 1078 follow-up participants were included in the ESCAPE project from Paris-Region, Grenoble, Lyon and Marseille (Siroux et al. 2011).

SAPALDIA is a cohort study in Switzerland. In 1991, 9651 participants aged 20-65 were recruited for a detailed interview and health examination (SAPALDIA1). The follow-up (SAPALDIA2) was conducted in 2001-2003 at which 8047 participants provided health information. 2461 follow-up participants were included in the ESCAPE project from Basel, Geneva and Lugano(Ackermann-Liebrich et al. 2005).

NO₂ exposure assessment

Definition of the Land-use regression (LUR) methods: a LUR combines monitoring of air pollution at a small number of locations and development of stochastic models using predictor variables usually obtained through geographic information systems (GIS). The model is then applied to a large number of unsampled locations in the study area (Hoek et al. 2008). To avoid the exaggerated influence of a high NO₂ point in the models validation process, the predictor variables were truncated. All the details of the development of the models are described in a previous publication (Beelen et al. 2013) and more general information on LUR can be found in Hoek et al. 2008.



Figure S1 Study areas (in brackets: number of participants including in the present analysis)

Study area	Country	Study area description; major city	Population density of the major city (inhabitants/km ²)
Norwich	United Kingdom	Norwich and surrounding areas	4 129
Ipswich	United Kingdom	Ipswich and surrounding areas	3 247
Antwerp	Belgium	Antwerp and surrounding areas	2 479
Paris	France	Paris and suburban areas	21 154
Lyon	France	Lyon and suburban areas	10 460
Grenoble	France	Grenoble and suburban areas	8 837
Marseille	France	Marseille city	3 555
Geneva	Switzerland	Geneva city and surrounding smaller towns	12 628
Verona	Italy	City of Verona and surrounding areas	1 277
Pavia	Italy	City of Pavia and surrounding areas	1 147
Turin	Italy	Turin city and five smaller municipalities	6 902
Oviedo	Spain	Oviedo city	1 186
Galdakao	Spain	Galdakao and surrounding smaller towns	923
Barcelona	Spain	Barcelona city	15 982
Albacete	Spain	Albacete city	152
Huelva	Spain	Huelva city	987

Table S1 Description of the study areas and population density

Adapted from Cyrys et al., *Atmospheric Environment*, 2012 (Cyrys et al. 2012)

Table S2: Definition of neighborhood and distribution of the study population by neighborhood and city

City	Type of neighborhood	Study participants	Neighborhoods with
	(average population	by heighborhood	one participant (%)
	size)	mean (mm-max)	
Norwich	I SOA ^a (1200)	2.3 (1 – 6)	18
Ipswich	LSOA (1200)	3.0 (1 – 11)	11
Antwerp	Statistical sector (670)	2.1 (1 – 9)	27
Paris		1.9 (1 – 10)	37
Lyon	$\mathbf{DIS}^{b}(2000)$	2.1 (1 – 10)	25
Grenoble	IKIS (2000)	4.6 (1 – 16)	4
Marseille		1.7 (1 – 6)	35
Geneva	Sous-secteur (2000)	4.0 (1 – 18)	25
Verona	Saziona di consimanto	1.1 (1 – 3)	80
Pavia	(160)	1.4(1-7)	56
Turin	(109)	1.0(1-2)	89
Oviedo		2.4(1-8)	14
Galdakao		2.6 (1 – 12)	14
Barcelona	(1000)	1.1 (1 – 3)	77
Albacete	(1000)	4.3 (1 – 13)	2
Huelva		2.7 (1 – 8)	8

^{*a*} Lower layer Super Output Area ^{*b*} IRIS is a French acronym for 'aggregated units for statistical information'.

Model	Type of linear regression	Random effect	SEP	Table (column)
Pooled data				
Model 1			Each SEP indicator separately	2 (1)
Model 2	Multi-level	City	Education level mutually adjusted for unemployment	2 (2)
Model 3			Occupation class mutually adjusted for unemployment	2 (3)
Model 4			Each SEP indicator separately	2 (4)
Model 5	Multi-level	City +	Education level mutually adjusted for unemployment	2 (5)
Model 6		nerghoornood	Occupation class mutually adjusted for unemployment	2 (6)
City-specific				
Model 7	Multi laval	Neichborhood	Education level mutually adjusted for unemployment	3a
Model 8	wuun-level	neignoornood	Occupation class mutually adjusted for unemployment	3b
Model 9	Single-level	-	Each SEP indicator separately	S6

Table S3 Description of the main analysis

Results

Supplementary analysis

We found an interaction between education and unemployment for only 4 cities (Norwich, Antwerp, Verona and Paris). We found an interaction between occupational class and sex only in Pavia (women in lower occupational class were more exposed than men). Finally, we found an interaction between unemployment and age in Grenoble (younger participants living in neighborhoods with higher unemployment rate were more exposed to NO₂) and in Huelva (only older participants living in neighborhoods with higher unemployments with higher unemployment were exposed to NO₂).

Cities	Ν			Occupational class		
		OC-I	OC-II	OC-III	OC-IV	Not in labor force*
Norwich	242	20.0	18.0	16.6	16.0	16.0
Ipswich	338	18.7	18.6	16.2	15.9	16.1
Antwerp	539	21.8	20.9	19.6	17.5	16.5
Paris	785	23.0	20.9	19.1	18.2	20.8
Lyon	210	22.3	20.2	18.9	16.3	20.0
Grenoble	690	23.2	20.5	19.0	17.5	20.1
Marseille	119	22.5	19.6	18.8	16.7	19.7
Geneva	612	23.0	21.0	18.9	17.4	19.1
Verona	179	22.5	21.4	18.6	16.3	16.4
Pavia	190	21.8	20.6	18.4	15.2	17.4
Turin	176	23.4	21.9	18.6	17.1	14.8
Oviedo	315	21.5	21.5	19.8	16.5	16.2
Galdakao	408	22.0	20.0	18.6	16.6	15.1
Barcelona	284	21.8	19.7	17.9	16.1	16.2
Albacete	419	20.9	19.8	18.7	15.7	14.5
Huelva	233	22.0	19.0	18.6	16.1	15.4
Pooled cities	5692	22.2	20.4	18.6	16.5	17.8

Table S4: Mean age at completed education by occupational class (crude)

Occupation class (OC): OC-I: Managers and Professionals, OC-II: Technicians and associate professionals, OC-III: other non-manuals, OC-IV: skilled, semi-skilled and unskilled manuals.

*Category "not in the labor force" was excluded to calculate the p-value for trend.

All p-values for trend across the occupational classes were significant (p <0.0001)

	n	High	Medium	Low	P-value for trend
Norwich	242	10.0	10.6	13.9	0.004
Ipswich	338	8.1	10.8	12.1	< 0.0001
Antwerp	500	8.4	7.2	9.0	0.41
Paris	785	10.3	10.3	11.1	0.05
Lyon	210	9.4	9.1	8.9	0.47
Grenoble	690	9.6	9.6	10.1	0.21
Marseille	119	12.8	11.3	12.3	0.74
Geneva	612	4.1	4.3	4.6	< 0.0001
Verona	179	4.4	4.9	4.5	0.89
Pavia	188	3.3	3.6	3.3	0.99
Turin	170	6.1	8.0	8.4	0.001
Oviedo	315	13.5	14.2	14.6	0.01
Galdakao	408	10.5	10.6	10.9	0.27
Barcelona	284	10.3	10.8	11.9	0.001
Albacete	419	13.3	14.5	15.4	0.001
Huelva	233	18.9	22.1	24.1	< 0.0001
Pooled cities	5692	9.4	10.1	10.7	< 0.0001

Table S5a: Mean unemployment rate (%) by education level (crude)

The neighborhood unemployment rate has been assigned individually to participants using their residential addresses.

Cities	Ν			Occupational	class		
		OC-I	OC-II	OC-III	OC-IV	Not in labor	P-value
						force*	for trend
Norwich	242	8.9	9.2	13.4	12.6	10.6	0.0002
Ipswich	338	9.1	8.9	10.7	11.1	13.9	0.02
Antwerp	500	8.0	6.9	8.3	9.7	7.3	0.03
Paris	785	10.6	10.5	10.9	11.1	9.0	0.36
Lyon	210	9.5	9.2	9.5	7.7	9.8	0.06
Grenoble	690	9.4	9.6	9.8	11.6	10.0	0.0003
Marseille	119	12.2	10.9	12.8	13.2	11.6	0.66
Geneva	612	4.1	4.3	4.4	4.8	4.5	0.0001
Verona	179	4.8	4.8	4.9	3.5	4.5	0.15
Pavia	188	3.2	3.8	3.0	3.7	3.5	0.69
Turin	170	6.8	6.6	7.5	8.1	8.2	0.12
Oviedo	315	13.2	13.6	13.8	15.0	14.8	0.0002
Galdakao	408	10.1	10.7	10.6	11.2	10.0	0.04
Barcelona	284	10.2	10.3	10.4	11.6	11.3	0.004
Albacete	419	13.4	13.7	13.8	16.0	14.7	0.0005
Huelva	199	18.5	20.1	20.9	24.8	22.5	< 0.0001
Pooled cities	5692	9.2	9.1	10.1	11.8	10.1	< 0.0001

Table S5b: Mean unemployment rate (%) by occupational class (crude)

Occupation class (OC): OC-I: Managers and Professionals, OC-II: Technicians and associate professionals, OC-III: other non-manuals, OC-IV: skilled, semi-skilled and unskilled manuals.

The neighborhood unemployment rate has been assigned individually to participants using their residential addresses.

*Category "not in the labor force" was excluded to calculate the p-value for trend.

Table S6a: Odd ratios (OR) for high exposure (95% CI) in association to educational level mutually adjusted for neighborhood unemployment rate (n=5692)

City	n	Educationa		Neighborhood Unemployment [*]	
		Medium	Low	P-value	
				for trend	
Norwich	242	0.45 (0.21; 1.00)	0.44 (0.17; 1.15)	0.05	1.59 (1.11; 2.62)
Ipswich	338	1.04 (0.49; 2.18)	0.57 (0.19; 1.67)	0.36	1.21 (0.78; 1.86)
Ântwerp	500	0.72 (0.40; 1.31)	0.69 (0.36; 1.32)	0.23	3.68 (2.49; 5.44)
Paris	785	1.00 (0.64; 1.55)	0.47 (0.29; 0.75)	0.002	1.33 (1.04; 1.69)
Lyon	210	0.49 (0.20; 1.17)	0.37 (0.14; 0.95)	0.04	1.95 (1.07; 3.56)
Grenoble	690	0.83 (0.42; 1.63)	0.51 (0.30; 0.89)	0.64	1.63 (1.17; 2.26)
Marseille	119	0.57 (0.15; 2.14)	0.20 (0.04; 0.96)	0.05	2.19 (1.23; 3.88)
Geneva	612	0.80 (0.42; 1.51)	0.87 (0.48; 1.56)	0.62	1.60 (1.04; 2.45)
Verona	179	0.60 (0.23; 1.54)	0.23 (0.08; 0.68)	0.009	1.38 (0.96; 2.00)
Pavia	188	0.65 (0.29; 1.44)	0.35 (0.15; 0.81)	0.02	1.37 (0.89; 2.09)
Turin	170	0.68 (0.24; 1.91)	1.41 (0.51; 3.89)	0.55	1.03 (0.68; 1.56)
Oviedo	315	0.77 (0.45; 1.32)	0.36 (0.16; 0.83)	0.02	0.52 (0.27; 1.01)
Galdakao	408	0.75 (0.41; 1.38)	0.49 (0.24; 0.97)	0.04	2.80 (1.53; 5.11)
Barcelona	284	0.87 (0.45; 1.69)	0.77 (0.35; 1.68)	0.48	0.53 (0.29; 0.95)
Albacete	419	0.74 (0.39; 1.42)	0.63 (0.31; 1.28)	0.21	0.39 (0.22; 0.72)
Huelva	233	1.16 (0.49; 2.75)	0.65 (0.20; 2.09)	0.43	2.06 (1.16; 3.65)

Cities are sorted from north to south.

A multilevel logistic regression model (PROC GLIMMIX) was performed with neighborhood at level-2 (random intercept for neighborhood level); adjusted for cohort, age, sex. High exposure (reference category) was defined as a concentration above the 75th percentile of the distribution by cities; p-value for trend were calculated by introducing the categorical variables in continuous.

Table S6b: Odd ratios (OR) for high exposure (95% CI) in association to occupational class mutually adjusted for neighborhood unemployment rate (n=5692)

City	n			Neighborhood Unemployment t∞		
		00.11	00 11	00.04	P-value	
		OC-II	OC-III	OC-IV	for trend	
Norwich	242	1.02 (0.39; 2.68)	0.43 (0.16; 1.12)	0.42 (0.15; 1.20)	0.09	1.71 (1.17; 2.51)
Ipswich	338	1.91 (0.79; 4.62)	1.23 (0.54; 2.81)	0.81 (0.17; 1.50)	0.27	1.23 (0.81; 1.86)
Ântwerp	500	1.00 (0.49; 2.04)	1.23 (0.75; 2.03)	0.45 (0.18; 1.08)	0.34	3.96 (2.65; 5.90)
Paris	785	0.91 (0.58; 1.41)	0.88 (0.53; 1.46)	0.68 (0.30; 1.56)	0.24	1.33 (1.04; 1.69)
Lyon	210	0.41 (0.16; 1.08)	0.42 (0.16; 1.11)	0.45 (0.15; 1.36)	0.65	1.94 (1.05; 3.59)
Grenoble	690	1.19 (0.66; 2.15)	0.89 (0.44; 1.81)	1.07 (0.50; 2.27)	0.75	1.60 (1.15; 2.23)
Marseille	119	0.43 (0.10; 1.77)	0.06 (0.01; 0.48)	0.50 (0.10; 2.64)	0.08	2.40 (1.34; 4.31)
Geneva	612	0.93 (0.45; 1.92)	0.88 (0.45; 1.73)	0.55 (0.28; 1.12)	0.68	1.62 (1.06; 2.48)
Verona	179	1.31 (0.38; 4.49)	1.07 (0.38; 3.03)	0.14 (0.03; 0.83)	0.06	1.28 (0.87; 1.87
Pavia	188	1.58 (0.59; 4.21)	0.25 (0.10; 0.65)	0.22 (0.07; 0.69)	0.004	1.36 (0.88; 2.10)
Turin	170	0.34 (0.06; 1.93)	0.84 (0.29; 2.45)	0.83 (0.24; 2.86)	0.84	1.02 (0.70; 1.49)
Oviedo	315	0.30 (0.10; 0.93)	0.53 (0.29; 0.99)	0.52 (0.24 1.12)	0.20	0.49 (0.25; 0.96)
Galdakao	408	0.50 (0.20; 1.24)	0.64 (0.31; 1.33)	0.63 (0.31; 1.30)	0.35	2.71 (1.49; 4.91)
Barcelona	284	1.69 (0.69; 4.15)	0.96 (0.45; 2.04)	0.91 (0.40; 2.07)	0.74	0.52 (0.29;0.93)
Albacete	419	0.93 (0.37; 2.36)	0.38 (0.16; 0.90)	0.54 (0.27; 1.09)	0.19	0.38 (0.21; 0.69)
Huelva	233	1.13 (0.33; 3.87)	1.27 (0.47; 3.39)	1.64 (0.57; 4.78)	0.42	1.08 (1.04; 3.26)

Cities are sorted from north to south.

A multilevel logistic regression model (PROC GLIMMIX) was performed with neighborhood at level-2 (random intercept for neighborhood level); adjusted for cohort, age, sex. High exposure (reference category) was defined as a concentration above the 75th percentile of the distribution by cities; p-value for trend were calculated by introducing the categorical variables in continuous.

Occupational class (OC): OC-I: Managers and Professionals (ref), OC-II: Technicians and associate professionals, OC-III: other non-manuals, OC-IV: skilled, semi-skilled and unskilled manuals. P-value for trend were calculated by introducing the categorical variables in continuous.

City	n	Educatio	onal level (ref=high)			Neighborhood unemployment rate			
	· · · · · · ·	Medium	Low	P-value	OC-II	OC-III	OC-IV	p-value	
				for				for	
				trend				trend	
Norwich	242	-3.0 (-9.3;3.8)	2.4 (-5.7; 11.3)	0.77	0.3 (-8.1; 9.4)	-1.4 (-9.2; 7.1)	-3.9 (-12.2; 5.1)	0.83	9,4 (5,1; 13,8)
Ipswich	338	3.8 (-0.9; 8.7)	2.7 (-3.1; 8.7)	0.28	1.3 (-4.4; 7.4)	7.2 (1.5; 13.2)	3.6 (-2.6; 10.3)	0.28	5,0 (1,1; 9,0)
Antwerp	500	-4.4 (-8.6; -0.04)	-1.5 (-6.1; 3.3)	0.44	-1.7 (-7.1; 4.0)	2.1 (-2.6; 7.1)	-3.0 (-8.1; 2.4)	0.90	15,0 (11,8; 18,2)
Paris	785	-7.5 (-13.0; -1.7)	-4.2 (-10.1; 2.2)	0.12	-3.6 (-13.7;7.7)	-1.3 (-8.2; 6.2)	-4.1 (-10.2;2.5)	0.46	13,7 (9,7; 17,8)
Lyon	210	-16.5 (-29.9; -0.6)	-28.1 (-40.2; -13.4)	0.001	-25.5 (-39.2; -8.9)	-7.3 (-23.2; 11.8)	-12.7 (-27.7; 5.3)	0.02	12,8 (2,3; 24,4)
Grenoble	690	1.1 (-4.3; 6.8)	1.2 (-4. 4; 7.1)	0.68	2.8 (-4.3; 10.5)	0.9 (-5.7; 8.0)	-0.6 (-6.7; 5.8)	0.44	9,3 (5,1; 13,7)
Marseille	119	-14.9 (-25.4; -2.8)	-19.2 (-29.9; -6.9)	0.004	-2.4 (-20.2; 19.4)	-10.4 (-24.4; 6.2)	-6.1 (-19.1; 8.9)	0.37	12,2 (7,1; 17,6)
Geneva	612	-0.5 (-5.8; 5.1)	-3.6 (-8.9; 2.1)	0.22	2.4 (-5.1; 10.5)	-0.5 (-6.4; 5.7)	-0.5 (-6.5; 5.9)	0.71	9,3 (4,5; 14,3)
Verona	179	-12.9 (-31.1; 10.1)	-25.1 (-39.8; -6.7)	0.01	-32.8 (-49.8; -10.0)	-6.9 (-27.7; 20.0)	0.4 (-27.0; 37.9)	0.008	14,0 (3,7; 25,5)
Pavia	188	-2.2 (-9.1; 5.3)	-6.1 (-12.4; 0.7)	0.08	-9.5 (-16.7; -1.6)	-9.3 (-16.0; -2.1)	2.1 (-7.3; 12.5)	0.003	2,7 (-0,9; 6,4)
Turin	170	4.5 (-3.4; 13.0)	8.2 (-0.6; 17.8)	0.06	12.1 (1.5; 23.8)	10.0 (0.8; 20.1)	9.6 (-2.1; 22.7)	0.02	2,8 (-0,7; 6,5)
Oviedo	315	-9.6 (-19.0; 0.9)	-22.3 (-31.1; -12.3)	< 0.0001	-27.2 (-35.7; -17.7)	-13.3 (-23.4; -1.7)	-17.1 (-29.8; -2.1)	< 0.0001	-14,4 (-24,0; -3,6)
Galdakao	408	-2.6 (-9.4; 4.8)	-1.5 (-9.4; 7.1)	0.70	3.7 (-4.9; 13.1)	8.1 (-1.6; 18.7)	3.8 (-8.4; 17.6)	0.39	21,5 (13,8; 29,7)
Barcelona	284	0.3 (-6.7; 7.7)	-5.0 (-12.5; 3.2)	0.25	-2.2 (-10.2; 6.4)	2.7 (-5.1; 11.0)	4.4 (-5.1; 14.9)	0.71	-7,2 (-12,1; -2,0)
Albacete	419	-20.4 (-32.3; -6.2)	-29.6 (-40.5; -16.7)	< 0.0001	-21.0 (-34.3; -5.0)	-14.9 (-29.7; 3.2)	-11.4 (-30.7; 13.3)	0.007	-8,3 (-18,1; 2,6)
Huelva	233	-0.5 (-8.4; 8.29)	-1.1 (-10.0; 8.6)	0.82	19.6 (8.3; 32.1)	8.6 (-1.9; 20.2)	10.8 (-3.0; 26.6)	0.001	1,6 (-2,6; 5,9)

Table S7: Association between individual- and neighborhood SEP and NO₂ (μ g m-³) using a single-level linear regression model (each SEP variable considered separately; n=5692)

Cities are sorted from north to south.

Each SEP variables were considered separately, adjusted for cohort, age and sex.

Results are expressed in percent change in NO₂ (μ g*m-³) concentration. Negative value means a decrease in NO₂ (in percent) compared to the reference class for the categorical variable; p-value for trend were calculated by introducing the categorical variables in continuous. The unemployment rate has been transformed in z-score, the change in NO₂ is showed for 1 standard deviation.

Occupation class (OC): OC-I: Managers and Professionals, OC-II: Technicians and associate professionals, OC-III: other non-manuals, OC-IV: skilled, semi-skilled and unskilled manuals.

Table S8: Percent change (95% CI) in NO₂ concentration (μ g m⁻³) in association neighborhood deprivation (alone and mutually adjusted for either educational level or occupational class)

Cities	n	Alone	Adjusted for	Adjusted for	
			educational level	occupational class	
Norwich	242	6.8 (3.3; 10.4)	7.2 (3.6; 10.9)	7.1 (3.5; 10.9)	
Ipswich	338	1.2 (-0.4; 2.7)	1.1 (-0.5; 2.6)	1.2 (-0.4; 2.8)	
Paris	782	19.4 (15.7; 23.1)	19.4 (15.7 ; 23.1)	19.4 (15.7 ; 23.1)	
Lyon	206	26.4 (12.4; 42.1)	26.1 (12.3 ; 41.7)	26.9 (12.9 ; 42.7)	
Grenoble	690	15.0 (9.4; 20.9)	14.9 (9.3 ; 20.8))	14.8 (9.2 ; 20.7)	
Marseille	119	18.3 (9.7; 27.5)	18.4 (9.9 ; 27.6)	18.1 (9.7 ; 27.2)	
Verona	176	3.2 (-7.5; 15.1)	3.2 (-7.5 ; 15.2)	2.1 (-8.6 ; 14.0)	
Pavia	188	-0.5 (-3.6; 2.8)	-0.5 (-3.6 ; 2.8)	-0.4 (-3.6 ; 2.8)	
Oviedo	315	-12.2 (-17.8; -6.1)	-11.8 (-17.5; -5.8)	-11.9 (-17.7;-5.8)	
Galdakao	408	1.3 (-3.4; 6.2)	2.4 (-3.7; 8.9)	1.2 (-3.5; 6.0)	
Barcelona	284	2.7 (-0.2; 5.7)	2.7 (-0.2; 5.8)	2.5 (-0.4; 5.6)	
Albacete	419	-13.7 (-24.7; -1.2)	-12.7 (-23.7; -0.2)	-13.4 (-24.4; -0.9)	
Huelva	233	-1.1 (-6.6; 4.6)	-0.9 (-6.4 4.8)	-1.8 (-7.1 3.8)	

A multilevel linear regression model (PROC MIXED) was performed with neighborhood at level-2 (random intercept for neighborhood level); adjusted for cohort, age and sex.

Results are expressed in percent change in NO_2 (µg m-³) concentration. The deprivation indices have been transformed in country-specific z-scores, the change in NO_2 is showed for 1 standard deviation. Positive value means higher exposition to NO_2 . A 95% confidence interval (CI) that does not include zero indicates the presence of significant differences. Deprivation index corresponds to the Carstairs Index for GB cities (Carstairs, 1995); The French European Deprivation Index for the French cities (Pornet et al. 2012); Italian Deprivation Index for Italian cities (Caranci et al. 2010) and Index of vulnerability for the Spanish cities (Alguacil Gómez et al. 2013). Deprivation index (DI) information were not available for Antwerp, Turin and Geneva

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Annex 1: Paris-Region: a case study

Methods:

We described the departments regarding their geographical characteristics (population density, green areas) and socioeconomic indicators (unemployment, poverty, Gini index).

We ran a standard multilevel linear regression model with random effects that takes into account the hierarchical structure of the data by disentangling the residual variability at the individual, neighborhood level. We presented the results for the model including simultaneously the individualand area-SEP markers and accounting for the neighborhood clustering. As NO₂ concentrations were positively skewed, we transformed the variables using natural log transformation. For ease of interpretation, we converted the regression coefficients (β s) 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 considered three sub-regions rather than the departments as they present particular sociodemographic and geographic situations and also to have enough participants in each categories.

Results:

Figure A: Maps of Paris-Region



Paris Region is organized in three principal geographic areas: City of Paris (75), the inner suburbs (composed of three administrative "departments": Hauts-de-Seine (92), Seine-St-Denis (93) and Val de Marne (94)) and the outer suburbs (composed of four departments: Seine-et-Marne (77), Yvelines (78), Essonne (91) and Val d'Oise (95).

Table A. Characteristics of the departments in Paris-Region

				Department-level				Neighborhood-level		Individual-level data	
	Depart ment	N	Population density	% of green areas	% of unemployment	% Poverty rate	Gini index	Neighborhood Unemployment	NO ₂ mean ±sd	% of participants with high Education	% of participants with high Occupation
City of Paris	75	389	21347	21	8	16	0.45	11.9	42.7 ±8.9	58.9	50.1
Inner suburbs	92	76	11315	18	6.2	12.0	0.40	9.2	35.9 ±14.2	47.4	47.4
	93	35	7892	12	10.2	27.0	0.33	15.4	41.8 ± 20.1	37.1	37.1
	94	32	9833	9	6.7	15.0	0.35	9.4	33.7 ±12.0	46.9	59.4
Total inner suburbs		143	10,146 ±1416	14.5	7.3	16.3	0.37	10.8	37.2 ±15.8	44.8	47.6
Outer suburbs	77	28	1761	59	5.1	11	0.32	9.7	19.8 ±5.6	14.3	28.6
	78	63	2400	54	4.9	9	0.36	7.1	21.7 ±7.4	39.7	34.9
	91	48	1856	48	4.8	12.0	0.33	7.5	24.4 ±7.6	35.4	43.8
	95	35	3511	35	6.7	16.0	0.32	9.3	27.5 ±12.1	34.3	37.1
Total outer suburbs		174	2371 ±630	49.3	5.3	11.6	0.34	8.1	23.7 ±9.0	33.3	36.8
Paris Region		706	14,401 ±8156	26.7	7.2	15.0	0.41	10.7	36.4 ± 13.4	42.1	46.3

Table A: The sub-regions of Paris-Region are characterized by specific sociodemographic and socioeconomic situations. The outer suburbs are characterized globally by a low population density and high superficies of green areas. The unemployment (at department level and neighborhood level) and poverty rate are also less marked in this area compared to Paris or the inner suburbs. Regarding the participants, those living in the outer suburbs have lower education level and held less skilled occupations compared to Paris or the inner suburbs.

As expected, the more the participants lived far from Paris, the less they were exposed to NO_2 . They were twice less exposed than those residing within Paris city (23.7 vs. 42.7). That is to say, even if Paris and its inner suburbs are more polluted areas they concentrate the most educated participants with the higher skills. This could explain the reverse association between education/occupation and NO_2 exposure.

Neighborhood unemployment is higher than unemployment measured at department level, however its distribution is the same (higher in Paris and inner suburbs than in the outer suburbs). At department level, NO_2 mean increases as expected with higher density and decreases with higher green areas. Regarding, the socioeconomics characteristics, the NO_2 increases with higher unemployment and higher poverty rate.

			Individual-le	evel	Neighborhood- level		Department-level			
		NO ₂	Individual Education level	Individual Occupation class	Unemployment rate	Population density	Green areas	Unemployment rate	Poverty rate	Gini index
Individual-level	NO_2	0								
	Education level	0.03 ns	0							
	Occupation class	0.05 ns	0.46*	0						
Neighborhood- level	Unemployment	0.39*	-0.08°	-0.03 ns	0					
	Population density	0.66*	0.08°	0.12"	0.35*	0				
	Green areas	-0.62*	-0.11"	-0.12"	-0.35*	-0.69*	0			
Department-level	Unemployment rate	0.62*	0.07 ns	0.06 ns	0.49*	0.73*	0.79*	0		
	Poverty rate	0.45*	0.04 ns	0.02 ns	0.45*	0.39*	0.65*	0.90*	0	

Table B: Pearson correlation between individual, neighborhood and "department" characteristics

P-value: NS non-significant, ° [0.05-0.01[; "[0.01-0.001[; *p<10-5

Table B: As expected, mean NO_2 concentrations exposure estimated at residential address increased with higher population density and less greens areas at department level in the Paris-Region. At department level, participants with higher education level or higher occupation class appeared to live in higher density areas with less green spaces. At this level, there was no correlation between NO_2 and education level or occupation class. Unemployment rate at neighborhood level was positively correlated with unemployment (<0.0001) and poverty rate (<0.0001) at department level. Green areas was positively associated to unemployment at department (not at neighborhood level). Unlike in the US, wealthier people generally live in more urban areas.

Individual-SEP markers were relatively well correlated to each other (r=0.46, p<0.0001), but they were weakly or not correlated to area-SEP (i.e. unemployment (both at neighborhood and department level) and poverty rate. This discrepancy could suggest a selection bias where only the high-SEP person living in disadvantaged neighborhood participated to the study. However, low correlation between individual- and area-SEP has been also found in other European studies, suggesting that, unlike in the US, the urban segregation that could explain environmental health inequalities at individual-level was not verified in Europe.

	n	Educational level (ref=high)			Neighborhood Unemployment t∞
		Medium	Low	P-value	
				for trend	
Paris-Region	785	0.1 (-2.6; 2.9)	-0.3 (-3.1; 2.6)	0.84	13.7 (9.7; 17.8)
City of Paris	420	1.5 (-2.0; 5.2)	1.0 (-2.5; 4.6)	0.53	4.8 (1.5; 8.2)
Inner Suburbs	156	0.3 (-1.7; 2.4)	0.3 (-1.7; 2.4)	0.67	7.3 (1.1; 13.9)
Outer suburbs	209	-1.2 (-5.9; 3.8)	-2.0 (-7.5; 3.8)	0.48	5.4 (-1.7; 13.0)

Table C: Percent increase in NO2 (μ g m-³) concentration (95%CI) in relation to educational level with adjustment for neighborhood unemployment rate in Paris-Region (n=706)

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 education level, p-value for trend were calculated by introducing the categorical variables in continuous. $^{\infty}$ Unemployment has been transformed in z-score, the increase/decrease in NO₂ is showed for 1 standard deviation in the unemployment rate We found the similar results by pooling participants in Paris-Region compared to pooling them by sub-regions that were not artefacts and with characteristics that could influence the association. The unemployment rate however became no longer significant in the outer suburbs.

Table D: Percent increase in NO2 (μ g m-³) concentration (95%CI) in relation to occupational class with adjustment for neighborhood unemployment rate in Paris-Region (n=706)

City	n		Neighborhood Unemployment t∞			
		OC-II	OC-III	OC-IV	P-value for trend	
Paris-Region	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)
City of Paris	420	-1.5 (-5.0; 2.1)	-3.4 (-7.3; 0.7)	-3.1 (-9.2; 3.5)	0.16	5.0 (1.7; 8.4)
Inner Suburbs	156	-0.3 (-1.8; 1.3)	1.5 (-0.4; 3.5)	-0.9 (-3.5; 1.8)	0.35	7.2 (1.0; 13.8)
Outer suburbs	209	-3.2 (-8.4; 2.3)	-4.4 (-10.6; 2.2)	-2.8 (-11.4; 6.6)	0.34	5.4 (-1.7; 13.0)

A multilevel linear regression model (PROC MIXED) was performed with neighborhood at level-2 (random intercept for neighborhood level); adjusted for study, age, sex

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

 $^{\infty}$ Unemployment has been transformed in z-score, the increase/decrease in NO₂ is showed for 1 standard deviation in the unemployment rate

We found the similar results by pooling participants in Paris-Region compared to pooling them by sub-regions that were not artefacts and with characteristics that could influence the association. However, the associations were no longer significant.