



Air pollution, health and social deprivation: A fine-scale risk assessment



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ABSTRACT

Risk assessment studies often ignore within-city variations of air pollutants. Our objective was to quantify the risk associated with fine particulate matter (PM_{2.5}) exposure in 2 urban areas using fine-scale air pollution modeling and to characterize how this risk varied according to social deprivation. In Grenoble and Lyon areas (0.4 and 1.2 million inhabitants, respectively) in 2012, PM_{2.5} exposure was estimated on a 10 × 10 m grid by coupling a dispersion model to population density. Outcomes were mortality, lung cancer and term low birth weight incidences. Cases attributable to air pollution were estimated overall and stratifying areas according to the European Deprivation Index (EDI), taking 10 µg/m³ yearly average as reference (counterfactual) level. Estimations were repeated assuming spatial homogeneity of air pollutants within urban area. Median PM_{2.5} levels were 18.1 and 19.6 µg/m³ in Grenoble and Lyon urban areas, respectively, corresponding to 114 (5.1% of total, 95% confidence interval, CI, 3.2–7.0%) and 491 non-accidental deaths (6.0% of total, 95% CI 3.7–8.3%) attributable to long-term exposure to PM_{2.5}, respectively. Attributable term low birth weight cases represented 23.6% of total cases (9.0–37.1%) in Grenoble and 27.6% of cases (10.7–42.6%) in Lyon. In Grenoble, 6.8% of incident lung cancer cases were attributable to air pollution (95% CI 3.1–10.1%). Risk was lower by 8 to 20% when estimating exposure through background stations. Risk was highest in neighborhoods with intermediate to higher social deprivation. Risk assessment studies relying on background stations to estimate air pollution levels may underestimate the attributable risk.

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1. Introduction

Exposure to particulate matter increases respiratory and cardiovascular morbidity and mortality (Pope and Dockery, 2006; Künzli et al., 2010; Peters, 2011), including lung cancer (Lepeule et al., 2012; Raaschou-Nielsen et al., 2013). Effects are also observed among children, both for respiratory (MacIntyre et al., 2011) and cardiovascular morbidity (Pieters et al., 2015). There is increasing evidence for effects of air pollution on adverse pregnancy and birth outcomes (Shah and Balkhair, 2011), in particular birth weight (Wilhelm et al., 2012; Dadvand et al., 2013; Pedersen et al., 2013). For some of the well-characterized effects (such as short-term effects of PM_{2.5} on mortality), no threshold of exposure below which the effects cease to exist has been identified (WHO, 2013).

Dose-response functions from epidemiological studies can be translated into a number of attributable cases at the population level through risk assessment studies. These risk assessment studies require data on population exposure, which are usually based on air quality monitoring networks. These networks provide a (very) limited spatial resolution within each urban area and do not fully take into account local sources, since the stations considered generally exclude those close to traffic or other sources. Studies at the level of countries, continents or of the world generally rely on environmental (e.g., dispersion) models and possibly satellite measurements, which also often have a poor spatial resolution at the urban scale. These approaches make the strong hypothesis that the people living in each study area are exposed to the same pollutants concentrations, which has been proven not to be the case in urban areas (Jerrett et al., 2005).

Within 12 European urban areas in which fine-scale (LUR) models had been developed, Pedersen et al. (2013) quantified the effect of PM_{2.5} exposure during pregnancy on term low birth weight and estimated that the proportion of attributable term low birth weight cases was 22% (95% confidence interval, CI, 8–33%),

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the WHO yearly air quality guideline of $10 \mu\text{g}/\text{m}^3$ being taken as the counterfactual value. To our knowledge, only one other risk assessment study has considered term low birth weight as an outcome, investigating the effects of a transport policy aiming at reducing road traffic in Barcelona (Rojas-Rueda et al., 2013). For events such as mortality or lung cancer, many more risk assessment studies exist, very few of which relied on fine-scale exposure data such as Land-Use Regressions (LUR) or dispersion models (Forastiere et al., 2011; Rojas-Rueda et al., 2012).

The issue of environmental justice, or socio-economic status facing air pollution, has become a public health priority. Within Europe, relationships between air pollution exposure and socio-economic status vary according to city (Deguen and Zmirou-Navier, 2010). In some areas, the highest exposure to air pollution has been reported to correspond to the population with intermediate social deprivation (Havard et al., 2009). In other areas, it corresponded to areas with highest social deprivation, a pattern similar to that observed in several American studies (Kruize et al., 2007; Namdeo and Stringer, 2008); areas in which the highest air pollution exposure was observed in areas with lowest deprivation or highest socio-economic status have also been described (Forastiere et al., 2007). A recent study conducted in four large French cities emphasized these contrasted associations: in Paris, the population most exposed to air pollution was the one with the lowest social deprivation, while the opposite was found in Marseille and Lille. In Lyon urban area, the most exposed neighborhoods were those with an intermediate social deprivation status (Padilla et al., 2014). Differences in air pollution levels according to social deprivation are likely to entail differences in the health burden associated to air pollution between neighborhoods with different deprivation levels –however only risk assessment studies relying on fine-scale information on air pollution, social deprivation (and possibly population density) can assess the resulting contrasts in attributable risk between neighborhoods.

The main aim of this work was to perform a risk assessment study of the long-term effects of air pollution in two cities, relying on a fine-scale dispersion model, and comparing this approach to the more classical one relying on background monitoring stations (i.e., homogeneous values within the urban area). Our second objective was to identify possible social gradients in $\text{PM}_{2.5}$ exposure and attributable risk at the neighborhood level. The adverse health events considered were non-accidental mortality, lung cancer incidence and term low birth weight.

2. Materials and methods

2.1. Study areas

The study was conducted in Grenoble (670,000 inhabitants) and Lyon (2,120,000 inhabitants) urban areas in the south-East of France, which are respectively the 11th and 2nd largest in France in term of population (INSEE, 2013a). The study area was defined according to the air pollution dispersion model coverage (Fig. 1).

2.2. Assessment of air pollution levels

We relied on Sirane $\text{PM}_{2.5}$ dispersion model (Soulhac et al., 2011, 2012). The source input data of the model include road traffic, heating systems and punctual emission sources such as industries. The pollutants dispersion modeling takes into account urban structures (in particular buildings characteristics, street widths), as well as several meteorology variables on a hourly-basis like wind speed, wind direction and fluctuation, or ground temperature. The model output is provided on a $10 \times 10 \text{ m}$ grid. Model validation was checked by comparing the 2012 model estimates at

the locations of the permanent monitoring stations to the measurements of these stations. The relative error was in the 1.7–6.4% range in Grenoble (two locations) and in the 0.8–1.7% range in Lyon (two locations).

In addition, the measurements from a background air quality monitoring station (AQMS) were used to perform a sensitivity analysis consisting in applying an approach relying on an exposure model without spatial contrasts within each urban area, which corresponds to the approach used in most former risk assessment studies at the urban scale (INVS et al., 2013).

Information on population density was available at the same spatial resolution than the dispersion model, and was based on data from INSEE and the National Institute of Geographic and Forestry Information (IGN, 2007; INSEE, 2010).

2.3. Health events considered

We considered all-cause non-accidental mortality (ICD10: A00–R99), a public health relevant outcome almost systematically investigated by risk assessment studies; lung cancer (ICD10: C33–34) incidence, which ranks first among cancers in terms of mortality in France and is known to be caused by atmospheric pollution. Term low birth weight was chosen as a new relevant health outcome to be considered in risk assessment studies, focused on a sensitive population; very few previous risk assessment studies have been conducted on this health event (Pedersen et al., 2013; Rojas-Rueda et al., 2013) for which WHO recently indicated that evidence is increasing regarding an effect of particulate matter exposure (WHO, 2013). Data on death cases in 2007 were obtained from the death registry dedicated unit of the French Institute of Health and Medical Research (INSERM). Low birth weight cases were estimated by multiplying to the total number of births in each municipality in 2007 (INSEE, 2013b) the proportion of term low birth weight (i.e. below 2500 g for a birth after the end of the 37th gestational week), as estimated from the 2010 national perinatal survey, a survey of all births occurring in a one-week period in the whole country; this proportion was 2.524% (INSERM, 2012). The local cancer registry (Registre du cancer de l'Isère) provided the lung cancer incident cases in Grenoble urban area. Such registry did not exist for the Lyon urban area, so that we restricted the risk assessment for lung cancer incidence to Grenoble area. Three cases could not be geocoded by the registry, which represents 1.5% of all cases.

Data on mortality and term low birth weight were available at the municipality scale, while cancer incident cases were available at the IRIS (housing Blocks Regrouped for Statistical Information) scale, which is the most accurate (finest) geographical census unit available. The IRIS are homogeneous neighborhoods containing on average 2000 inhabitants, and are similar to the US census block group (INSEE, 2008).

2.4. Dose-response functions

Our criteria to select dose-response functions were that they had to be derived from robust studies such as large studies or meta-analyses with limited potential for confounding. For non-accidental mortality we selected the meta-risk from the latest WHO expert meeting (World Health Organization, 2014); the function for lung cancer incidence was also issued from a meta-analysis (Hamra et al., 2014), while the function for term low birth weight was based on the pooled study by Pedersen et al. (2013); since this study yielded a higher OR than a large meta-analysis (Dadvand et al., 2013), we also reported estimates using this other meta-analysis. The relative risks used are listed in Table 1.

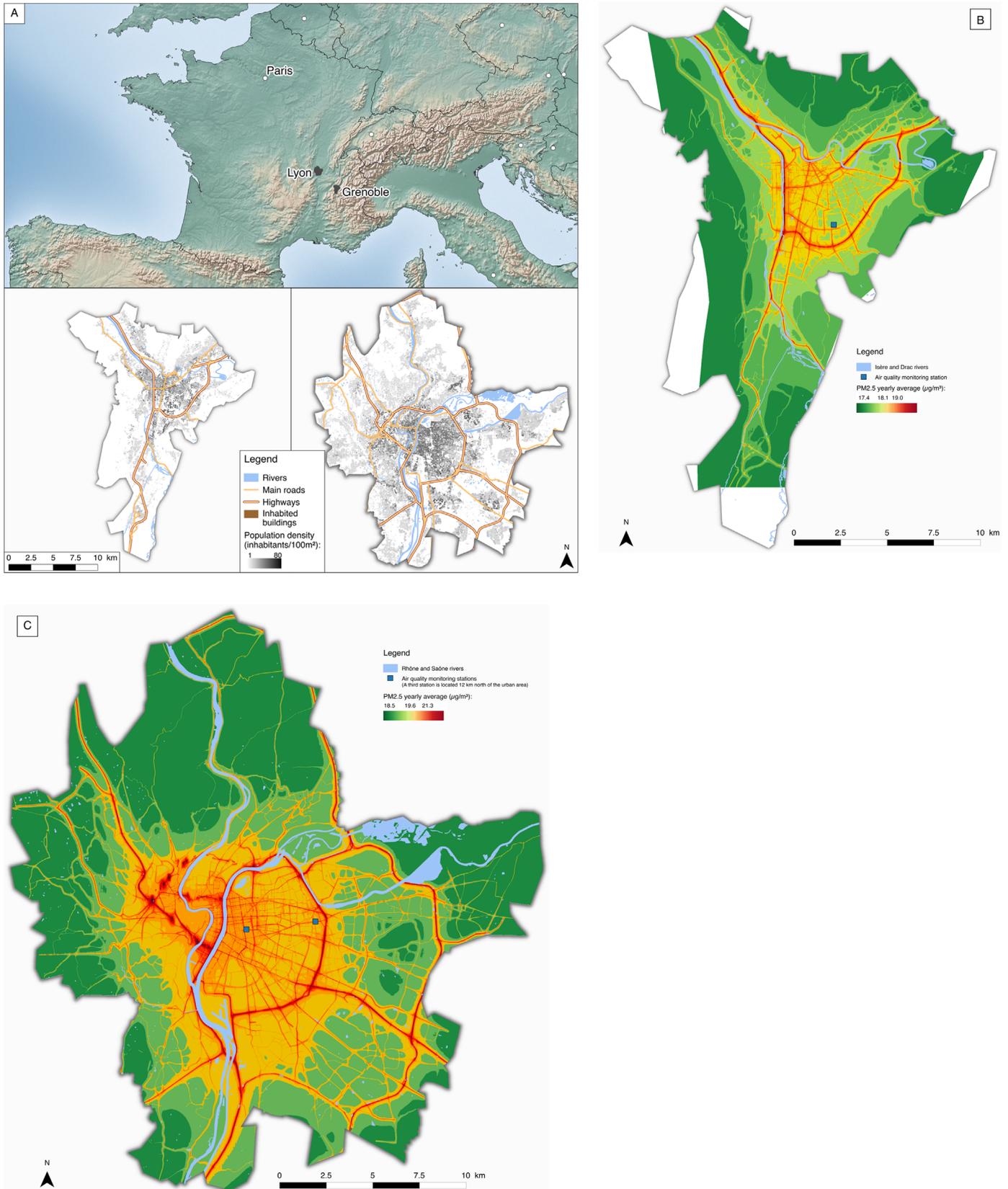


Fig. 1. Study areas (A) and air pollution models for fine particulate matter (PM_{2.5}) concentrations in Grenoble (B) and Lyon (C) urban areas (PM_{2.5} yearly averages for the year 2012).

2.5. Risk characterization

We estimated the number of adverse health events attributable to over-exposure to air pollution, compared to a reference level.

The reference level corresponded to a yearly PM_{2.5} average of 10 µg/m³, the current World Health Organization (WHO) air quality guideline (WHO, 2005).

The number of cases attributable to air pollution NAC_{i,j} at each

Table 1
Dose-response functions used for long-term effects of air pollution exposure to fine particulate matter (PM_{2.5}).

Health event	Study	Relative risk (95% CI) for a 10 µg/m ³ increase in exposure	
Non-accidental mortality	World Health Organization, (2014) ^a	1.066	(1.040–1.093)
Lung cancer incidence	Hamra et al. (2014) ^a	1.09	(1.04–1.14)
Term low birth weight ^b	Pedersen et al. (2013)	1.392	(1.124–1.769) ^c
	Dadvand et al. (2013)	1.10	(1.03–1.18) ^d

^a Meta-analysis-based relative risks.

^b Occurrence of low birth weight (< 2500 g) births among term births (those occurring after the end of the 37th gestational week).

^c The original odds-ratio was reported for a 5 µg/m³ increase in exposure: 1.18 (1.06–1.33).

^d Odds-ratio. Main estimates as reported in Table 2 by Dadvand et al. This odds-ratio is used in a sensitivity analysis (see discussion).

geographical coordinate (i,j) was estimated as

$$E1 : NAC_{i,j} = n_{i,j} \times \left(\frac{D}{N} \right) \times \left(\frac{RR_{i,j} - 1}{RR_{i,j}} \right)$$

.Where $n_{i,j}$ was the population density (inhabitants/100 m²), D the total number of disease cases in the smallest geographical unit available containing the location (i,j), N the number of inhabitants in this geographical unit (deduced from the population density data). This formula assumes that for each neighborhood (for lung cancer estimates) or city (for the other outcomes), cases are distributed in the cells of the dispersion model output proportionally to their population density. $RR_{i,j}$ is the customized relative risk at location (i,j), which depended on the PM_{2.5} concentration $c_{i,j}$ observed at this location:

$$RR_{i,j} = RR_{E-R} \left(\frac{C_{i,j} - C_{ref}}{10} \right)$$

.Where RR_{E-R} corresponded to the relative risk associated with an increase by 10 µg/m³ in PM_{2.5} concentration selected for the outcome considered (see Table 1), and c_{ref} was equal to the 10 µg/m³ reference level from the WHO air quality guideline (see above). All attributable cases $NAC_{i,j}$ were then summed over each study area.

2.6. Sensitivity analyses

The impact of air pollution was also assessed under alternative hypotheses, labelled H2 to H4. The H2 hypothesis assumed a homogeneous spatial distribution of population density. Hence the number of attributable cases was estimated as:

$$E2 : NAC_{i,j}^{H2} = \left(\frac{D}{NGP} \right) \times \left(\frac{RR_{i,j} - 1}{RR_{i,j}} \right)$$

.Where NGP was the total number of grid points in the area. H3 assumed that both the spatial distribution of the population density and the PM_{2.5} concentrations were homogeneous in each area, hence a number of attributable cases corresponding to:

$$E3 : NAC_{i,j}^{H3} = \left(\frac{D}{NGP} \right) \times \left(\frac{RR_{median} - 1}{RR_{median}} \right)$$

.Where RR_{median} was the median PM_{2.5} concentration in the study area (Grenoble or Lyon urban area), estimated from the population-weighted area specific distribution of PM_{2.5} concentrations at each point of the grid.

We estimated the number of attributable cases under what we termed the classical approach (H4 hypothesis), in which exposure

assessment relied on the air quality monitoring network. One PM_{2.5} background station was available in Grenoble and three in Lyon. Starting from H3 assumptions, in H4 the relative risk RR_{median} was replaced by RR_{AQMS_avg} , the relative risk corresponding to the yearly average of PM_{2.5} levels recorded by the station(s):

$$E4 : NAC_{i,j}^{H4} = \left(\frac{D}{NGP} \right) \times \left(\frac{RR_{AQMS_avg} - 1}{RR_{AQMS_avg}} \right)$$

Finally, all estimations of the number of lung cancer cases were repeated with a degradation of the spatial resolution of the incident lung cancer cases, the only health event for which data at the IRIS (neighborhood) were available (Fig. 3). These disease cases initially available at the neighborhood scale were aggregated at the municipality or urban area scale, by homogeneously distributing the cases in the populated grid cells of each municipality, or in the populated cells throughout the whole urban area. This analysis was done in order to investigate the influence of the spatial resolution of information on health events.

2.7. Socio-economic inequalities

Area-level socio-economic status was estimated through the European Deprivation Index (EDI) (Pornet et al., 2012). The EDI quantifies the deprivation status and relies on ten characteristics available at the IRIS –or neighborhood– level, which were combined for all IRIS in the whole country based on a European survey (EU-SILC; Pornet et al., 2012). The variables cover various socio-economic characteristics such as the proportion of overcrowded homes, the occupational class, employment status or basic amenities presence (Pornet et al., 2012).

To evaluate the relationship between exposure to air pollution and the EDI, we grouped IRIS into deciles defined by the EDI at the IRIS level, and described the population-weighted air pollution levels in each EDI decile. In addition, we ranked the IRIS in each urban area by their median exposure level to PM_{2.5}, and compared the ordered result with the EDI score by means of Spearman's rank correlation coefficients. We also estimated the attributable risk of PM_{2.5} by EDI decile, at the same neighborhood scale.

Data management and analyses were performed with Stata software (StataCorp LP, TX USA); QGIS software was used for the spatial operations and cartography (QGIS 2.4, OSGeo Foundation, Beaverton, OR, USA).

3. Results

3.1. Study population, air pollution exposure and health events

The part of Grenoble urban area considered had a surface of 245 km² and included 385,000 inhabitants distributed in 25 municipalities, out of which 157,000 inhabitants (41% of the total) lived inside Grenoble city. Each of the 169 IRIS –or neighborhoods– included an average population of 2280 (interquartile range: 1940–2760). In Lyon area (480 km²), 470,000 out of the 1.2 million inhabitants considered, or 39% of the total, lived in Lyon city, while the total population was spread in 64 municipalities. The number of IRIS in the urban area was 495, with an average population of 2470 (interquartile range: 1970–2990). The two study areas are represented in Fig. 1.

The 5th, 50th and 95th percentiles of the population density-weighted PM_{2.5} levels estimated by the dispersion model in 2012 were 17.4, 18.1, 19.0 µg/m³ in Grenoble and 18.5, 19.6, 21.3 µg/m³ in Lyon urban areas, respectively. The average PM_{2.5} levels recorded in 2012 by the background air quality monitoring stations were 17.5 µg/m³ in Grenoble and 18.1 µg/m³ in Lyon, lower than the

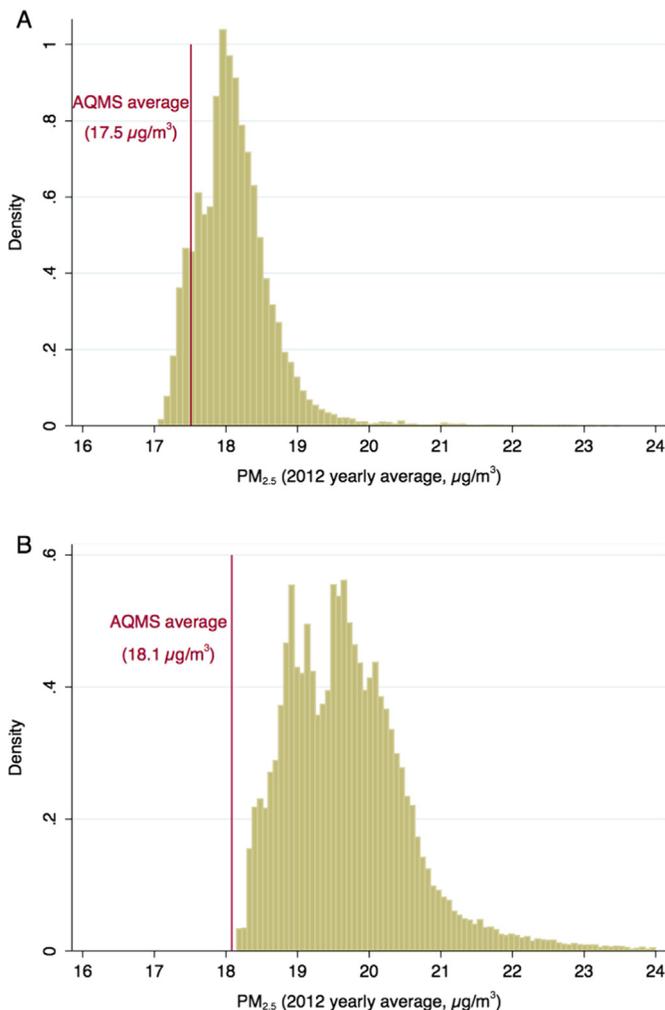


Fig. 2. Distribution of population exposure to fine particulate matter (PM_{2.5} yearly average in 2012) in Grenoble (A) and Lyon (B) urban areas. The mean yearly level from the local background monitoring station(s) is indicated by the vertical line. AQMS: Air Quality Monitoring Station.

median exposure from the dispersion model (Fig. 2).

The numbers of non-accidental deaths in 2007 was 2254 and 8148 in Grenoble and Lyon study areas, respectively, which corresponds to death rates of 5.9‰ and 6.7‰, respectively (compared to 8.4‰ for metropolitan France). The number of incident lung cancer cases in Grenoble urban area was 195, which corresponded to an incidence of 50.6 cases/100,000 inhabitants. The incidence varied between IRIS, and was 26.1 and 78.9 for the first and last deciles, respectively (Fig. 3). The numbers of term low birth weight cases, which were estimated from a nationwide prevalence estimate (2.524%, see Materials and Methods, Section 2.3), were 133 and 474 in Grenoble and Lyon urban areas, respectively.

3.2. Attributable risk of PM_{2.5} exposure

Based on the relative-risk functions chosen (Table 1) and the estimated PM_{2.5} levels, the estimated attributable risk of air pollution on all-cause non-accidental mortality corresponded to 114 cases in Grenoble (95% CI 71–157), or 5.1% of the total (95% CI 3.2–7.0%); the corresponding figures for Lyon were 491 cases (95% CI 305–675) or 6.0% of the total (95% CI 3.7–8.3%). The number of lung cancer incident cases that could be attributed to PM_{2.5} levels was 13.2 in Grenoble (95% CI 6.1–19.7), or 6.8% of the total (95% CI

3.1–10.1%; no estimate for Lyon). The attributable number of term low birth weight cases was 31.4 in Grenoble (23.6% of all term low birth weight births, 95% CI 9.0–37.1%). In Lyon, 131 term low birth weight cases were assumed to be attributable to PM_{2.5}, which represented 27.6% of the total (95% CI 10.7–42.6%, Table 2).

The sensitivity analyses showed that when population density was assumed to be homogeneous at the urban area level (H2 hypothesis), the attributable risk of death or term low birth weight birth was lower by 4.7–5.6% compared to under H1, depending on the urban area and health event. For lung cancer in Grenoble, the attributable risk was increased by 1.5% with H2 compared to H1. When exposure was assumed to be homogeneous within each urban area and corresponded to the model area-specific median exposure (H3 hypothesis), the risk attributable to PM_{2.5} was lower than under H1. Compared to the fine-scale approach (H1 hypothesis), the attributable risk estimated with H3 was lower by 7.5–8.6% in Grenoble, depending on the health event, and by 8.3–9.4% in Lyon. A similar situation was observed under H4, which assumed that everyone was exposed to the yearly level measured by the local background monitoring station(s). Under H4, the difference with H1 was similar to the difference between H3 and H1 in Grenoble while it was higher in Lyon, with a number of attributable cases lower by 18.0–19.8% under H4 compared to H1, depending on the health event (Table 3).

We repeated this sensitivity analysis restricting the study area to the two administrative cities of Lyon and Grenoble; this resulted in a higher attributable risk when assuming a homogeneous population density, with differences between H1 and H2 varying from 1.1% to 2.4% depending on the municipality and health event (Table S1).

For lung cancer incidence, ignoring the spatial distribution of cases in Grenoble urban area did not result in a notable difference (1% change) in terms of attributable risk (Table 4, Fig. 3).

3.3. Stratification of estimates on social deprivation

Air pollution was associated with the neighborhood social deprivation index, exposure being lowest in the neighborhoods in the decile of the social deprivation index (EDI) corresponding to the lowest deprivation, and highest in the fifth to seventh deciles (Table 5, Fig. 4). The Spearman's rank coefficient of correlation between PM_{2.5} median exposure and EDI score, by IRIS, was 0.40 in Grenoble (n=169 IRIS) and 0.23 in Lyon (n=495, Fig. 5, Fig. S1).

Stratification of the attributable risk of PM_{2.5} on the EDI showed similar contrasts. For mortality and term low birth weight, and depending on the social deprivation decile, the maximum between-EDI decile differences in attributable risk were in the 11.8–12.0% and 9.8–10.9% ranges in Grenoble and Lyon urban areas, respectively. For example, the anticipated death risk attributable to PM_{2.5} was 4.8% in the IRIS from the third and eighth EDI deciles, while it was 5.4% (a relative increase by 12.5%) in the sixth decile (Table 5). For lung cancer incidence, the maximum between EDI decile difference in terms of attributable risk was 12.1% when the spatial distribution of lung cancer cases was at the urban area scale, 33.0% when the spatial distribution was the neighborhood (IRIS) scale and 32.1% when the spatial distribution was the municipality scale (Table 5, Fig. S2).

4. Discussion

4.1. Summary

This study is among the first to perform a risk assessment of fine particulate matter relying on a spatially finely resolved exposure model. We estimated PM_{2.5} exposure distribution from a

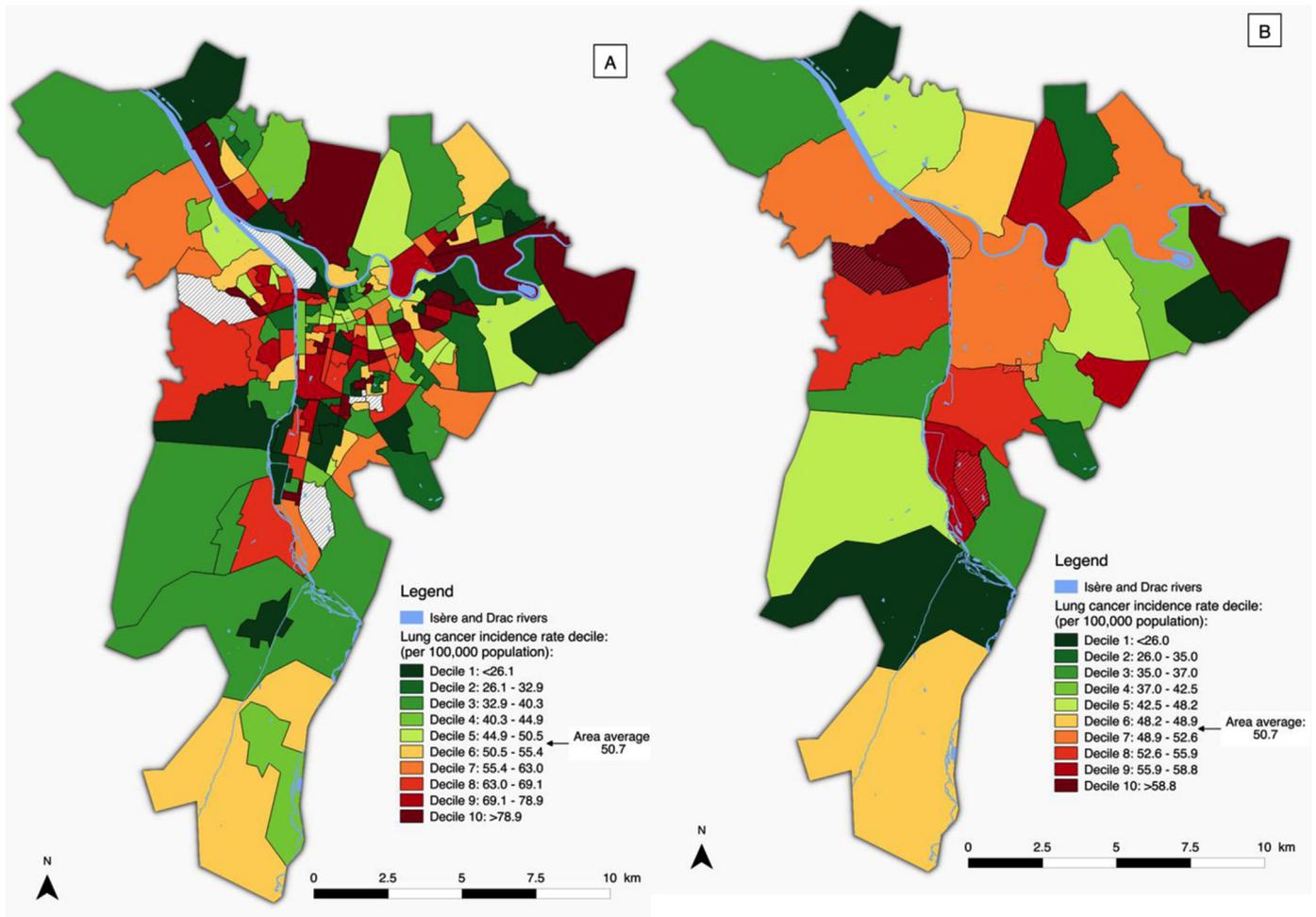


Fig. 3. Lung cancer incidence in Grenoble urban area, taking into account the neighborhood (IRIS)-specific information on the distribution of cases (A) and assuming spatial homogeneity in the distribution of cases in neighborhoods (IRIS) from the same municipality (B). IRIS: housing Blocks Regrouped for Statistical Information, or neighborhood.

Table 2
Estimated number of cases attributable to fine particulate matter ($PM_{2.5}$) exposure in 2012 in Grenoble and Lyon urban areas (non-accidental mortality, lung cancer incidence and term low birth weight incidence), taking into account fine-scale variations in $PM_{2.5}$ levels.

Health event	Observed number of health events (2007)	Number of attributable cases (% of total) carriage return associated with $PM_{2.5}$ levels ^a	95% CI	(% of total)
Non-accidental mortality				
Grenoble	2250	114 (5.1%)	71–157	(3.2–7.0%)
Lyon	8150	491 (6.0%)	305–675	(3.7–8.3%)
Lung cancer incidence				
Grenoble	195	13.2 (6.8%)	6.1–19.7	(3.1–10.1%)
Term low birth weight cases				
<i>Pedersen et al. (2013)</i> dose-response function				
Grenoble	133 ^b	31.4 (23.6%)	12.0–49.4	(9.0–37.1%)
Lyon	474 ^b	131 (27.6%)	50.8–202	(10.7–42.6%)
<i>Dadvand et al. (2013)</i> dose-response function				
Grenoble	133 ^b	9.9 (7.4%)	3.2–16.8	(2.4–12.6%)
Lyon	474 ^b	42 (8.9%)	13.5–70.5	(2.8–14.9%)

^a Compared to the counterfactual situation corresponding to compliance with WHO guidelines (yearly average level, $10 \mu\text{g}/\text{m}^3$).

^b Estimated number of birth weights < 2500 g among term births (≥ 37 gestational weeks).

fine-scale dispersion model with a 10-m resolution, coupled to knowledge of the population density at the same scale. In addition, we provided an estimation of the number of term low birth weight cases attributable to air pollution, which had to our knowledge very little been done (Pedersen et al. 2013; Rojas-Rueda et al., 2013). Exposure assessment based on background air quality

monitoring stations tended to underestimate population exposure, and consequently the attributable risk, by 10–20% according to the area. Regarding information on cases location, including fine-scale information on the spatial resolution of disease cases (lung cancer) did not entail a difference in term of attributable risk compared to aggregating information on cases at the municipality or urban area

Table 3Sensitivity analyses of the risk assessment of fine particulate matter (PM_{2.5}) exposure under three alternative hypotheses related to the spatial resolution.

Health event and hypothesis ^a	PM _{2.5} exposure: 5th–50th–95th percentile (µg/m ³)	Number of attributable cases (NAC)			
		NAC	(% of total)	95% CI	(% of total)
Non-accidental mortality					
Grenoble area (n=385,000)					
H1 (reference)	17.4–18.1–19.0	114	(5.1%)	71–157	(3.2–7.0%)
H2	17.1–17.5–18.9	108	(4.8%)	67–149	(3.0–6.6%)
H3	17.5–17.5–17.5	105	(4.7%)	65–145	(2.9–6.4%)
H4	17.5–17.5–17.5	106	(4.7%)	65–146	(2.9–6.4%)
Lyon area (n=1,220,000)					
H1 (reference)	18.5–19.6–21.3	491	(6.0%)	305–675	(3.7–8.3%)
H2	18.3–18.9–21.0	465	(5.7%)	289–639	(3.5–7.8%)
H3	18.9–18.9–18.9	449	(5.5%)	278–617	(3.4–7.6%)
H4	18.1–18.1–18.1	410	(5.0%)	254–565	(3.1–6.9%)
Lung cancer incidence					
Grenoble area (n=385,000)					
H1 (reference)	17.4–18.1–19.0	13.2	(6.8%)	6.1–19.7	(3.1–10.1%)
H2	17.1–17.5–18.9	13.4	(6.9%)	6.2–20.0	(3.2–10.3%)
H3	17.5–17.5–17.5	12.2	(6.3%)	5.6–18.2	(2.9–9.3%)
H4	17.5–17.5–17.5	12.2	(6.3%)	5.7–18.3	(2.9–9.4%)
Term low birth weight cases					
Grenoble area (n=385,000)					
H1 (reference)	17.4–18.1–19.0	31.4	(23.6%)	12.0–49.4	(9.0–37.1%)
H2	17.1–17.5–18.9	30.0	(22.6%)	11.5–47.4	(8.6–35.6%)
H3	17.5–17.5–17.5	29.2	(22.0%)	11.1–46.3	(8.3–34.8%)
H4	17.5–17.5–17.5	29.4	(22.1%)	11.2–46.5	(8.4–35.0%)
Lyon area (n=1,220,000)					
H1 (reference)	18.5–19.6–21.3	131	(27.6%)	50.8–202	(10.7–42.6%)
H2	18.3–18.9–21.0	124	(26.1%)	48.2–193	(10.2–40.7%)
H3	18.9–18.9–18.9	121	(25.5%)	46.5–188	(9.8–39.6%)
H4	18.1–18.1–18.1	111	(23.4%)	42.6–175	(9.0–36.9%)

^a H1: Fine-scale approach taking into account spatial variations of both population density and PM_{2.5} as presented in Table 2; H2: Same as H1 but assuming spatial homogeneity of population density; H3: Same as H2, but assuming spatially homogeneous air pollution levels (area-specific median level of dispersion model estimate); H4: Same as H2, but assuming spatially homogeneous air pollution levels, as estimated by the area-specific background air quality monitoring stations (one station in Grenoble and 3 stations in Lyon; see Fig. 1).

level as is usually done. The impact of PM_{2.5} on mortality, lung cancer and term low birth weight tended to be highest in areas with a moderate to high social deprivation index, and lowest in areas with lowest social deprivation.

4.2. Underlying assumptions and data

We supposed that mean level at the home addresses was a good proxy of the average exposure to PM_{2.5} present in the outdoor air. We restricted our study to fine particulate matter (PM_{2.5}).

Table 4Estimated impact of fine particulate matter (PM_{2.5}) exposure on lung cancer incidence with varying assumptions on the spatial resolution of the information on lung cancer incidence (Grenoble urban area only).

Spatial resolution of the lung cancer cases	PM _{2.5} exposure: 5th–50th–95th percentile (µg/m ³)	Number of attributable cases (% of total)		95% CI	(% of total)
By neighborhood (IRIS)^a					
H1 (reference)	17.4–18.1–19.0	13.2	(6.7%)	6.1–19.7	(3.1–9.9%)
H2	17.1–17.5–18.9	13.4	(6.8%)	6.2–20.0	(3.1–10.1%)
H3	17.5–17.5–17.5	12.2	(6.2%)	5.6–18.2	(2.8–9.2%)
H4	17.5–17.5–17.5	12.2	(6.2%)	5.7–18.3	(2.9–9.2%)
By municipality^b					
H1 (reference)	17.4–18.1–19.0	13.2	(6.7%)	6.1–19.7	(3.1–9.9%)
H2	17.1–17.5–18.9	13.0	(6.6%)	6.0–19.4	(3.0–9.8%)
H3	17.5–17.5–17.5	11.8	(6.0%)	5.5–17.7	(2.8–8.9%)
H4	17.5–17.5–17.5	11.9	(6.0%)	5.5–17.8	(2.8–9.0%)
Whole urban area					
H1 (reference)	17.4–18.1–19.0	13.1	(6.6%)	6.1–19.6	(3.1–9.9%)
H2	17.1–17.5–18.9	12.5	(6.3%)	5.8–18.7	(2.9–9.4%)
H3	17.5–17.5–17.5	12.1	(6.1%)	5.6–18.1	(2.8–9.1%)
H4	17.5–17.5–17.5	12.2	(6.2%)	5.7–18.2	(2.9–9.2%)

H1: Fine-scale approach taking into account spatial variations of both population density and PM_{2.5} as presented in Table 2; H2: Same as H1, assuming spatial homogeneity of population density; H3: Same as H2, assuming spatially homogeneous air pollution levels (area-specific median level of dispersion model estimate); H4: Same as H2, assuming spatially homogeneous air pollution levels, as estimated by the area-specific background air quality monitoring stations (one station in Grenoble and three stations in Lyon; see Fig. 1).

^a The neighborhood (IRIS, or housing Block Regrouped for Statistical Information) is the finest scale for which lung cancer cases were available; IRIS included on average 2280 inhabitants (interquartile range: 1940–2760) and Grenoble area included a total of 169 IRIS.

^b For the municipality-scale setup, lung cancer cases from each IRIS were aggregated in the corresponding municipality (total of 25 municipalities in Grenoble urban area).

Table 5
Stratification on the social deprivation status of the population-weighted median exposure to PM_{2.5} and of the risk attributable to fine particulate matter (PM_{2.5}; part of the number of attributable cases (NAC) on the total, by EDI decile).

	Social deprivation decile										NAC (Part of total)
	1 (least deprived)	2	3	4	5	6	7	8	9	10 (most deprived)	
Grenoble											
Population (thousands)	40.0	38.9	37.1	38.2	39.4	39.8	38.5	36.2	38.7	38.2	
	10.4%	10.1%	9.6%	9.9%	10.2%	10.3%	10%	9.4%	10%	9.9%	
PM _{2.5} exposure	17.54	17.66	17.84	18.06	18.23	18.29	18.31	18.08	18.01	18.14	
Non-accidental mortality attributable to PM _{2.5}	11.2	11.0	10.8	11.4	11.9	12.1	11.8	10.8	11.4	11.5	114
	5.0%	4.9%	4.8%	5.1%	5.3%	5.4%	5.2%	4.8%	5.1%	5.1%	5.1%
Lung cancer incidence attributable to PM _{2.5}	1.17	1.18	1.24	1.35	1.12	1.42	1.46	1.44	1.35	1.48	13.2
	6.0%	6.1%	6.4%	6.9%	5.7%	7.3%	7.5%	7.4%	6.9%	7.6%	6.8%
Term low birth weight cases attributable to PM _{2.5}	3.11	3.05	2.99	3.13	3.28	3.32	3.23	2.97	3.15	3.17	31.4
	23.4%	22.9%	22.5%	23.5%	24.7%	25.0%	24.3%	22.3%	23.7%	23.8%	23.6%
Lyon											
Population (thousands)	124.1	120.7	123	120.7	122.9	122.9	123.9	121.6	122.5	119	
	10.2%	9.9%	10.1%	9.9%	10.1%	10.1%	10.1%	10%	10%	9.7%	
PM _{2.5} exposure	18.77	19.15	19.58	19.74	19.9	20.02	19.92	19.93	19.56	19.26	
Non-accidental mortality attributable to PM _{2.5}	46	47	49.7	48.7	50.8	51	51.4	51	49.1	46.7	491
	5.6%	5.8%	6.1%	6.0%	6.2%	6.3%	6.3%	6.3%	6.0%	5.7%	6.0%
Term low birth weight cases attributable to PM _{2.5}	12.3	12.5	13.2	12.9	13.5	13.5	13.6	13.5	13.0	12.4	131
	25.9%	26.4%	27.8%	27.2%	28.5%	28.5%	28.7%	28.5%	27.4%	26.2%	27.6%

EDI: European Deprivation Index.

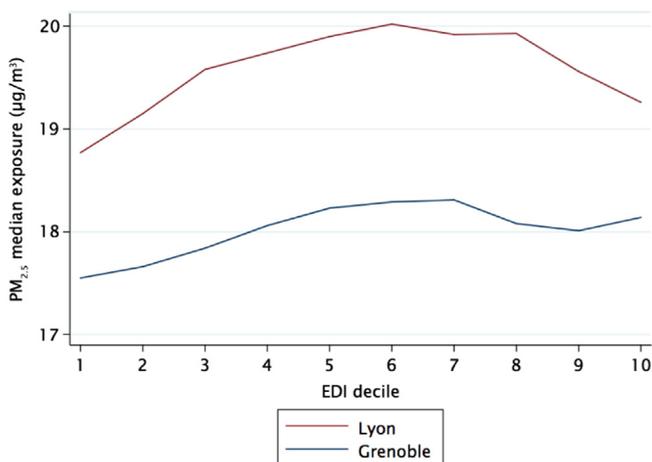


Fig. 4. Median exposures to fine particulate matter (PM_{2.5}) by neighborhoods grouped in social deprivation (EDI index) decile, in Grenoble and Lyon (see Table 5 for exact values). EDI: European Deprivation Index.

Associations with the outcomes considered have been reported for other atmospheric pollutants, including PM₁₀, nitrogen (di)oxide (Pedersen et al., 2013; Nafstad et al., 2003; Hystad et al., 2013), and ozone. PM₁₀ include the smaller PM_{2.5} fraction that we considered, and, at least for lung cancer and low birth weight, there is evidence that any effect of the coarse PM fraction, additional to that of PM_{2.5}, if any, is likely to be low (Hamra et al., 2014; Pedersen et al., 2013). For NO₂, the literature is less clear, so that one cannot exclude an effect on some of the outcomes we considered in addition to that of PM_{2.5}; our option not to estimate an effect of NO₂ may have led to an underestimation of the effects of atmospheric pollutants as a whole.

Data on mortality are exhaustive in France; for data privacy

reasons, it was not possible to obtain mortality data at a finer scale than the municipality. If we assume that the conclusions of the sensitivity analysis done with lung cancer (for which we could rely on incidence data at the IRIS, or neighborhood scale) also apply to other health outcomes, then the aggregation of death and low birth weight cases at the municipality scale is unlikely to have strongly biased our attributable risk estimates. However, this lack of fine-scale resolution on death cases may have modified the distribution of attributable cases according to social deprivation and the social contrasts in health burden. Indeed, stratification of the number of attributable lung cancer cases on the social deprivation decile showed that depending on the spatial resolution of the lung cancer incidence (neighborhood, city or urban area), the distribution of the attributable risk varied depending on the social deprivation status (Fig. S2B).

Results of risk assessment studies such as ours are generally highly sensitive to the dose-response function chosen. Residual confounding cannot be excluded in the dose-response functions we relied on. For example, these dose-response functions were not adjusted for noise, a possible risk factor for cardiovascular deaths correlated to air pollution levels (Foraster et al., 2011). We have used the meta-risk for mortality estimated for the world, which was very close to that estimated from European studies only (RR of 1.06 per 10 µg/m³, 95% CI 1.02–1.11).

For lung cancer incidence, the presence of a local cancer registry allowed us to obtain data at the smallest geographical unit available, instead of the municipality level. The meta-analysis by Hamra et al. (2014) providing an estimate for the association between outdoor PM_{2.5} concentrations and lung cancer was based on studies which were not all corrected for active smoking, the main risk factor associated with lung cancer risk. The authors reported consistent meta-estimates when restricting the analysis to studies adjusting for smoking status and other individual characteristics (Hamra et al., 2014). In a more recent study, Cui et al. (2015)

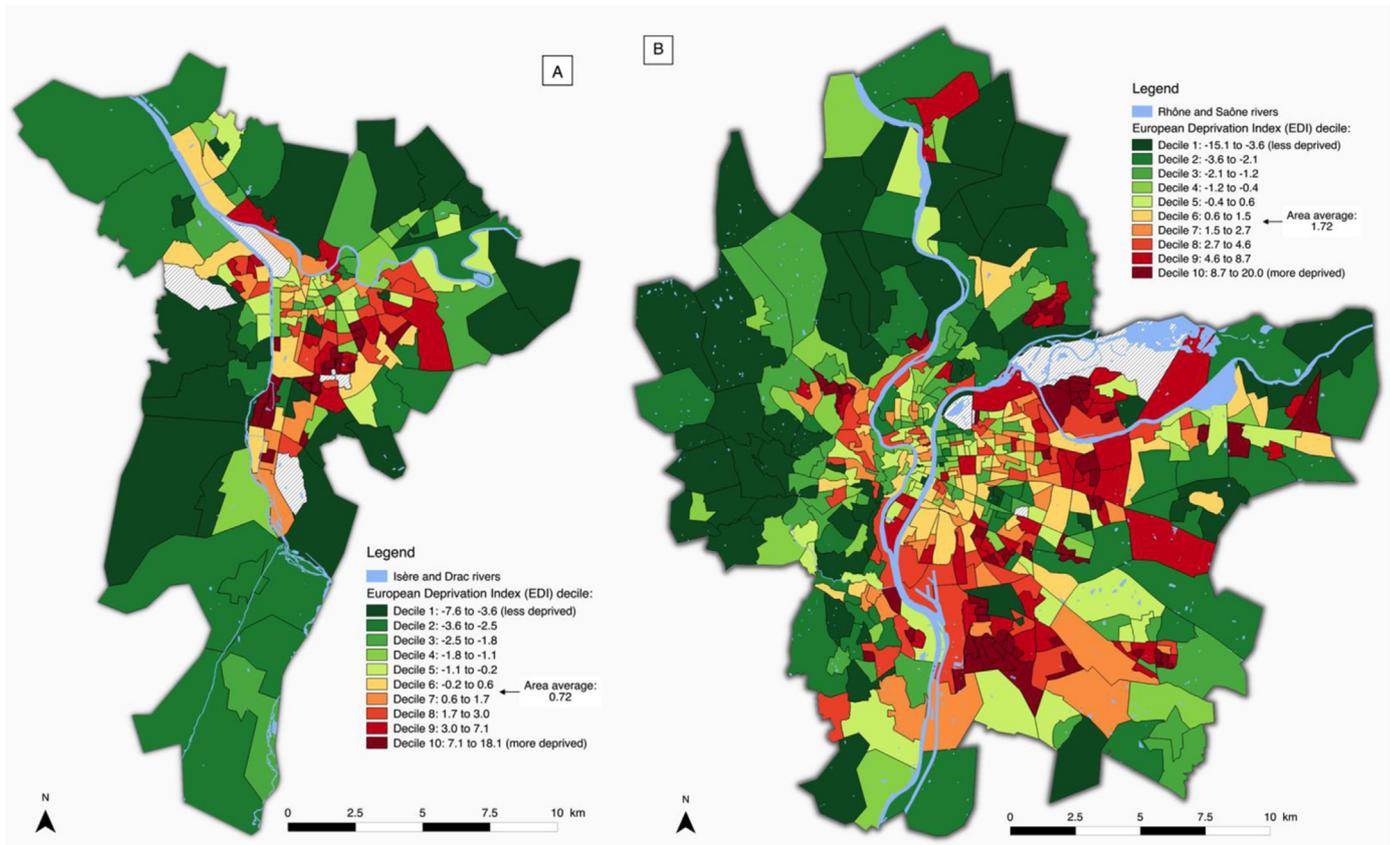


Fig. 5. Social deprivation status (European Deprivation Index, EDI) at the IRIS scale in Grenoble (A) and Lyon (B) urban areas. IRIS: housing Blocks Regrouped for Statistical Information, or neighborhood.

conducted a meta-analysis of ambient $PM_{2.5}$ concentrations and lung cancer with 10 out of 12 selected studies matching the studies used by Hamra et al. who relied on 14 studies. Point estimates were identical, Cui et al. (2015) reporting a relative risk of 1.09 (95% CI: 1.06–1.11), compared to 1.09 for Hamra et al. (95% CI: 1.04–1.14).

Data on term low birth weight cases incidence are not available at the municipality level in France so that we relied on a recent national perinatal survey (INSERM, 2012). One cannot exclude the possibility of geographic variations in term low birth weight incidence between Grenoble and Lyon urban areas. However, although an error in the city-specific incidence could impact the number of term low birth weight cases attributable to $PM_{2.5}$, it would not impact the proportion of cases attributable to $PM_{2.5}$. Like in other risk assessment studies, results expressed in terms of proportion of attributable cases are more robust to any deviation from the hypotheses related to the baseline incidence of the health events considered. The choice of the dose-response relationship has a much larger impact on the attributable risk, as shown by our sensitivity analysis relying on the dose-response from Dadvand et al. (2013). The dose-response function for $PM_{2.5}$ effects on term low birth weight incidence used in our main analysis was based on a recent European study of about 50,000 births with harmonized fine scale air pollution modeling relying on land use regression and adjusted for a large number of potential confounders (Pedersen et al., 2013). It was much higher than that from previous meta-analyses; for example, Dadvand et al. (2013) reported an OR for term low birth weight of 1.10 (95% CI, 1.03–1.18) for each increase by $10 \mu\text{g}/\text{m}^3$ in $PM_{2.5}$ concentrations, compared to 1.39 (95% CI, 1.12–1.77) for the Pedersen et al. study. Applying the dose-response function from Dadvand et al. yielded an estimated proportion of term low birth weight cases attributable to $PM_{2.5}$ concentrations of 8.9% (95% CI 2.8–14.9%) in Lyon area, compared

to 27.6% (95% CI, 10.7–42.6%) with the dose-response function we chose. For both studies, the dose-response relationship corresponded to an exposure to $PM_{2.5}$ during pregnancy, while our attributable risk estimates relied on yearly exposures. Again, confounding (in any direction) cannot be excluded, as these studies did not adjust the $PM_{2.5}$ effect for any influence of noise or meteorological factors, which have been recently reported to possibly impact low birth weight risk (Gehring et al., 2014; Strand et al., 2011).

Since population density data were available from the 2007 census, we chose to use 2007 also for the number of disease cases. There was no strong trend in any of the health events considered on a 10-year period around 2007 (not detailed). Thus, this difference between the years considered is unlikely to limit the validity of our findings.

4.3. Which approach should be used to assess air pollution in future risk assessment studies?

To our knowledge, most former risk assessment studies at the urban scale did not use exposure models such as fine-scale dispersion models or land-use regressions with a spatial resolution capable of catching street-scale contrasts of exposure (Pascal et al., 2013; Sousa et al., 2012). One risk assessment study conducted in Estonia relied on a dispersion model with a 200 m spatial resolution (Orru et al., 2009).

Regarding the population-density weighting for air pollution exposure assessment, we could not identify another study applying a weighting at a fine, street level scale, although a study estimating the benefits of a reduction in air pollution in Barcelona metropolitan area coupled air pollution levels to population density data (Pérez et al., 2009).

The typical approach used in former risk assessment studies at the urban scale consists in estimating exposure to air pollution with data from the air quality monitoring network. The reliance on air quality monitoring stations in risk assessment may at first sight seem justified by the fact that many of the dose-response functions used in risk assessment derive from epidemiological studies in which exposure was assessed from air quality monitoring stations. We believe that this should not be used as an argument not to move towards reliance on finer scale models in risk assessment studies. First, more and more epidemiological studies now provide dose-response functions based on fine-scale air pollution modeling (e.g., Raaschou-Nielsen et al., 2013; Pedersen et al., 2013). Second, it is generally assumed that the reliance on background air quality monitoring stations in etiological studies will mainly lead to Berkson-type error. Berkson-type error is not expected to bias strongly dose-response function, meaning that dose-response functions derived from station-based studies are in theory close to those observed with models entailing less exposure misclassification (Thomas et al., 1993). Consequently, there is no reason to combine an unbiased dose-response function to an estimate of the distribution of air pollution levels that tends to underestimate exposure. Even if dose-response functions from studies relying on background monitoring stations were biased, it is unclear that using also monitoring stations to estimate exposures in risk assessment studies would limit the impact of the bias in the dose-response on the attributable risk.

In France and in other countries, the monitoring stations used in such studies are background monitoring stations. As documented in our study, in a typical urban area setting, such stations tend to underestimate population exposure to outdoor air pollution levels, and hence the risk attributable to atmospheric pollution. In Grenoble, the mean exposure level was underestimated by 3.3% while in the larger Lyon area, the average of background monitoring stations entailed an estimate 8.1% lower than the density-weighted average provided by our approach. This resulted in an underestimation of the attributable risk by 8–20% according to area and outcome. The amplitude and even possibly the direction of this bias may differ in other cities and countries, depending on the principle guiding the location of stations and their selection for the study (e.g., on whether or not traffic stations are used).

In our analysis relying on a dispersion model coupled to data on population density (H1), we quantified the impact of the absence of information on the population distribution by estimating the attributable risk with the sole dispersion model (H2). Under this hypothesis, attributable risk varied from –1.5% to 5.6%, depending on the health event and urban area. The absence of information for both the population distribution (population density) and spatial contrasts in the exposure model was quantified (H3), and our results showed that the health impact was underestimated by 7.5–9.4% depending on the health event and urban area, compared to our fine-scale approach. All in all, this suggests that it is safer to simultaneously take fine-scale variations in air pollution and in population density into account, and not only either one.

4.4. Air pollution and social deprivation in urban areas

Different patterns have been reported between and within Europe and the USA in terms of associations between air pollution exposure and social deprivation. In many American areas, the more deprived population was exposed to higher concentrations of air pollutants (Padilla et al., 2014). The literature in Europe is less abundant and results show heterogeneity. In a review, Deguen and Zmirou-Navier (2010) concluded that the direction and amplitude of the association varied according to the area. As an illustration, two studies conducted in the Netherlands and the

United Kingdom found higher exposures to air pollution for the most deprived populations (Kruize et al., 2007; Namdeo and Stringer, 2008) while a study in Strasbourg reported highest exposure for the middle compared to the lowest and highest social classes (Havard et al., 2009). Our findings in Lyon urban area were similar to those from Padilla et al. (2014) in the same city, who compared yearly averages of ambient NO₂ concentrations between 3 quintiles of social deprivation. The authors also used Sirane dispersion model for exposure assessment, while social deprivation was estimated with another method based on principal component analyses resulting in nine socio-economic characteristics, some of which being close or identical to those considered in the deprivation index we used (i.e. rates of unemployment, single-parent households), and also available at the neighborhood level. PM_{2.5} levels were highest in the neighborhoods with intermediate to high social deprivation (6th to 8th deciles of the EDI) while in Grenoble area exposure was higher for neighborhoods with a deprivation above the area median. To our knowledge, no previous study had described associations between social deprivation and air pollution in Grenoble area. The amplitude of the spatial variations in PM_{2.5} levels were relatively modest within each urban area (the 95th percentile of exposure was 1.6 µg/m³ higher than the 5th percentile, an increase by 9% in Grenoble, and 2.8 µg/m³ higher in Lyon, a 15% increase), which is typical of fine particulate matter, a pollutant which often has more limited spatial variations at the urban level than other pollutants such as NO₂. This limited spatial variability of PM_{2.5} concentrations puts an upper bound to contrasts in air pollution levels associated with neighborhood-level deprivation. Moreover, our study only took into account the between-neighborhood contrasts in PM_{2.5} levels; other differences exist between subjects with contrasted deprivation level, such as behavioral or environmental exposure to other factors influencing the occurrence of the health outcomes we considered (e.g., smoking prevalence, which is in France twice as high among unemployed citizens, compared to white collars; INPES (Guignard et al., 2010)). The effect of these differences is to some extent taken care of in our estimate related to lung cancer, which is based on lung cancer incidence data at the neighborhood scale, but not in our estimates of mortality and low birth weight incidence, which are based on cases aggregated at the municipality scale.

All in all, these studies suggest that there is no universal pattern in the association between air pollution exposure and social deprivation, and that associations differ even within a single region. In the two cities, still, it appeared that air pollution exposure was more strongly an issue of middle-class and lower-class neighborhoods, compared to upper-class (least deprived) neighborhoods.

4.5. Conclusion

Our estimates correspond to the long term effects of atmospheric pollutants, although for term low birth weight the window of sensitivity is likely to correspond to pregnancy. Consequently, should a decrease in PM_{2.5} concentration down to the WHO guideline of 10 µg/m³ be achieved quickly, most of the beneficial attributable risk on low birth weight occurrence, and a minor part of that on mortality, are expected to occur on the mid-term, during the following year. Our uncertainty estimates may be too optimistic in the case of term low birth weight, for which there is heterogeneity between studies in dose-response functions, with the existence of a meta-analysis reporting weaker associations than in the European study we relied on.

Risk assessment studies relying on background monitoring stations tend to underestimate the health burden of particulate matter air pollution. Use of exposure models with a fine, street

level spatial resolution coupled with knowledge of the population density at the same scale, is a feasible and relevant approach.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.envres.2016.01.030>.

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