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Air pollution, health and social deprivation in an urban setting

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THÈSE

Pour obtenir le grade de

DOCTEUR DE LA COMMUNAUTÉ UNIVERSITÉ GRENOBLE ALPES

Spécialité : **Modèles, méthodes et algorithmes en biologie,
santé et environnement**

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Présentée par

Xavier MORELLI

Thèse dirigée par **Rémy Slama**

préparée au sein de l'Unité mixte Inserm–Univ. Grenoble Alpes,
U823, Institut Albert Bonniot

Dans l'École Doctorale

« **Ingénierie pour la Santé, la Cognition et l'Environnement** »

Pollution de l'air, santé et défaveur sociale en zone urbaine

Air pollution, health and social deprivation in an urban setting

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Publications and communications

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Oral communication

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Poster

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General introduction

1. Health in urban areas

Nowadays, 75% of the European population lives in an urban area. In urban areas, maintaining a sustainable environment is a major challenge for public health (WHO, 1997). Air pollution and noise represent two human-related sources of mortality and morbidity with generally higher exposure levels and hence corresponding to a higher disease burden in urban than in rural area (WHO, 2011, 2013). One possibly notable exception is ozone, whose effects may be higher (for a given concentration increase) in rural rather than urban areas (Madrigano et al., 2015).

Other environmental factors may impact health, and go along with the urban sprawl (Frumkin, 2002). In city centers, more heat is generated by the concentrated human activity, due to the absence of vegetation and trees (less shade and less cooling through the evapotranspiration phenomenon) and the concentration in dark surfaces absorbing and radiating heat (roadways, rooftops). This results in a “heat island” effect which has consequences on health ranging from benign disorders to an increased mortality (Kovats et Hajat, 2008; Tan et al., 2010). Moreover, access to water in both quality and quantity represents an essential basic need (WHO, 2004). Water quality may also be an issue in urban areas from industrialized countries (e.g., contamination by chlorination by-products, a possible cause of bladder cancer; Villanueva et al., 2007). Lack of green space may also be associated with deleterious health effects (Maas et al., 2006; Nieuwenhuijsen et al., 2014). The spread of infectious diseases is also modified in urban compared to rural areas. The health effects of these environmental nuisances may be increased by a possibly higher proportion of subjects with poor social support or sociodemographic status in urban areas.

Notwithstanding the relevance for public health of these various exposures, this thesis will focus on air pollutants, and also to a lesser extent noise exposure.

2. Air pollution and health in urban settings

Atmospheric pollution is the introduction of chemicals or biological molecules or other materials harmful to environment or health into the Earth's atmosphere. Human-related sources of air pollution can be categorized in several ways. One can distinguish mobile sources, stationary sources and agriculture. Mobile sources include road transport, namely personal and light- and heavy-duty vehicles. Stationary sources include heating (central heating, stoves) and industrial sources (thermal power stations, waste facilities). Road traffic is a source of various gaseous pollutants: suspended particles, nitrogen oxides (NO_x), sulfur dioxide (SO₂), carbon monoxide (CO), volatile organic compounds (VOCs) such as benzene, polycyclic aromatic hydrocarbons, heavy metals and others. Secondary pollutants such as ozone (O₃) are created from the reaction between these pollutants. Most of those pollutants are regulated in Europe (European Union (Official Journal), 2008).

In the modern era, the health effects of air pollution exposure have been known or questioned at least as early as in the first half of the nineteenth century (in the case of lead dust exposures in occupational settings; Lestel, 2002). Extraction of fossil fuels and construction of coal burning factories led to increasing amounts of pollutants released in the atmosphere in western Europe and particularly in industrial areas from the nineteenth Century onwards. The health effects of combustion-related air pollutants have been suspected as early as in the first half of the twentieth century. Episodes of very high air pollution events (for current European standards) occurred for example in Belgium in late 1930s, a phenomenon called "Les brouillards de la Meuse" ("*Meuse's region fogs*") which led to several dozens of premature deaths (Nemery et al., 2001). In the USA, a similar situation appeared in late 1948 in Donora, Pennsylvania, with a couple of dozens of premature deaths due to industries operating under specific weather conditions limiting the dispersion of the pollutants in the air.

Another well-described event was the 1952 London Great Smog. This five-day high air pollution event originated from specific weather conditions coupled to the use of bad quality, post-war coal for heating. Effects on health were observed on a broader time scale (up to a couple of months) after the air pollution peak (Bell and Davis, 2001). This event was one of the first in modern history to raise the authorities' awareness regarding the impact of atmospheric pollution on health. Studies showed that this pollution peak led to approximately 12,000 anticipated deaths due to respiratory tract infections (bronchopneumonia, acute purulent bronchitis in addition to chronic bronchitis) in Greater London. Currently, a large majority of the European population living in urban areas is still exposed to concentrations in air pollutants exceeding the air quality guideline values (WHO, 2013).

While the effects of air pollution exposure remain an issue in occidental countries, the health burden of air pollution poses a more and more serious threat in developing countries, such as China or India (WHO, 2002). In these large countries, the health burden of air pollution is likely to be larger because of the population size and less sophisticated heating systems, power plants and the air quality regulations in general. In late 2013, a seven-day, weather-driven episode of smog in northeastern China (Harbin, 5 million inhabitants and 8th largest city in the country) resulted in fine particulate matter concentrations of up to 1,000 $\mu\text{g}/\text{m}^3$, which is two orders of magnitude above everyday values in background areas of France or Europe.

Numerous epidemiological studies have investigated the effects of air pollution on health. These, together with toxicological studies, have allowed better characterizing the effects of some air pollutants, particularly those of particulate matter, or PM. Particulate matter are often classified as PM₁₀ –for particles with an aerodynamic diameter of less than 10 μm , PM_{2.5} –those with an aerodynamic diameter of less than 2.5 μm , or UFP –for ultrafine particles of less than 0.1 μm . Exposure to air pollution has both short- and long-term effects. Short-term effects occur a few days following the exposure, while long-term effects consist in a contribution of the

exposure to appearance of chronic diseases, some of which ultimately result in premature death. Effects are observed on mortality, cardiovascular and respiratory morbidity, cancer incidence (with a very high level of proof), and other health outcomes, with a lower level of evidence (WHO, 2013).

Exposure to particulate matter increases respiratory and cardiovascular morbidity and mortality (Pope et Dockery, 2006; Künzli et al., 2010; Peters, 2011; Lepeule et al., 2012). These effects are observed in adults but also children, both for respiratory morbidity (McIntyre et al., 2011) but also, as recently suggested, for cardiovascular morbidity (Pieters et al., 2015).

There is increasing evidence regarding the effects of air pollution on adverse pregnancy and birth outcomes (Shah et Balkhair, 2011), in particular birth weight (Dadvand et al., 2013; Pedersen et al., 2013) and preeclampsia (Pedersen et al., 2014). More recent studies also suggest an effect of PM air pollution exposure on the neurodevelopment and cognitive function (Ranft et al., 2009; Freire et al., 2010; Raz et al., 2015) and diabetes (Rückerl et al., 2011; Raaschou-Nielsen 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).

In 2012, the International Agency for Research on Cancer (IARC, Lyon, France) classified diesel engine exhaust and atmospheric pollution in general as well as particulate matter (in 2013) as carcinogenic for humans (Group 1¹; IARC, 2012; Benbrahim-Tallaa et al., 2012; IARC, 2013; Loomis et al., 2013).

¹ IARC's carcinogenicity assessment is as follows: Group 1: *recognized*, Group 2A: *probable*, Group 2B: *possible carcinogen*, Group 3: *not classifiable*, Group 4: *probably not carcinogenic to humans*. Group 1 also includes other air pollutants such as tobacco and asbestos.

3. Noise, another by-product of traffic

As for air pollution, an important part of the population in Europe is exposed to high levels of noise, which has an impact on health (Basner et al., 2014). In Europe, an estimated 54% of the urban population is thought to be exposed to levels exceeding the 55 decibel (dB) L_{DEN}^1 annual average, which constitutes a threshold above which noise exposure is considered to impact health (Babisch, 2012). Environmental noise, which is in part due to road traffic (and planes or trains in specific areas), is one of the three main sources of exposure, the others being social noise and occupational noise. Most studies of health effects focus on occupational exposures, although road traffic noise and airport noise exposures have also been considered in some studies.

In addition to the auditory consequences, namely hearing impairment, exposure to high levels of noise has effects on health, from simple annoyance, (sleep) disturbance and cognitive impairment, especially among children, to cardiovascular diseases risk factors which ultimately lead to hypertension, arteriosclerosis and possibly myocardial infarction and stroke (Sørensen et al., 2011, 2012; van Kempen et Babisch, 2012). An effect on birth outcomes has also been suggested (Gehring et al., 2014).

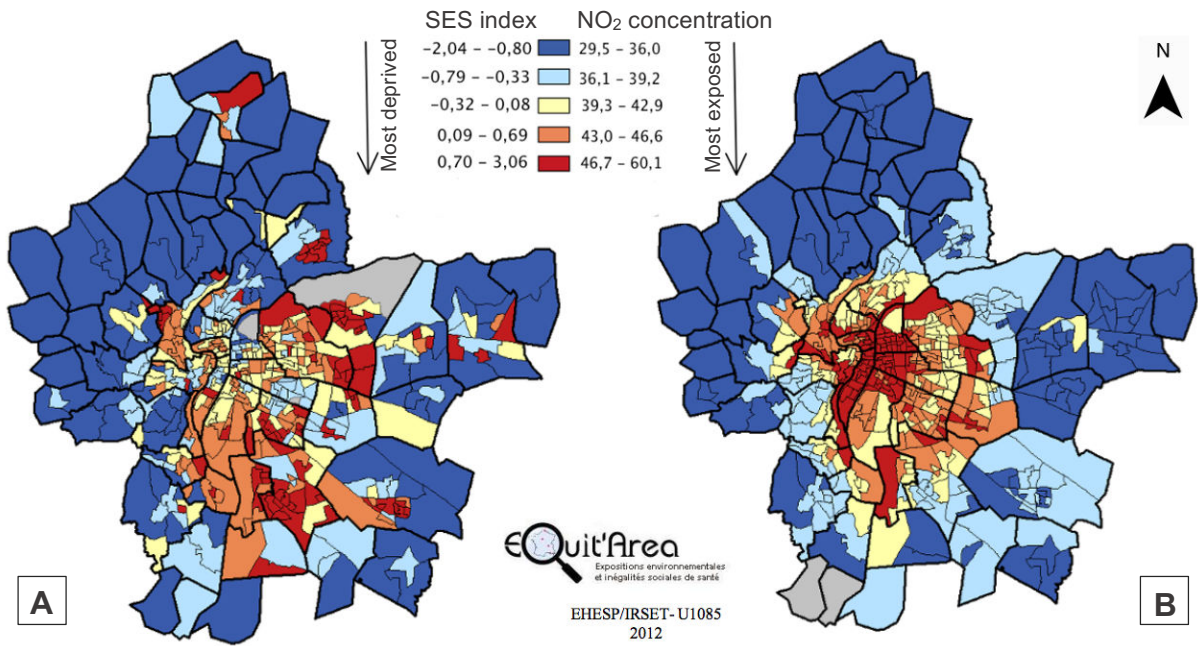
Air pollution and noise levels vary over time and space and share the same main sources (road traffic), which is likely to entail a (spatial at least) correlation between exposures (Davies et al., 2009). Since both noise and air pollutants such as PM may have similar health effects (such as effects on the cardiovascular function), confounding bias may exist, which constitutes a challenge in epidemiological studies (Foraster et al., 2014). Very few studies have attempted to simultaneously assess both exposures and to consider their health effects (Foraster et al., 2014). The amount of correlation may moreover vary between urban areas.

¹ L_{DEN} : Average level during day, evening and night, with a weighting according to the hour.

4. Social inequalities in the exposure to air pollution in urban areas

Several studies showed that exposure to air pollution differs according to the social deprivation status. The trend observed in the USA seems to be consistent, in the direction of higher exposure among the most deprived populations (Brochu et al., 2011; Hajat et al., 2015). Studies conducted in Europe found different patterns of air pollution exposure according to the city, with the more exposed corresponding alternately to the most deprived (Kruize et al., 2007; Namdeo et Stringer, 2008), to the intermediately deprived (Havard et al., 2009), or sometimes to the least deprived populations (Forastiere et al., 2007). The few studies conducted in France also found different patterns at the country level –depending on the city– in the distribution of the exposure to air pollution according to social deprivation (Havard et al., 2009; Deguen et Zmirou-Navier, 2010; Padilla et al., 2014). For example, Padilla et al. (2014) found that in Lille and Marseille, the most deprived were the most exposed to nitrogen dioxide (NO₂), while in Lyon the neighborhoods with an intermediate socio-economic status were the most exposed (Figure 1); in Paris, the least deprived were exposed to the highest concentrations in air pollution.

Figure 1: Spatial distribution of a socio-economic index (SES, A) and of concentrations in nitrogen dioxide (NO₂, B) at the neighborhood (IRIS) scale in Lyon urban area (NO₂ data 2002–2009, socio-economic data 1999 and 2006 census; Equit'Area project).

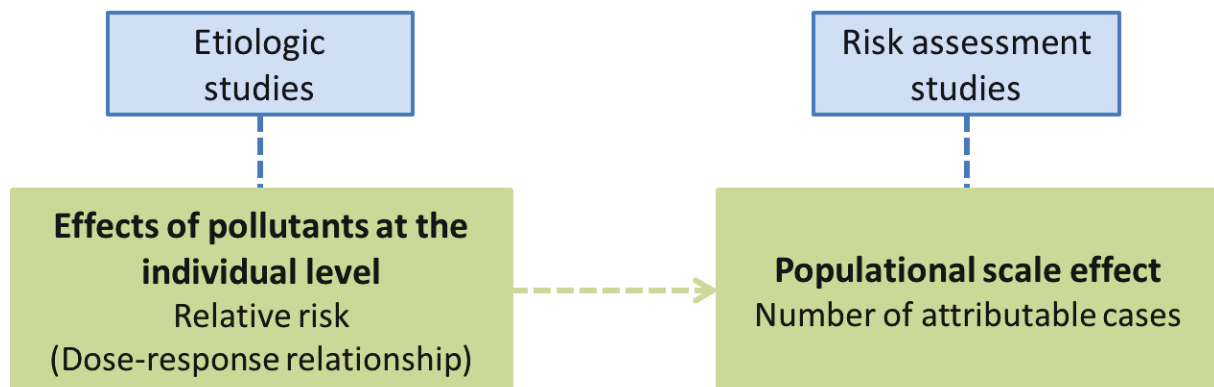


5. Evaluation of the impact of air pollution and of measures to reduce air pollution

Etiologic epidemiological studies typically highlight exposure–risk relationships for an individual exposure. Such studies do not constitute an integrated tool allowing the translation of the population exposure in an urban area into an estimate of the public health burden. This can be done through *risk assessment* studies. Such studies require, among other things, knowledge of the distribution of the exposure, which opens the possibility to quantify the impact of air pollution in urban areas.

The concept of Risk Assessment¹ was proposed by the US National Research Council in 1983 (NRC, 1983). This approach consists in four steps: 1. Identification of the danger; 2. Choice of the Exposure–Risk Function (ERF); 3. Estimation of the exposure and 4. Risk characterization (Figure 2).

Figure 2: Etiologic versus risk assessment studies.



In France, a derived methodology inspired from a 2001 World Health Organization (WHO) guide for health impact assessment (HIA) was established by the Institute for Public Health

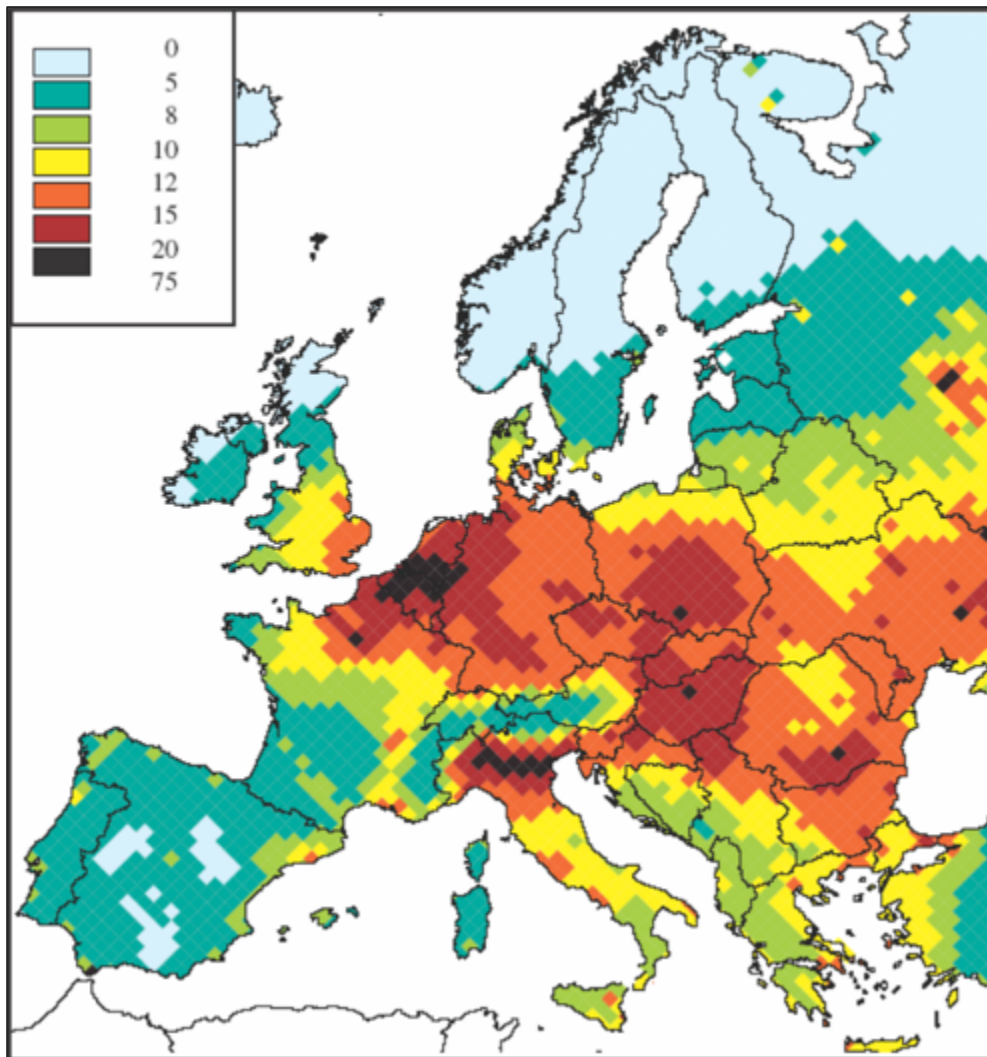
¹ In France, national authorities instigated routinely conducted risk assessment studies of air pollution in urban areas. The French Institute for Public Health Surveillance (InVS, now *Santé Publique France*) adapted this approach into *Health Impact Assessment studies*, or "Etudes d'impact sanitaire".

Surveillance (*Institut de Veille Sanitaire*, InVS, now *Santé Publique France*) in order to quantify the impact of air pollution on the population living in urban areas (INVS, 2013). This method corresponds to the counterfactual HIAs, where the health burden is calculated based on a comparison with a hypothetical situation where the exposure would be lower, typically reduced to an air quality guideline value¹. Projects like Apheis or Aphekom were conducted based on this approach, which assumes that the population exposure to air pollution corresponds to the average outdoor levels recorded by one or several air quality monitoring stations (AQMS) distributed across the study area.

Health impact assessment has a major role to characterize the impact of an exposure with a proven adverse health effect at the population scale. HIA studies occur downstream of the etiologic studies and translate an individual effect of air pollution, in term of relative risk (or odds-ratio), into a population-scale effect, expressed as a number of disease cases attributable to the exposure. Such estimates are meaningful for decision making in the field of public health, and also facilitate communication of the public health burden in the media. In Europe, examples of such studies include a trinational evaluation in France, Austria and Switzerland, based on figures from 1996 (Künzli et al., 2000); the Clean Air For Europe (CAFE) project, which reported 42,000 premature deaths per year in France (based on data available for year 2000; Figure 3); the Aphekom project, which reported losses of life expectancy due to air pollution in the 3.6–7.5 months range depending on the city in France (based on 2004-2006 data); the Environmental Burden of Disease in Europe (EBoDE) project, which reported for six European countries a yearly average of disability-adjusted life years (DALYs, or “healthy” life years lost) due to fine particulate matter in the 4,500–10,000 range per million people, depending on the country (Hänninen et al., 2014; Lim et al., 2012).

¹ For PM_{2.5} (yearly average), the WHO air quality guideline is 10 µg/m³, the European regulatory limit is 25 µg/m³, and the US regulatory limit is 12 µg/m³ (1997-2012 US limit value: 15 µg/m³).

Figure 3: Average of the PM_{2.5} concentrations modeled for the CAFE project (Clean Air For Europe, 4-year average for 1997, 1999, 2000, 2003; concentrations in µg/m³).



Many other similar assessments have been conducted elsewhere in Europe, for example in 19 cities (Medina et al., 2004), in London (Tonne et al., 2008), Stockholm (Johansson et al., 2009), Tallinn (Ortu et al., 2009), Rome (Cesaroni et al., 2012) or elsewhere in Italy (Baccini et al., 2011; Fattore et al., 2011), Barcelona (Rojas-Rueda et al., 2011, 2012, 2013), Munich (Fensterer et al., 2014). Studies in French cities have been conducted by public health agencies, including in Lyon (CIRE, 2006a) and Grenoble (CIRE, 2006b); the study in Lyon concluded that 212 all-cause deaths were attributable to short term exposure to NO₂ (annual average based

on 2001-2002 data), while the study in Grenoble concluded that 155 all-cause deaths were attributable to long term exposure to PM₁₀ (annual average based on 1999-2000 data).

These risk assessment studies can not only be used to document the current health impact of a pollutant, but could also be used to document the expected efficiency of future urban scenarios in terms of reduction of the health impact, thus pushing the evaluation of the health impact beyond the sole comparison to a reference level based on a regulation, like the WHO guideline value or a national limit value. To our knowledge, five risk assessment studies (including one Mexican study) have been conducted considering such hypothetical future scenarios of reduction of air pollution levels, most of these consisting in a compliance with air pollutants' limit values (Ballester et al., 2008; Pérez et al., 2009; Boldo et al., 2011; Rojas-Rueda et al., 2012; Riojas-Rodriguez et al., 2014). In addition, a study in Italy by Baccini et al. (2011) also evaluated a decrease in PM₁₀ levels, but focused on short-term health events.

6. Methodological challenges in the assessment of exposure to air pollution

The accurate characterization of the effect of air pollution on health relies centrally on the quality of the exposure assessment. Exposure misclassification can strongly impact statistical power of epidemiological studies, bias dose-response functions and hence also health impact estimates (de Klerk et al., 1989; Nieuwenhuijsen, 2015). Among the gaseous air pollutants, modeling ultrafine particles (also known as nanoparticles, or PM_{0.1}) appears as a challenge. The latter are not regulated yet. Because of a large surface/mass ratio, this class of particles is suspected to have a more deleterious health impact than larger particles (Geiser et al., 2005).

In France, concentrations in pollutants are routinely monitored by the Air Quality Surveillance stations network (*Associations Agréées de Surveillance de la Qualité de l'Air*, AASQA). For health impact assessment, reliance on such data entails exposure misclassification because of

the limited spatial resolution of this network. For example, concentrations in fine particulate matter (PM_{2.5}) are routinely monitored in Grenoble and Lyon by one and three background stations, respectively, while the areas to cover are 250 and 500 km², respectively.

Advances in computing power and modeling techniques opened new perspectives regarding the assessment of air pollution exposure in urban areas with strong spatial contrasts in exposures (Brauer et al., 2003; Nieuwenhuijsen et al., 2006; Sellier et al., 2014). As an illustration, the Air Rhône-Alpes AASQA has developed fine-scale dispersion modeling of air pollution in the major urban areas of the region, including Grenoble and Lyon urban areas. The atmospheric dispersion model, called Sirane (Soulhac et al., 2011), provides a 10-meter grid of population density and yearly averages of the concentrations in nitrogen dioxide (NO₂), ozone (O₃) and particulate matter (PM₁₀, PM_{2.5}). This thesis focuses on particulate matter, more specifically the ultrafine particles (UFP) and PM_{2.5}. To our knowledge, most risk assessment studies conducted at the urban area scale relied on air quality monitoring stations (Künzli et al., 2000; Medina et al., 2004; Fattore et al., 2011; Fensterer et al., 2014), with few exceptions (Tonne et al., 2008; Johansson et al., 2009; Orru et al., 2009; Rojas-Rueda et al., 2012, 2013). Since the monitoring stations considered in risk assessment studies are usually background monitoring stations, the distribution of the estimated exposure levels is expected to differ from those from dispersion models (Perez et al., 2013). Research needs to be done to assess the magnitude of the misclassification bias by comparing health impact estimates obtained with monitoring stations data to those achieved by the use of a fine-scale dispersion model. Alternatives to dispersion models exist, in particular personal dosimeters (Nieuwenhuijsen et al., 2014) and land use regression (LUR) models (Brauer et al., 2003). LUR models take advantage of geographic information systems (GIS) data, which often are readily available, and concentrations measurements based on a small to moderate number of monitoring sites, making it possible to estimate individual exposures for large study populations. Such models have been developed

for pollutants such as nitrogen dioxide, PM₁₀, PM_{2.5}, PM_{2.5} absorbance (e.g. in the context of EU projects such as TRAPCA or ESCAPE; Eeftens et al., 2012). The ability of LUR models to describe the spatial variability in the above-mentioned pollutants appears satisfactory, with cross-validation R² often in the 0.6-0.8 range –although attention has been drawn upon the *optimism* of R² and cross-validation R² statistics in the context of studies relying upon a limited number of measurement sites (Basagana et al., 2012). For other pollutants such as ultrafine (nano-)particles, LUR models are currently much more rare (Hoek et al., 2011). The ability to develop such models will depend upon the possibility to estimate the yearly average in one site based on a limited number of shorter-term measurements. To our knowledge, this issue has been poorly documented, in particular for very short-term measurements of UFP (Rückerl et al., 2011). Documenting this temporal variability is also of interest for noise measurements, as a satisfying stability would pave the way for the development of a LUR-type approach for traffic-related noise.

7. General aims of the thesis

There were three general aims in this thesis:

- 1) To describe the correlations between short-term measurements of noise, ultrafine particles concentrations, traffic counts, and to assess the temporal variability of these measures for modeling purposes.
- 2) To perform a risk assessment study quantifying the health impact of air pollution on the health of the citizens in the Grenoble and Lyon urban areas with a fine-scale modeling approach; in addition, to discuss the impact of the spatial resolution of exposure models on the estimates of risk assessment studies, and investigate the potential socio-economic disparities in exposure to air pollution and its associated health burden.
- 3) To study the effects of hypothetical scenarios of reduction of fine particulate matter on the population exposure, and to translate these changes in air pollution levels into health benefits.

The thesis is organized into three chapters, corresponding to each general aim:

Chapter I: Short-term associations between traffic-related noise, particle number and traffic flow in three European cities;

Chapter II: Air pollution, health and social deprivation: a fine-scale health risk assessment based on the current situation;

Chapter III: Estimating the health benefits of hypothetical scenarios on the health of the population in urban areas.

Chapter I: Short-term associations between traffic-related noise, particle number and traffic flow in three European cities

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Résumé du Chapitre I

En Europe, plus de 75% de la population vit en zone urbaine, dont le trafic routier génère pollution atmosphérique et bruit. Plus de 80% des européens habitant dans les zones urbaines sont exposés à des niveaux de particules en suspension dépassant les valeurs guides de l'Organisation Mondiale de la Santé (OMS, ou *WHO*). Par ailleurs, environ 54% des européens vivant en zone urbaine seraient exposés à des niveaux moyens de bruit annuel dépassant les 55 dB (niveau moyen durant la journée, le soir et la nuit avec une pondération selon l'heure ; L_{DEN}), seuil au-delà duquel l'exposition prolongée tend à entraîner des effets délétères sur la santé (Babisch, 2012). De nombreuses études ont mis en évidence les effets de la pollution atmosphérique sur la santé humaine, à court comme à long terme (WHO, 2013). La littérature scientifique sur les effets de l'exposition au bruit extérieur est moins abondante, mais suggère très fortement l'existence d'une relation causale entre exposition au bruit et effets sur la santé (Basner et al., 2013).

En épidémiologie, la pollution atmosphérique (issue du trafic) et le bruit routier représentent l'un pour l'autre un facteur de confusion potentiel : l'étude de l'association entre bruit et santé pourrait être biaisé par le rôle de la pollution de l'air, et vice-versa. De nouvelles études sont nécessaires pour distinguer les rôles respectifs de ces deux expositions environnementales sur la santé (Foraster et al., 2013 ; Tétreault et al., 2013). Un certain nombre d'études ont évalué la corrélation à long terme entre bruit routier et particules en suspension ; cependant, peu de données existent quant à leur corrélation à court terme, malgré les probables effets sur la santé des expositions à court terme (Huang et al., 2013).

L'objectif de ce chapitre était de décrire la corrélation entre des mesures à court terme de bruit, de concentrations en particules ultrafines ($\leq 0,1 \mu m$) et de flux de trafic en zone urbaine. Un second objectif était d'investiguer la variabilité temporelle de ces mesures.

Nous avons effectué des mesures simultanées de bruit routier, de concentrations en particules ultrafines et de flux routiers motorisés sur des durées de 20 min et à 141 sites de mesure. Ces mesures ont été répétées de une à trois fois, et ce dans trois villes européennes de taille moyenne (Bâle, Gérone, Grenoble ; respectivement 193 000, 96 700 et 156 000 habitants). Le niveau de répétabilité des mesures était estimé par des coefficients de corrélation intra-classes (ICC), basés sur les modèles à effets aléatoires (McGraw et Wong, 1996). La corrélation entre les mesures simultanées était estimée à l'aide de nuages de points et de coefficients de corrélation de Pearson. En outre, certaines caractéristiques étaient recueillies pour chaque site,

telles sa typologie (fond urbain ou en proximité du trafic), la largeur de la rue, la distance à la route principale la plus proche, ainsi que d'autres caractéristiques géographiques selon différentes tailles de buffer (ou périmètres de cercles concentriques) telles que la longueur cumulée de routes principales au sein du buffer ou bien leur charge de trafic (en Trafic Moyen Journalier Annuel, TMJA).

Pour chacun des trois marqueurs d'exposition environnementale, les mesures rapportaient des niveaux plus élevés dans les sites à proximité du trafic. Les concentrations en UFP ne variaient pas selon d'autres caractéristiques, tandis que les mesures de bruit et de flux de trafic tendaient à varier selon la largeur de la route la plus proche et la distance à la route principale. Les mesures à court terme de bruit routier (coefficient de corrélation intra-classe quantifiant l'accord entre des mesures consécutives, $r = 0,86-0,97$ selon la ville) et de flux de trafic ($r = 0,93-0,94$) étaient stables au cours du temps, ce qui n'était pas le cas des particules ultrafines ($r = -0,11$ à $0,14$). Les corrélations de Pearson entre les mesures simultanées de 20 min de particules ultrafines et de bruit routier étaient dans l'intervalle $0,43-0,55$ selon la ville ; les corrélations entre le bruit et les flux de trafic variaient de $0,54$ à $0,72$; enfin, les corrélations entre les particules ultrafines et les flux de véhicules étaient plus faibles, variant de $0,15$ à $0,37$ selon la ville.

A notre connaissance, cette étude est la première à décrire les corrélations entre des mesures simultanées de trois marqueurs d'exposition environnementale. Les mesures de 20 min de bruit routier et de trafic, mais pas de particules ultrafines, étaient relativement stables à des intervalles de temps variant de quelques jours à plusieurs mois, dans trois villes européennes de taille moyenne. Dans ces villes, sur le court terme, le bruit et les particules ultrafines ont mis en évidence des corrélations modérées, ce qui pourrait permettre à de futures études épidémiologiques de démêler leurs potentiels effets conjoints à court terme sur la santé humaine. Pour le bruit et les flux routiers, la corrélation temporelle très importante confirme la validité de mesures à court terme pour caractériser des expositions sur le long terme. A l'inverse, pour les particules ultrafines, les importantes variations temporelles indiquent que les marqueurs d'émissions issues du trafic nécessitent des mesures sur de plus longues périodes (et probablement répétées au fil du temps pour prendre en compte les variations saisonnières) afin de produire des estimations fiables.

Abstract

Outdoor noise and particulate matter concentration share common sources, including road traffic in urban areas, raising the potential for mutual confounding in epidemiological studies of their health effects. While some studies evaluated their long-term correlation, little is known about their short-term correlation.

Our aim was to study the correlation of short-term noise, ultrafine ($<0.1\mu\text{m}$) particulate matter number concentration (UFP), and traffic flow in urban areas. A secondary aim was to document the temporal variability of these short-term measurements.

We simultaneously measured traffic noise levels, UFP concentrations as well as motor vehicles' flows for 20 minutes in 141 locations, on one to three occasions, in three middle size European cities (Basel, Girona, Grenoble).

The reproducibility of the short-term noise measurements and traffic counts over time was high, as reported by the intraclass correlation coefficient (ICC), which quantified the agreement between repeated measurements (ICC = 0.86-0.97, according to city, for noise and ICC = 0.93-0.94 for traffic counts); this was not the case for UFP number concentrations (ICC = -0.11 to 0.14). The Pearson correlations of simultaneous 20-min measurements of UFP number concentrations and noise levels were in the 0.43-0.55 range, depending on the city; correlations between noise levels and vehicle counts varied from 0.54 to 0.72; and correlations between UFP concentrations and vehicle counts were lower ($r = 0.15$ -0.37 depending on the city).

Measurements during as little time as 20 min of outdoor noise and traffic, but not of UFP, were strongly reproducible over durations of a couple of days or months in middle-size European cities. In these areas, on the short-term, noise levels and UFP concentrations exhibited relatively moderate correlations, which may allow adjustment for mutual confounding in epidemiological studies, thus allowing to disentangle their possible short-term health effects.

Keywords

Air pollution; spatiotemporal variation; traffic; traffic noise; ultrafine particles.

1. Introduction

A large body of evidence indicates that atmospheric pollutants impact human health, in particular cardiovascular, respiratory functions, and possibly reproductive and neurological diseases (World Health Organization, 2013). For some of these diseases, such as those related to the cardiovascular system, the specific role of traffic-related air pollution has been emphasized (Peters et al., 2004). Road traffic generates atmospheric pollutants such as ultrafine particles (typically in the 10-500 nm diameter range) and a large number of gaseous pollutants. In addition, traffic is a source of noise. Noise may also impact health, particularly cardiovascular health (Tétreault et al., 2013; Kempen et Babisch, 2012; Babisch, 2011; Basner et al., 2013) and possibly birth outcomes (Gehring et al, 2014).

In epidemiological terms, noise thus constitutes a potential confounder in the study of the association between atmospheric pollutants and health. Reciprocally, traffic-related air pollution constitutes a potential confounder in the association between noise and specific health factors. Clear identification of the respective role of these two stressors has not been accomplished (Foraster et al., 2013; Tétreault et al., 2013).

The correlation between traffic-related air pollution and noise levels has been previously considered (Allen et al., 2009; Can et al., 2011; Davies et al., 2009; Foraster et al., 2011; Sorensen et al., 2011). However, to our knowledge most research has focused on long-term averages, in an attempt to understand their mutual confounding effect in chronic diseases (Tétreault et al., 2013). In Girona, Spain, Foraster et al. reported a correlation of 0.62 between yearly averages of nitrogen dioxide (NO₂) levels based on measurements and modelled yearly averages of traffic noise levels. To our knowledge, the spatial association between noise and particulate matter levels (an atmospheric pollutant for which clear associations with cardiovascular health have been reported ; Brook et al., 2010) has so far been studied only once (Allen et al., 2009). The short-term correlations of noise and particulate matter have received

even less consideration. This study is of importance because air pollution and noise may also have short-term effects (Huang et al., 2013). To understand these associations, concurrent measurements of noise and air pollution as well as traffic density are needed. Comparisons of the associations between road traffic density and either noise or air pollution levels are also of interest, as road traffic is a major determinant of air pollution and noise in urban settings.

Thus, our aims were to describe the correlations between 20-min simultaneous measurements of noise, ultrafine particle number concentrations, and traffic flows, as well as the temporal variability of these measurements. We also investigated the potential determinants of ultrafine particle number concentrations and noise levels in each city.

2. Materials and Methods

2.1 Study areas

This work was part of the Tri-Tabs project (Tri-national project on traffic, air, noise and health), which involves the participation of three European centers: Basel (Switzerland; 193,000 inhabitants in the city in 2011 and 850,000 in the urban area), Girona (Spain; 96,700 and 336,000 inhabitants, respectively) and Grenoble (France; 156,000 and 670,000 inhabitants, respectively). For each city, at least 40 sites were carefully selected to capture the contrast of the road traffic noise and ultrafine particle number (UFP) concentrations, e.g. sites that are directly affected by road traffic flow; sites representing an urban background and a few sites in parks and gardens to represent regional background. Moreover, additional sites were chosen in the city-centre as well, with different predispositions to air pollution levels, traffic noise, and road traffic flows. We selected 60 sites in Basel, 40 sites in Girona and 41 sites in Grenoble. For each city, the number of measurements sites was similar to what is commonly used in the land-use regression (LUR) literature to characterize fine particulate matter or nitrogen dioxide levels even in larger cities (Eeftens et al. 2012). The choice of sites' locations was based on a deterministic approach, in order to cover the range of traffic, noise and air pollution levels in the urban area and have a homogeneous urban cover and avoid the proximity to sources of disturbance regarding the three exposure markers. To maximize comparability across measurements at the several sites, all measurements were done in non-rush hours. Up to 8 sites were measured each day. For a given site, each repeated measurement was done in a second campaign (Girona, Grenoble) or a third one (Basel). When weather conditions or construction work did not allow the measurement, this one was relocated to another day.

All locations were geocoded. Depending on the city, we conducted two (Grenoble, Girona) or three (Basel) repeated measurements in different campaigns, either at all sites (Basel) or at a sub-set of sites. For the second measurement campaign, 25 sites were selected in Girona and 26

in Grenoble. The measurements in Basel were taken at three different seasons, while measurements in Girona and Grenoble were repeated within close time intervals (see [Table 2](#) for the exact dates of the measurements campaign).

2.2 Noise, particulate matter and traffic measurements

The three variables of interest were UFP concentrations, traffic-related noise and road traffic flow. They were measured simultaneously at a given site, for a total duration of 20 min during non-rush hours (defined separately for the three cities) and during weekdays only. Ultrafine air pollution levels were assessed by measuring total UFP concentrations with a minidisc portable particle counter (FHNW, Windisch, Switzerland) in Basel and a Ptrak device (TSI, Shoreview, MN, USA) in Girona and Grenoble, which were deployed on a tripod at 1.5 m height.

Equivalent continuous levels of noise (LAeq averages, in dB(A)) were measured. The sound level meter used in Girona and Grenoble was CESVA SC30, while the one used for Basel was Pulsar 30, both being of the highest resolution (IEC class 1). The devices were deployed on a tripod at a 1.5 m height, separated from noise reflection surfaces from at least 1.5 m, and directed to the traffic. The devices were calibrated with each daily round of measurements. Measurements were corrected from peak values due to exogenous factors occurring during the monitoring, such as people talking close to the monitoring station.

Total traffic flow was counted by the study technician, summing automobile, heavy vehicles and motorcycles counts.

Some sites characteristics were retrieved from Geographic Information Systems; this included the width of the street (in meters), the distance to the closest main street (in meters), its annual average daily traffic (AADT), and street density (meters of roads in a 50-m radius around the measurement site). The other characteristics were collected during fieldwork, namely the site type (*Traffic* or *Background*) and the tramway lines proximity (tramway line presence –yes/no–

in a 50-m radius; in Basel and Grenoble only). The site type classification was based on pre-defined criteria related to distance to major roads, street density, building density and population density. Traffic sites were overrepresented as we anticipated more variation in air pollution and noise between them than between urban or regional background sites.

2.3 Data analysis

We computed scatter plots and Intraclass Correlation Coefficients (ICC) to assess the reproducibility of the measurements from one campaign to another. The ICC, a measure of reproducibility between repeated measurements, was calculated based on random effects models (McGraw and Wong 1996). Let Y_{ic} be the measurement taken in site i in campaign c .

We fitted the mixed effects model

$$Y_{ic} = \alpha + u_i + \varepsilon_{ic}$$

where $u_i \sim N(0, \sigma_u^2)$ and $\varepsilon_{ic} \sim N(0, \sigma_\varepsilon^2)$, and estimated the ICC as the correlation between two measurements in the same site at two different campaigns (Snijders et Bosker, 1999):

$$ICC = Cor(Y_{ic}, Y_{ic'}) = \frac{\hat{\sigma}_u^2}{\hat{\sigma}_u^2 + \hat{\sigma}_\varepsilon^2}$$

The variance components $\hat{\sigma}_u^2$ and $\hat{\sigma}_\varepsilon^2$ were estimated by restricted maximum likelihood. An ICC value of 1 indicates perfect agreement between all measurements in the same site. The correlation of simultaneous measurements of ultrafine particles, noise and traffic flow was assessed with scatter plots and Pearson's coefficients of correlation. Measurement sites were classified as being either Traffic or Background. The continuous characteristics of the measurement sites were dichotomized using the median as a cut-off, and the measurements were compared. The influence of these binary sites' characteristics on UFP concentrations, noise levels and traffic counts was assessed using Student's mean comparison test. This allowed

to investigate the role of some factors in possible correlation differences observed across cities.
Statistical analyses were performed using Stata 12 (Stata Corp., College Station, TX, USA).

3. Results

3.1 Measurement campaigns

Maps of the three areas are shown in [Figure 1](#). The sites characteristics are displayed in [Table 1](#). The proportion of traffic sites was 70% in Basel, 50% in Girona and 78% in Grenoble. There were more sites with a tramway line nearby in Basel than in Grenoble. Measurement sites in Grenoble were closer to main streets, while street density within a 50-m buffer was higher in Girona.

Summary statistics of the measurements grouped by city and campaign are presented in [Table 2](#). Median 20-min UFP concentrations during the first campaign were lower in Basel and Girona than in Grenoble: 14,800 particles/cm³ in Basel (Interquartile range, IQR: 9,180 to 19,600 particles/cm³), 13,700 particles/cm³ in Girona (IQR: 8,970 to 18,000 particles/cm³), and 17,000 particles/cm³ in Grenoble (IQR: 12,400 to 22,100 particles/cm³); medians of the traffic noise levels were 62 dB(A) in Basel (IQR: 55 to 66 dB(A)), 64 dB(A) in Girona (IQR: 60 to 68 dB(A)) and 67 dB(A) in Grenoble (IQR: 62 to 69 dB(A)). Median 20-min vehicle counts (including automobiles, heavy duty vehicles and motorcycles) were 30 vehicles in Basel (IQR: 9 to 102 vehicles), 54 vehicles in Girona (IQR: 17 to 262 vehicles) and 154 vehicles in Grenoble (IQR: 118 to 302 vehicles).

Figure 1: Maps of western Europe (A) and of the measurement sites locations in Basel (B), Girona (C) and Grenoble (D).

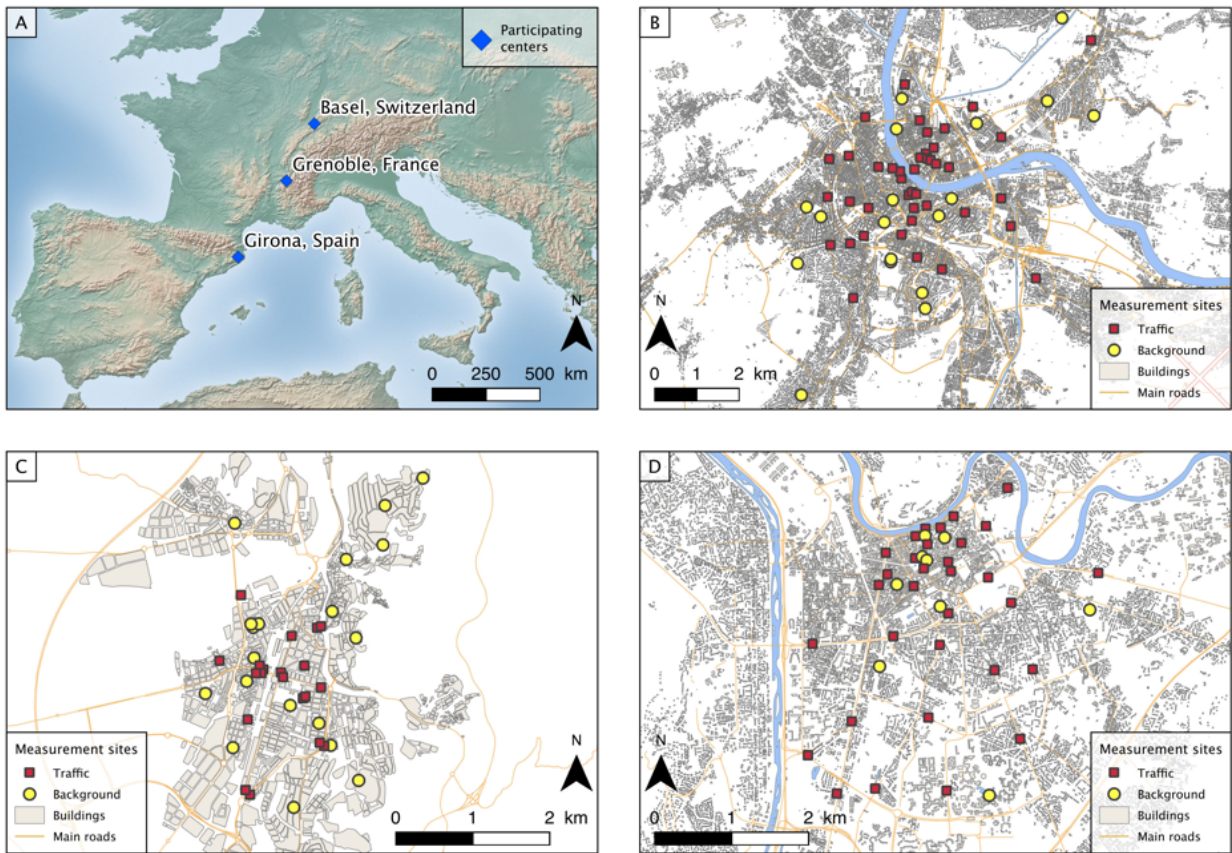


Table 1: Description of the measurement sites' characteristics.

Site characteristics	Basel			Girona			Grenoble			Overall		
	N (%)	Mean (SD)	p25-50-75	N (%)	Mean (SD)	p25-50-75	N (%)	Mean (SD)	p25-50-75	N (%)	Mean (SD)	p25-50-75
Nearest street width (m)	60 (100)	14 (5.4)	10 - 13 - 16	37 (93)	10 (5.8)	6.4 - 7.9 - 12	41 (100)	24 (18)	20 - 20 - 22	138 (98)	16 (12)	8.2 - 13 - 20
Main street distance (m)	60 (100)	56 (72)	5.5 - 22 - 83	40 (100)	161 (179)	36 - 119 - 205	41 (100)	21 (32)	3.9 - 11 - 21	141 (100)	77 (126)	6.2 - 22 - 98
Traffic at main street ^a	54 (90)	6.0 (6.4)	1.30 - 5.0 - 8.2	40 (100)	13.2 (8.6)	8.8 - 10.1 - 19.1	41 (100)	13.2 (9.7)	3.0 - 11.5 - 19.7	135 (96)	10.3 (8.9)	2.4 - 8.4 - 16.0
Street density ^b	60 (100)	71 (63)	0 - 94 - 100	40 (100)	229 (67)	175 - 224 - 272	41 (100)	122 (67)	97 - 99 - 159	141 (100)	129 (92)	90 - 100 - 185
Site type												
Background	18 (30)			20 (50)			9 (22)			47 (33)		
Traffic	42 (70)			20 (50)			32 (78)			94 (67)		
Tramway proximity ^c												
No	35 (58)			N.A. ^d			34 (83)			69 (68)		
Yes	25 (42)			N.A. ^d			7 (17)			32 (32)		

^a Annual Average Daily Traffic (AADT) estimated at the closest main street (in thousands).

^b Total road length (in meters) in a 50-meter radius.

^c Tramway line in a 50-meter radius.

^d There are no tramway lines in Girona.

Table 2: Summary statistics of particle number, noise and vehicle counts by city.

	Campaign	Basel			Girona			Grenoble		
		N	Mean (SD)	p25 - p50 - p75	N	Mean (SD)	p25 - p50 - p75	N	Mean (SD)	p25 - p50 - p75
Particle count (no./cm ³)	1	57	15,800 (7540)	9,180 - 14,800 - 19,600	30	13,700 (5950)	8,970 - 13,700 - 18,000	40	18,300 (8780)	12,400 - 17,000 - 22,100
	2	59	11,500 (7330)	6,370 - 9,450 - 15,500	23	9,900 (5680)	6,460 - 8,400 - 10,600	23	36,600 (18000)	25,500 - 32,800 - 44,400
	3	59	20,000 (13900)	7,320 - 17,500 - 30,300	N.A. ^a			N.A. ^a		
	All	175	15,800 (10600)	7,570 - 12,500 - 20,800	53	12,000 (6100)	7,550 - 9,870 - 17,500	63	25,000 (15600)	13,000 - 20,800 - 32,700
Noise (dB(A))	1	58	61 (6.5)	55 - 62 - 66	40	64 (6.1)	60 - 64 - 68	41	65 (6.5)	62 - 67 - 69
	2	60	60 (6.7)	55 - 61 - 65	25	63 (6.7)	58 - 64 - 67	25	66 (7.4)	65 - 67 - 69
	3	60	61 (6.8)	55 - 62 - 67	N.A. ^a			N.A. ^a		
	All	178	61 (6.6)	55 - 62 - 66	65	64 (6.3)	59 - 64 - 68	66	65 (6.8)	63 - 67 - 69
Total vehicle counts (no./20 min.)	1	58	74 (100)	9 - 30 - 102	40	154 (191)	17 - 54 - 262	38	222 (152)	118 - 207 - 302
	2	60	72 (98)	7 - 25 - 109	25	141 (191)	15 - 27 - 244	24	213 (121)	135 - 213 - 314
	3	60	87 (110)	8.5 - 46 - 119	N.A. ^a			N.A. ^a		
	All	178	78 (102)	8 - 34 - 114	65	149 (190)	15 - 46 - 244	62	218 (140)	118 - 210 - 314
Period of measurement		Start	End	Duration (days)	Start	End	Duration (days)	Start	End	Duration (days)
	1	3/25/2011	4/18/2011	24	6/23/2009	7/28/2009	35	09/28/2011	10/14/2011	16
	2	6/2/2011	6/30/2011	28	7/7/2009	7/30/2009	23	11/15/2011	11/23/2011	8
	3	11/25/2011	12/19/2011	24	N.A. ^(a)			N.A. ^(a)		

^a Not available: only two measurement campaigns were conducted in Girona and Grenoble.

3.2 Variability over time of ultrafine particle number concentrations, noise levels and traffic counts

The temporal variability of the three measured variables are presented in [Table 3](#) and in [Figure 2](#). Intraclass correlation coefficients (ICC) between repeated measurements of noise, UFP and traffic were in the same ranges in the three cities; for noise, the ICCs quantifying agreement between repeated measurements were in the 0.86 to 0.97 range; for traffic counts, ICCs were in the 0.93 to 0.94 range. Temporal variations were strongest for UFP concentrations, with ICCs in the -0.11 to 0.14 range. These variations are also indicated in [Figure 2](#) by the closeness of points to the $y=x$ line for noise levels and traffic counts, while the distribution of UFP concentrations is much more scattered around the $y=x$ line.

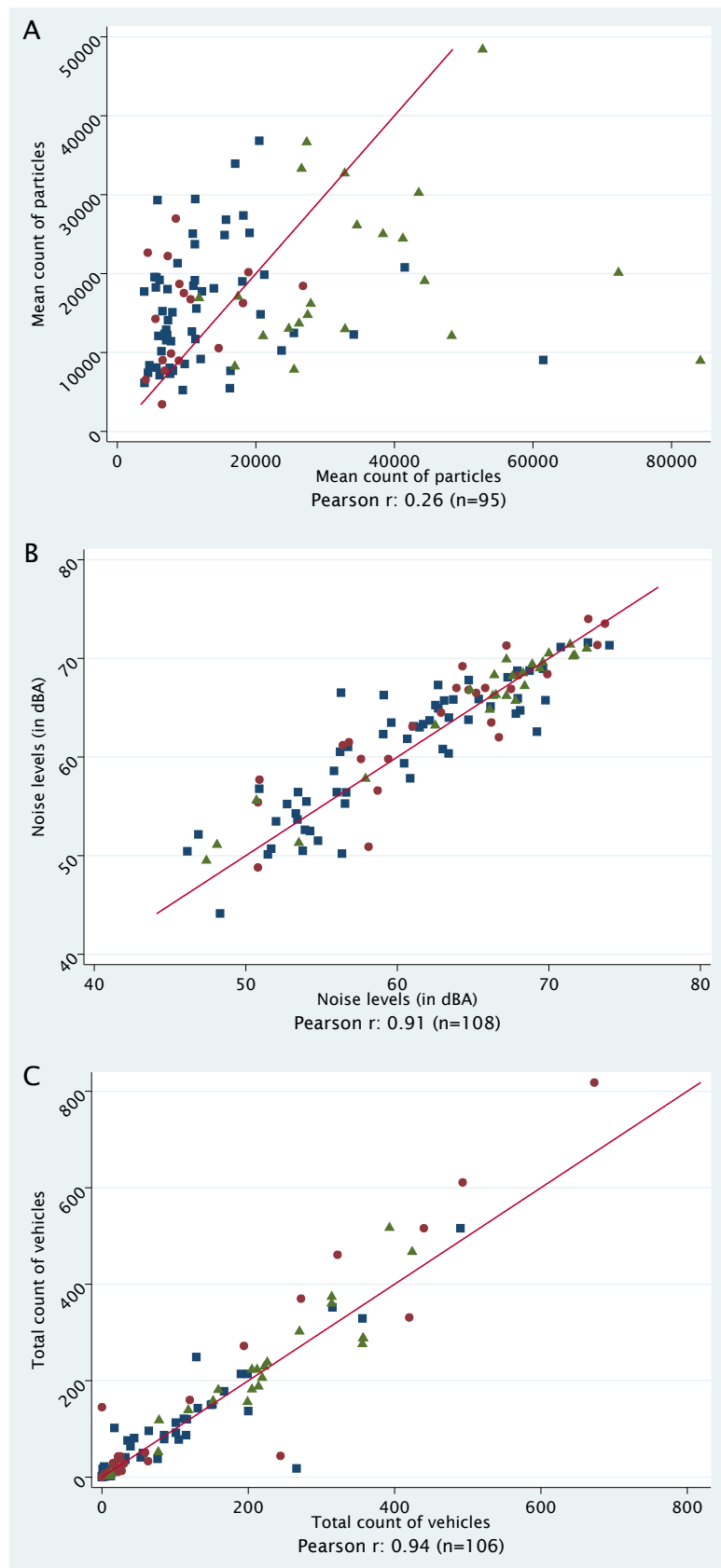
Table 3: Intraclass correlation coefficients between site-specific repeated measures at different periods of measurement.

Measurements	Basel (n=60)		Girona (n=25)		Grenoble (n=25)	
	r^a	p^b	r^a	p^b	r^a	p^b
Particle count	0.12	0.06	0.14	0.28	-0.11	0.69
Noise levels (dB(A))	0.86	$<10^{-4}$	0.87	$<10^{-4}$	0.97	$<10^{-4}$
Total vehicle counts	0.93	$<10^{-4}$	0.94	$<10^{-4}$	0.93	$<10^{-4}$

^a r corresponds to the intraclass correlation coefficient (ICC), based on the 2 (3 for Basel) measurements made at each site.

^b p -value corresponding to the test with null hypothesis H_0 : ICC=0, i.e. a test of independence of the repeated measurements.

Figure 2: Scatter plots of particle number (A), noise levels (B) and traffic counts (C) between the two campaigns, over the three cities (ultrafine particle number concentrations and traffic counts in number/20 min., noise in dB(A); third campaign in Basel excluded: see Supplemental Figure S1.) The squares, circles and triangles correspond to the measurements done in Basel, Girona and Grenoble, respectively. The red line indicates the $y=x$ line. Measurements of the first and second campaigns are displayed in the y and x axis, respectively.



3.3 Correlations of simultaneous levels of ultrafine particles concentrations, noise levels and traffic counts

Table 4 and Figure 3 show the Pearson correlation coefficients between the 20-min means of simultaneous measurements of noise levels, UFP concentrations and traffic counts. Correlations between noise measurements and traffic counts ranged from 0.54 to 0.72, according to city, while correlations of UFP concentrations with noise were in the 0.43-0.55 range and correlations of UFP concentrations with traffic counts were in the 0.15-0.37 range.

Table 4: Pearson correlation coefficients of particle number, noise and traffic counts, by city^a.

	Basel (n=178)		Girona (n=65)		Grenoble (n=63)		Overall (n=305)	
	r	p ^b	r	p ^b	r	p ^b	r	p ^b
Particle number versus Noise levels	0.46	<10 ⁻⁴	0.55	<10 ⁻⁴	0.43	<10 ⁻³	0.44	<10 ⁻⁴
Particle number versus Vehicle counts	0.26	<10 ⁻³	0.37	<0.01	0.15	0.27	0.29	<10 ⁻⁴
Noise levels versus Vehicle counts	0.60	<10 ⁻⁴	0.72	<10 ⁻⁴	0.54	<0.01	0.64	<10 ⁻⁴

^a Repeated measurements in each site were assumed independent in the estimation of the correlation coefficients. For detailed correlations by campaign, see Supplemental Table S1.

^b p-value corresponding to the test with null hypothesis H₀: r=0, i.e. a test of slope coefficient.

Figure 3: Scatter plots and correlations of simultaneously measured particle number, noise levels and traffic counts in Basel (A), Girona (B) and Grenoble (C) (data pooled from the 2 campaigns in Grenoble and Girona, 3 in Basel).

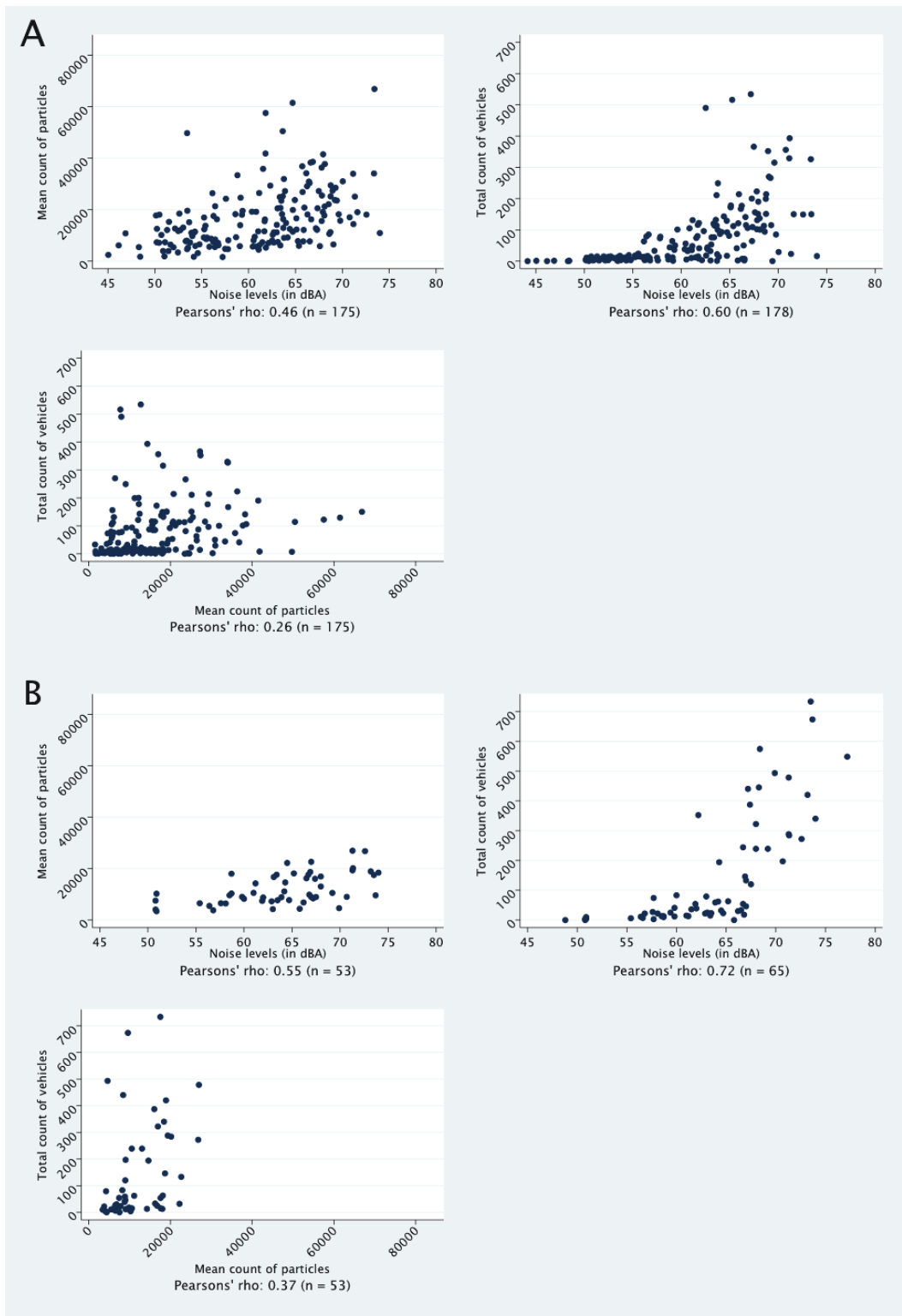
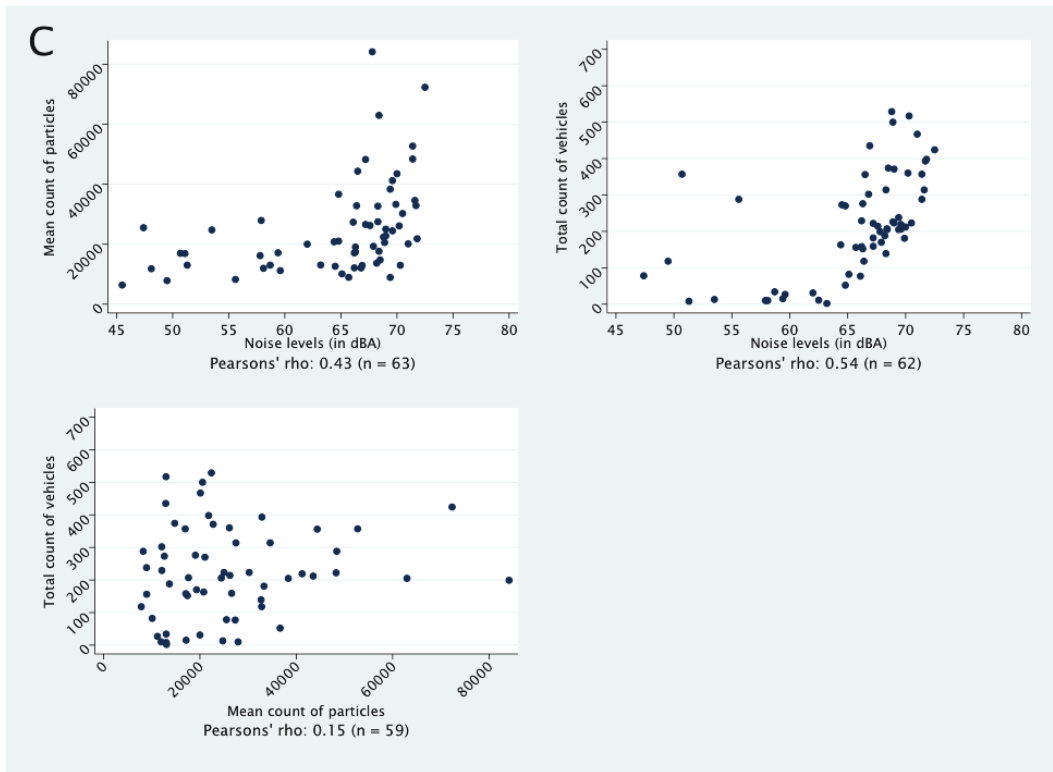


Figure 3 (continued)



3.4 Influence of the site characteristics on the ultrafine particle number concentrations, noise levels and traffic counts

Table 5 shows the differences in these environmental measurements according to the site characteristics. The levels of each of the three measurements were higher in traffic compared to non-traffic sites (p-values ranged from $<10^{-4}$ to 0.04 according to city). None of the other site characteristic considered was associated with UFP concentrations. Noise levels and traffic counts tended to vary with nearest street width and with main street distance, with strengths of association varying depending on the city.

Table 5: Influence of the site characteristics on particle number, noise and traffic count (characteristics of measurement sites were dichotomized using the median as cut-off; overall medians are displayed below; for city-specific median values, see Table 1).

	Basel (n=60)		Girona (n=40)		Grenoble (n=41)	
	Δ^a	p^d	Δ^a	p^d	Δ^a	p^d
Particle count (no./cm³)	(n=51-57)		(n=27-30)		(n=21-41)	
Site type (traffic vs. background)	6850	<0.01	4370	0.04	8760	0.01
Near street width (above vs. below 13.3m)	4670	0.03	2106	0.38	3420	0.35
Main street distance (below vs. above 22.4m)	2100	0.30	1770	0.43	3890	0.16
Main street traffic ^b (above vs. below 8370)	480	0.83	110	0.96	450	0.88
Street density ^c (above vs. below 99.8m)	730	0.72	2800	0.20	5250	0.06
Noise (dB(A))	(n=52-58)		(n=36-40)		(n=21-41)	
Site type (traffic vs. background)	6.91	<10 ⁻⁴	8.06	<10 ⁻⁴	11.9	<10 ⁻⁴
Near street width (above vs. below 13.3m)	8.58	<10 ⁻⁴	6.53	<10 ⁻³	2.12	0.47
Main street distance (below vs. above 22.4m)	7.86	<10 ⁻⁴	2.53	0.19	5.32	<0.01
Main street traffic ^b (above vs. below 8370)	0.44	0.81	1.48	0.45	5.72	<0.01
Street density ^c (above vs. below 99.8m)	8.49	<10 ⁻⁴	3.57	0.06	3.39	0.10
Total vehicle counts (no./20 min)	(n=52-58)		(n=36-40)		(n=19-38)	
Site type (traffic vs. background)	72	0.01	244	<10 ⁻⁴	163	0.01
Near street width (above vs. below 13.3m)	108	<10 ⁻⁴	208	<10 ⁻³	101	0.18
Main street distance (below vs. above 22.4m)	55	0.04	142	0.02	121	0.01
Main street traffic ^b (above vs. below 8370)	66	0.02	92	0.13	189	<10 ⁻⁴
Street density ^c (above vs. below 99.8m)	83	<0.01	92	0.13	49	0.32

^a Differences of the measurements means in each group, occurring in the first campaign. For differences of measurements between the first and the second campaign, see Supplemental Table S2. $\Delta = \text{mean}(\text{measurements_campaign1 in 1}^{\text{st}} \text{ group}) - \text{mean}(\text{measurements_campaign1 in 2}^{\text{nd}} \text{ group})$

^b Annual Average Daily Traffic.

^c Total road length (in meters) in a 50-meter radius buffer.

^d p-value corresponding to the test with null hypothesis $H_0: \Delta_1 = \Delta_2$, i.e. a test of difference of the measurements between the two groups.

4. Discussion

4.1 Summary

To our knowledge, this study is the first to describe the correlations of simultaneous short-term measurements of three local markers of traffic-related exposure, namely road traffic noise, ultrafine particle number (UFP) concentrations and traffic flows. The distributions of sites' characteristics and exposure levels were globally similar between the three cities, although UFP concentrations were about twice as high in Grenoble compared to Girona. While the Mediterranean city of Girona had the narrowest streets and highest street density in a 50 m buffer, UFP concentrations were lower than in the other cities. For each of the three cities considered, short-term levels of noise were moderately correlated to traffic counts and slightly less correlated to UFP concentrations, whereas UFP concentrations were weakly correlated with traffic counts. Twenty-minute measurements of outdoor noise and traffic, but not of UFP concentrations, were constant across a couple of days or months.

4.2 Protocol and results validity

We used a harmonized design with short-term measurements conducted at repeated times and with a common protocol to maximize comparison across the three cities. For the noise measurements, any interference such as unexplained, implausible or non-representative temporary peaks were reported and removed afterwards. There were however a few differences in design between areas: noise from trams in Basel and Grenoble could not always be excluded, which could partly explain the lower correlations of noise levels with traffic counts in these two cities; second, the time interval between repetitions was about six weeks in Grenoble, 1.5 week in Girona, and two to six months in Basel.

4.3 Temporal variations on repeated measurements of ultrafine particle number concentrations and traffic noise

Although these time intervals were different, the temporal intraclass correlation coefficients for the noise measurements and to a lesser extent the traffic counts were very high, and similar in all cities. This suggests that 20-min measurements of non-rush hour traffic density and traffic noise are a rather good marker for the characterization of the longer-term conditions. This is in line with previous studies on traffic counts and noise: Allen et al. (2009) reported constant measurements of noise over time ($n=22$, $r=0.84$, vs. $r=0.86-0.98$ in our study). It should be noted that some models of urban long-term noise are based on measurements of 15-20 minutes (Directive 49/2002/EC).

In contrast, UFP concentrations were not constant over time and this was observed in all three cities, including Girona with the short time interval between measurements. Thus, the 20-min protocol seems to be an efficient approach to characterize traffic counts and traffic-related noise, but not UFP concentrations. The reasons for the low correlations between repeated measures of UFP concentrations in specific sites may include the impact of meteorological conditions on UFP concentrations. A few studies have investigated such relationships, showing an influence of the local weather conditions on UFP concentrations. Sartini et al. (2013) found a 25% increase of UFP concentrations depending on the downwind exposure; Mishra et al. (2012) also reported an effect of wind direction –lower than that of traffic flows– on UFP concentrations. The impact of the other meteorological conditions has little been studied. A study by Reche et al. (2014) has reported a little impact of solar radiation, temperature and relative humidity on the correlations of outdoor average UFP concentrations between a site outside a school and a fixed urban background station; however both sites did not record the exact same parameter, thus limiting the interpretation of the results. Meteorological conditions have lower influences on traffic counts (only to the extent of the proportion of subjects changing their mode of transportation according to the weather) and on noise levels than on UFP

concentrations. Our study did not aim at characterizing the impact of meteorological conditions on noise or UFP concentrations, and in order to limit any impact of meteorological conditions on any of these parameters we did not perform measurements on rainy days or under windy conditions. Consequently, the temporal variability of the parameters studied would probably be higher if no restriction related to the meteorological conditions is applied. While this measurement protocol allows obtaining reproducible noise measurements, this reproducibility is not attained for UFP. Corrections for determinants of temporal variations in UFP concentrations such as meteorological conditions may be required to derive a long-term estimate from such short-term measurements of UFP concentrations; measuring UFP over longer time periods than 20 min would also be relevant.

4.4 Correlations between ultrafine particle number concentrations and traffic noise

Most of the studies assessing the relationship between noise and air pollution considered pollutants such as NO₂, NO_x or particulate matter (PM), according to a review by Tétreault et al. (2013). Most studies considered NO₂ as a proxy for local traffic emissions. As reviewed by Tétreault et al. (2013), coefficients of correlation between NO₂ and noise in the short-term had a similar level to the Pearson correlation that we report between UFP concentrations and noise, namely $r=0.53$, on 103 sites (Davies et al. 2009) in Vancouver, Canada. These correlations between NO₂ and noise were lower than the long-term correlations found in previous studies: indeed, Foraster et al. (2011) reported a coefficient of correlation of 0.62 between long-term averages of NO₂ and modelled noise on 77 sites. Very few studies were conducted on UFP concentrations, and these generally relied on measurements of shorter durations than ours. In a study of the relationship over time between 5-min measurements of ultrafine particles and noise in Chicago city and a suburb county in California, Allen et al. (2009) reported correlations between simultaneous UFP concentrations and noise measurements slightly weaker than ours

(n=36-46 sites, Pearson's r ranging from 0.26 to 0.41 depending on urban area vs. $r=0.43-0.55$ in our study). To our knowledge, the only other study assessing the correlation between 20-min measurements of UFP concentrations and noise focused on a single site and reported a Spearman coefficient of correlation of 0.38 (Can et al. 2011). In the study by Can et al., there was a distance of approximately 50 m between the locations of the instruments of measurement of UFP and noise. Thus, our results confirm that 20-min measurements of traffic noise and UFP concentrations are rather weakly associated and that the strength of the association is area-specific. We measured UFP concentrations and noise at street sites; correlations between measurements at facades or inside homes, which may be more representative of subjects' exposures (Foraster et al. 2013), may differ. Given the rather different propagation and diffusion properties of noise and UFP, one might expect correlations in front of residential sites to be even lower than in the street. Epidemiological studies of associations between short-term exposure to noise and health outcomes are, thus, unlikely to be strongly confounded by particle numbers –and vice versa. Thus it may well be possible to disentangle associations by adequate adjustment for particle numbers –and vice versa. Impact of differences in site characteristics and land-use factors across cities on UFP concentrations and noise levels may contribute to the different correlations observed. The range in the UFP–noise correlations showed that differences between the three cities were moderate given the city characteristics, which did not differ much. Other studies considered a wider range of land-use factors as determinants of the air pollution and noise levels (Weber et al. 2014).

4.5 Traffic counts

Many studies use or interpret traffic proximity or traffic density as proxies for exposure to primary emissions of traffic exhaust, such as UFP (Health Effects Institute, 2013). Our data show, however, that 20-min traffic counts are rather weak determinants of short-term UFP

particle number concentrations. Vehicle counts were more strongly associated with noise, measured at the street site. We cannot exclude that traffic counts and noise levels would correlate more strongly with long-term UFP averages, which were not considered in this study. Again, this correlation may be different at the facade of apartments where people live.

4.6 Conclusion

On the short-term, noise and ultrafine particulate matter levels exhibited only moderate correlations in three middle-sized cities in Europe, which may allow epidemiological studies to disentangle their possible short-term health effects by adequate adjustment for particle numbers –and vice versa. The very high temporal correlation of repeated measurements observed for noise and traffic counts confirms the validity of very short-term measurements to characterize the long-term mean conditions. On the contrary, the relatively strong temporal variations observed for the ultrafine particle number concentrations indicate that markers of fresh exhaust emissions need to be monitored over longer time periods (and probably repeated over time to take seasonal variations into account) to provide a stable estimate.

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Supplemental material

Table S1: Pearson correlations of particle, noise and traffic, by campaign and city.

Variables	Campaign	Basel (n=57-60)		Girona (n=23-40)		Grenoble (n=22-40)		Overall (n=104-136)	
		r	p	r	p	r	p	r	p
Particle count -									
Noise levels	1	0.42	<0.01	0.58	<10 ⁻³	0.51	<10 ⁻³	0.45	<10 ⁻⁴
	2	0.48	<10 ⁻³	0.50	0.02	0.54	0.01	0.48	<10 ⁻⁴
	3	0.51	<10 ⁻⁴	N.A. ^a		N.A. ^a		N.A. ^a	
Particle count -									
Vehicle counts	1	0.28	0.04	0.46	0.01	0.11	0.50	0.28	<0.01
	2	0.40	<10 ⁻³	0.32	0.13	0.31	0.16	0.44	<10 ⁻⁴
	3	0.16	0.22	N.A. ^a		N.A. ^a		N.A. ^a	
Noise levels -									
Vehicle counts	1	0.55	<10 ⁻⁴	0.71	<10 ⁻⁴	0.60	<0.01	0.65	<10 ⁻⁴
	2	0.61	<10 ⁻⁴	0.74	<10 ⁻⁴	0.49	<0.02	0.65	<10 ⁻⁴
	3	0.63	<10 ⁻⁴	N.A. ^a		N.A. ^a		N.A. ^a	

^a Not available: only two measurement campaigns were conducted in Girona and Grenoble.

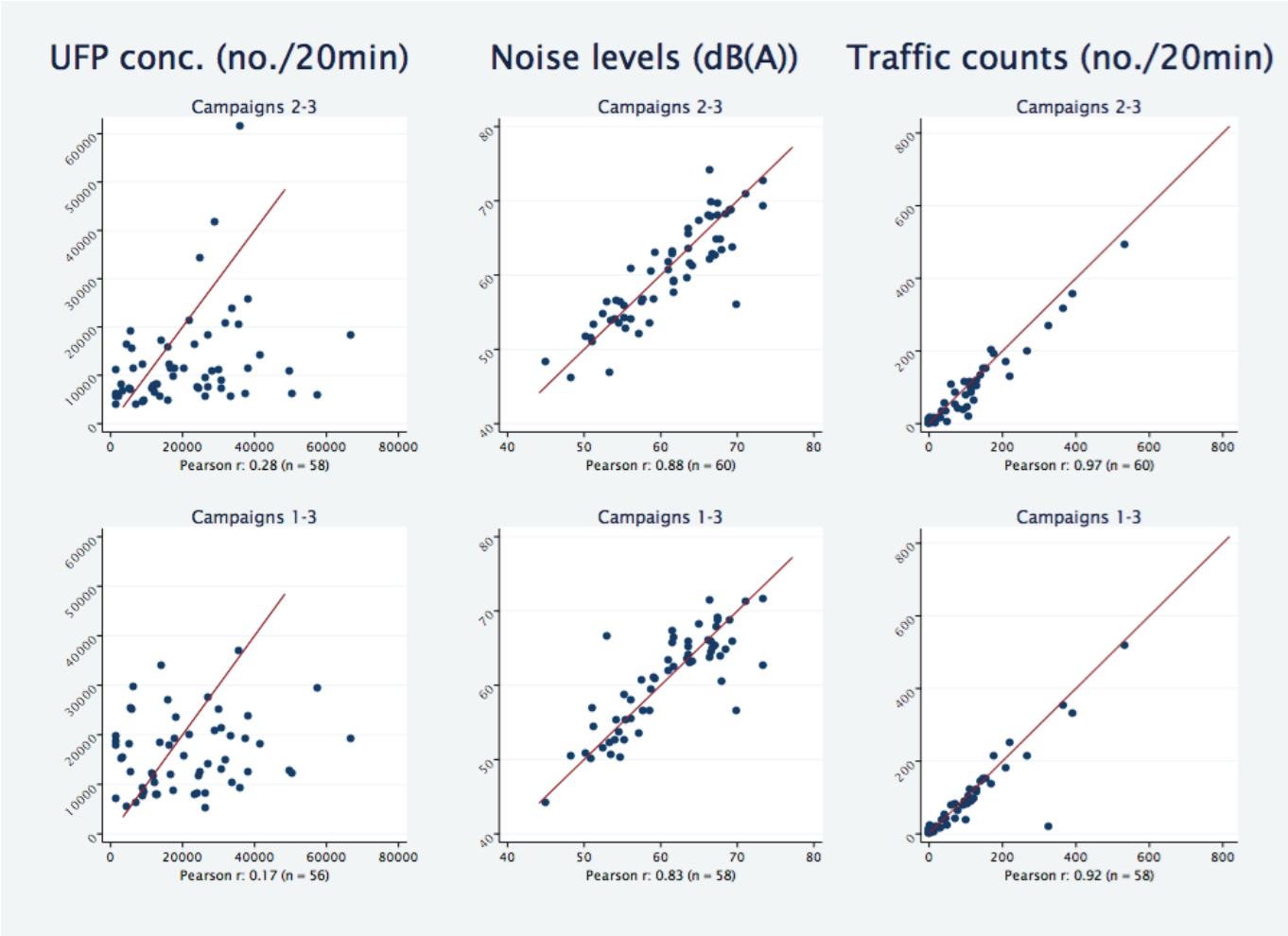
Table S2: Student t-tests of differences of particle count, noise and traffic levels between the first and the second campaign (20-minute measurements).

	Basel (n=56-58)		Girona (n=17-25)		Grenoble (n=22-25)	
	Δ^a	p	Δ^a	p	Δ^a	p
Particle counts	+3100	0.05	+4500	0.03	-14900	<0.01
Noise (dB(A))	+0.54	0.20	+0.91	0.18	+0.25	0.48
Total vehicle counts	+1.6	0.77	+22	0.16	+3.5	0.72

^a Mean of differences of the measurements between the first and the second campaigns (the third campaign in Basel was not considered).

$\Delta = \text{mean}(\text{measurements_campaign1} - \text{measurements_campaign2})$

Figure S1: Scatter plots of particle counts (A), noise levels (B) and traffic counts (C) between the two campaigns including the campaign 3, in Basel. The red line indicates the $y=x$ line.



UFP conc.: ultrafine particle number concentrations.

Chapter II: Air pollution, health and social deprivation: a fine-scale risk assessment

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Résumé du Chapitre II

De nombreuses études épidémiologiques se sont portées sur les effets de la pollution de l'air sur la santé humaine. Avec l'apport des études toxicologiques, elles ont permis une meilleure caractérisation des effets de certains polluants atmosphériques, en particulier ceux des particules en suspension (ou *particulate matter*, PM). Les PM sont souvent classées en PM₁₀ – pour les particules ayant un diamètre aérodynamique de moins de 10 µm, en PM_{2,5} – pour celles ayant un diamètre inférieur à 2,5 µm, ou encore en particules ultrafines (ou nanoparticules) pour celles ayant un diamètre inférieur à 0,1 µm. L'exposition aux PM augmente la mortalité et la morbidité respiratoire et cardiovasculaire (WHO, 2013). De nouvelles études indiquent que la pollution de l'air a aussi des effets sur les issues de grossesse, le neuro-développement et la fonction cognitive, ou encore le diabète (Shah et Balkhair, 2011 ; Raz et al., 2015 ; Raaschou-Nielsen et al., 2013). Par ailleurs, plusieurs études ont montré que l'exposition à la pollution de l'air différait selon le niveau de défaveur sociale. En Europe, aucune tendance claire n'émerge quant à la direction de cette association, à l'inverse des Etats-Unis, où les résultats des études convergent dans le sens d'une plus grande exposition parmi les plus défavorisés (Hajat et al., 2015). Les quelques études conduites en France ont trouvé des résultats différents selon la ville, allant d'une exposition plus importante chez les plus défavorisés (Lille, Marseille) à la situation inverse (Paris), ou encore une situation intermédiaire où les quartiers les plus exposés étaient ceux ayant un niveau de défaveur sociale intermédiaire.

En épidémiologie, les études étiologiques mettent en évidence des relations dose-réponse à l'échelle individuelle. Elles ne constituent pas un outil permettant de traduire l'exposition d'une population entière en un indicateur de « fardeau » de maladie. Ceci peut être réalisé au moyen d'études d'impact sanitaire (EIS). Ces études nécessitent, entre autres, une connaissance sur la distribution des expositions, ce qui rend possible la quantification de l'impact de la pollution de l'air à l'échelle des agglomérations. Le déroulement d'une EIS peut se décomposer en quatre étapes : 1. Identification du danger ; 2. Choix de la relation dose-réponse ; 3. Estimation des expositions, et 4. Caractérisation du risque. Les EIS se situent à l'aval des études étiologiques et traduisent un effet de la pollution de l'air à l'échelle de l'individu – en terme de risque relatif (ou odds-ratio) – en un effet à l'échelle de la population, exprimé par exemple en nombre de cas (de décès ou de maladie) attribuables à l'exposition. De telles estimations sont utiles dans le domaine de la prise de décision en santé publique, et facilitent en outre la communication du fardeau de maladie par le biais des médias.

La caractérisation adéquate des effets de la pollution de l'air sur la santé repose principalement sur la qualité de l'estimation des expositions. Un biais de classement peut impacter négativement la puissance statistique des études épidémiologiques, biaiser les fonctions dose-réponse et par conséquent les estimations d'impact sanitaire qui en découlent (Nieuwenhuijsen, 2015). En France, les concentrations en polluants sont enregistrées en routine par le réseau de surveillance de la qualité de l'air des AASQA (Associations Agréées de Surveillance de la Qualité de l'Air). Pour les EIS, reposer sur de telles données entraîne un biais de classement des expositions du fait de la résolution spatiale limitée du réseau de stations des AASQA. Ainsi, à Grenoble et à Lyon, respectivement une et trois stations de fond enregistrent les concentrations en particules fines ($PM_{2.5}$), tandis que les deux agglomérations couvrent 250 et 500 km². Concernant cette problématique, les avancées en expologie ont ouvert de nouvelles perspectives pour les zones urbaines aux fortes contrastes spatiaux. Par exemple, un modèle de dispersion atmosphérique à la résolution spatiale fine a été développé par l'AASQA Air Rhône-Alpes, couvrant notamment les agglomérations de Grenoble et Lyon. L'état actuel de la recherche montre que les connaissances sont encore limitées dans l'estimation de l'ordre de grandeur du biais de classement résultant d'une estimation des expositions au moyen de stations, par rapport à des modèles de dispersion.

L'objectif de ce chapitre était de mener une étude d'impact sanitaire des particules fines ($PM_{2.5}$) dans deux agglomérations au moyen d'une modélisation à l'échelle spatiale fine, et d'étudier les variations de cet impact selon un indicateur de défaveur sociale.

Dans les agglomérations de Grenoble et Lyon (respectivement 0,4 et 1,2 millions d'habitants), l'exposition aux $PM_{2.5}$ en 2012 a été estimée à une échelle de 10×10 m, en couplant un modèle de dispersion à des données de densité de population. Les événements de santé retenus étaient la mortalité non accidentelle ainsi que l'incidence du cancer du poumon (Grenoble) et des petits poids de naissances (à terme). Les nombres de cas attribuables à la pollution de l'air ont été estimés à l'échelle de l'agglomération, et en stratifiant par quartier selon l'indice de défaveur sociale EDI (European Deprivation Index). Les estimations d'impact sanitaire ont été répétées en considérant différents niveaux de résolution spatiale des polluants au sein des agglomérations.

Les niveaux médians de $PM_{2.5}$ étaient de 18,1 et 19,6 $\mu\text{g}/\text{m}^3$ à Grenoble et à Lyon, respectivement, correspondant à 114 et 491 décès non accidentels attribuables à l'exposition à long terme aux $PM_{2.5}$, ou respectivement 5,1% et 6,0% du total des décès (intervalles de confiance à 95%, IC 95% : 3,2–7,0% et 3,7–8,3%). Le nombre de petits poids de naissance (à

terme) attribuables à la pollution de l'air représentait 23,6% (IC 95% : 9,0–37,1%) du total à Grenoble, et 27,6% (IC 95% : 10,7–42,6%) du total à Lyon. A Grenoble, 6,8% des nouveaux cas de cancer du poumon étaient attribuables à la pollution de l'air (IC 95% : 3,1–10,1%). L'impact sanitaire était réduit de 8 à 20% en estimant l'exposition aux PM_{2.5} au moyen de stations de surveillance de la qualité de l'air. L'impact sanitaire était plus élevé dans les quartiers ayant un niveau de défaveur social intermédiaire, ou légèrement plus élevé que la moyenne.

Cette étude est parmi les premières à avoir estimé l'impact sanitaire des particules fines en se basant sur une modélisation des expositions à la résolution spatiale fine. De plus, nous avons calculé une estimation du nombre de cas incidents de petits poids de naissances à terme, ce qui a été très peu effectué jusqu'à présent. Les études d'impact sanitaires reposant sur les données des stations de fond seules tendent à sous-estimer le fardeau de maladie de la pollution aux particules fines. L'utilisation de modèles d'exposition à la résolution spatiale fine, en particulier à l'échelle de la rue, et couplée à des données sur la densité de population à la même échelle, apparaît comme une approche faisable et pertinente en zone urbaine.

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 10x10 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.

Keywords

Air pollution; dispersion model; risk assessment; health impact assessment; particulate matter; attributable risk; social deprivation; burden of disease

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 (Peters 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%), the WHO yearly air quality guideline of 10 µg/m³

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 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, National Institute of the Statistic and the Economic Studies, 2011). The study area was defined according to the air pollution dispersion model coverage (Figure 1).

2.2 Assessment of air pollution levels

We relied on Sirane 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 10x10 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, 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, 2013) 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, 2011). 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 2,000 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 (WHO, 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 the [Table 1](#).

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 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 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 $10 \mu\text{g}/\text{m}^3$ in $\text{PM}_{2.5}$ concentration selected for the outcome considered (see [Table 1](#)), and c_{ref} was equal to the $10 \mu\text{g}/\text{m}^3$ 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 $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$ concentration in the study area (Grenoble or Lyon urban area), estimated from the population-weighted area specific distribution of $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$ background station was available in Grenoble and three in Lyon. Starting from $H3$

assumptions, in *H4* the relative risk RR_{median} was replaced by $RR_{\text{AQMS}_{\text{avg}}}$, the relative risk corresponding to the yearly average of $PM_{2.5}$ levels recorded by the station(s):

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

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 ([Figure 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 2,280 (interquartile range: 1,940–2,760). 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 2,470 (interquartile range: 1,970–2,990). The two study areas are represented in [Figure 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 median exposure from the dispersion model ([Figure 2](#)).

The number of non-accidental deaths in 2007 was 2,254 and 8,148 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 ([Figure 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.

Figure 1A: Study areas (Grenoble urban area: bottom left corner; Lyon urban area: bottom right corner).

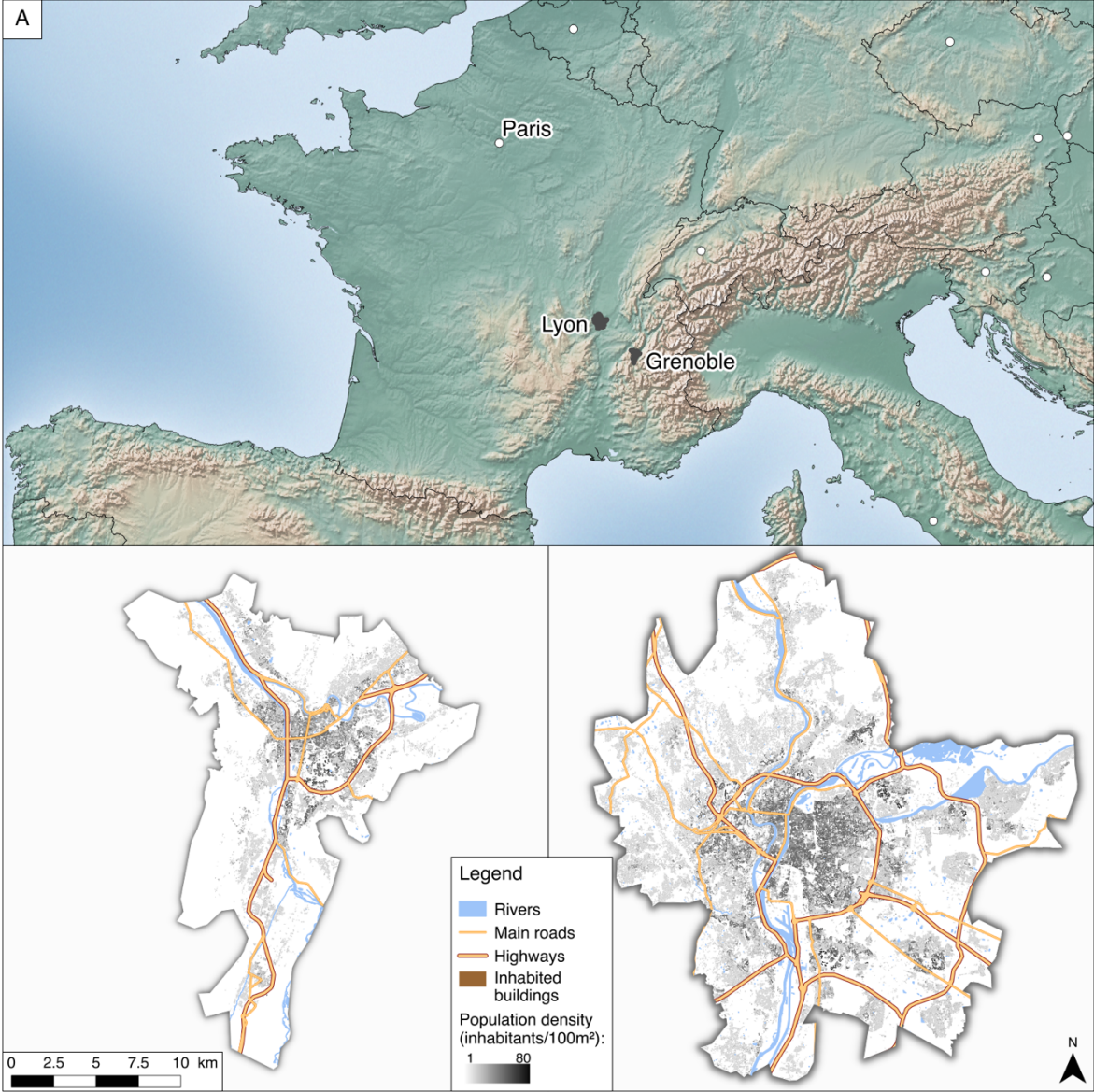


Figure 1B: Air pollution model for fine particulate matter (PM_{2.5}) concentrations in Grenoble urban area (PM_{2.5} yearly averages for the year 2012).

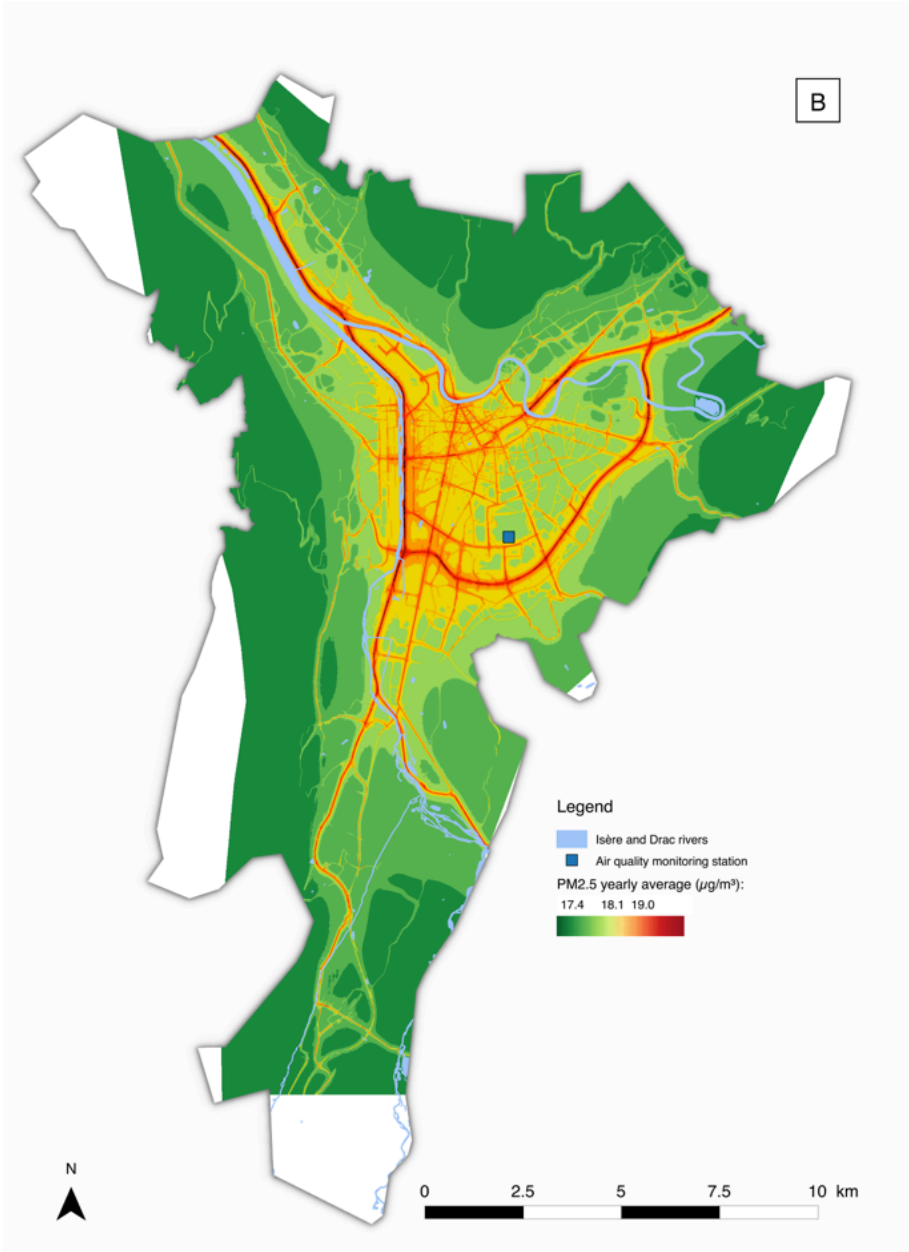


Figure 1C: Air pollution model for fine particulate matter (PM_{2.5}) concentrations in Lyon urban area (PM_{2.5} yearly averages for the year 2012).

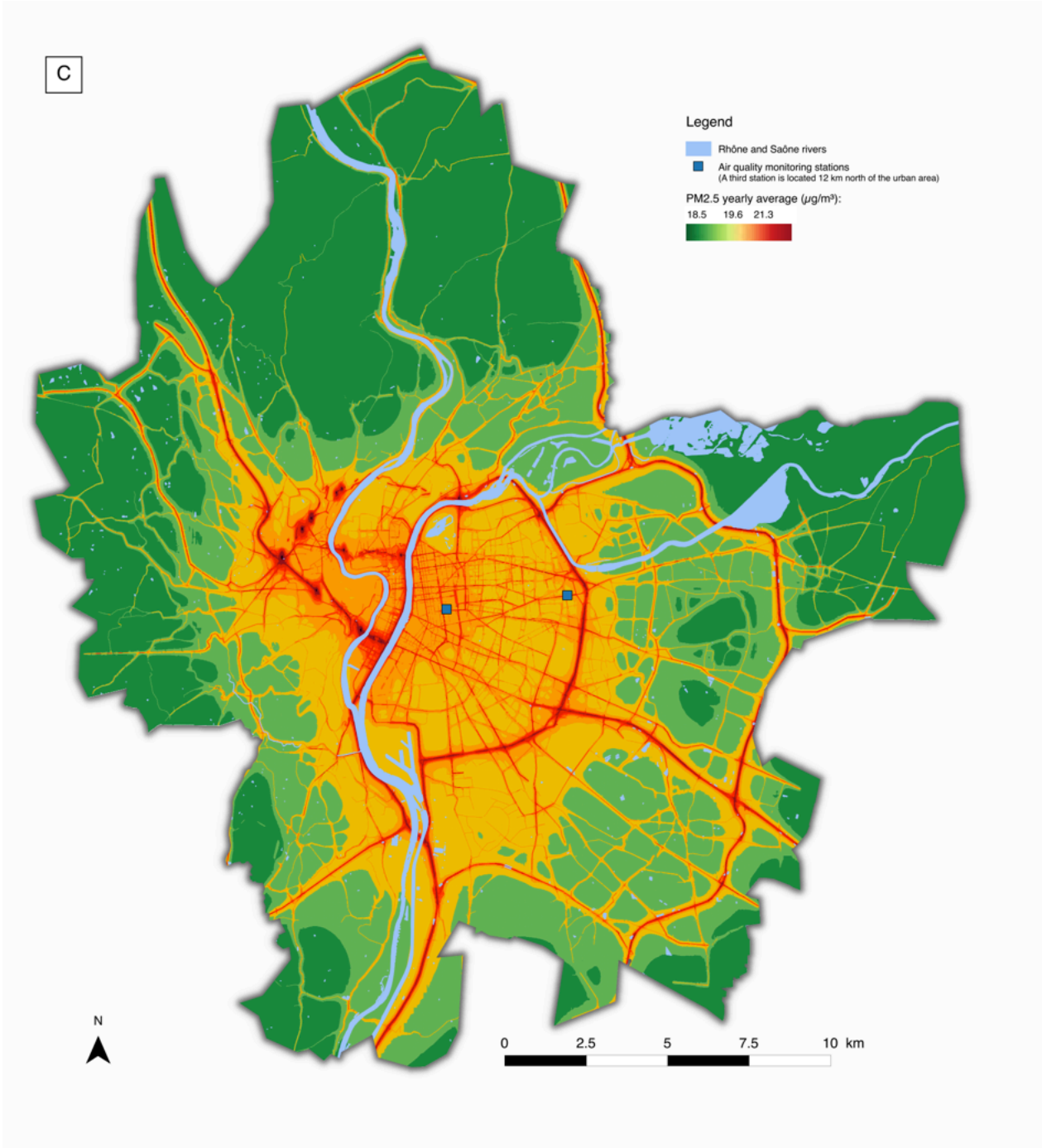


Figure 2: Distribution of population exposure to fine particulate matter (PM_{2.5} yearly average in 2012) in Grenoble (A) and Lyon (B) urban areas. The mean yearly level from the local background monitoring station(s) is indicated by the vertical line.

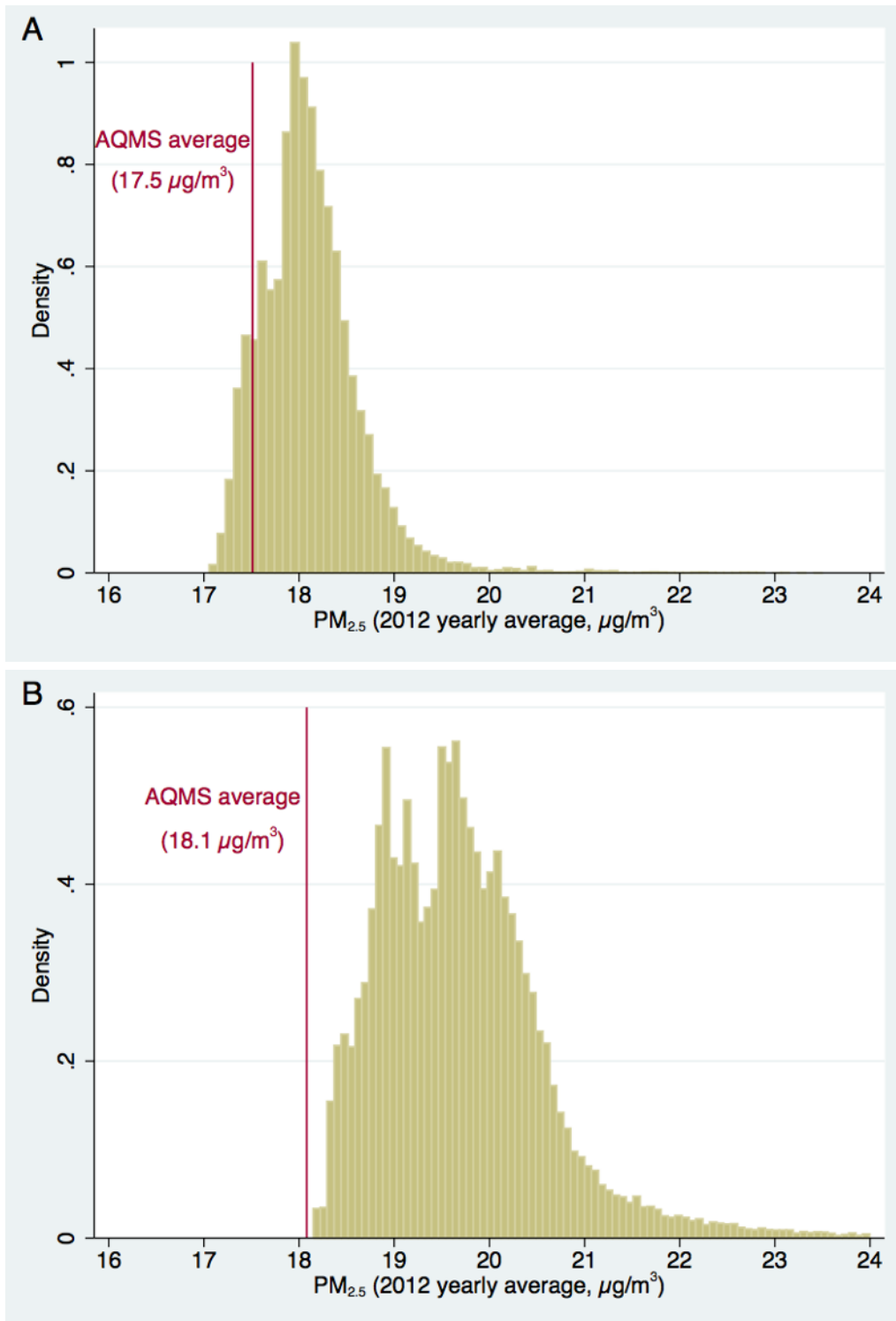
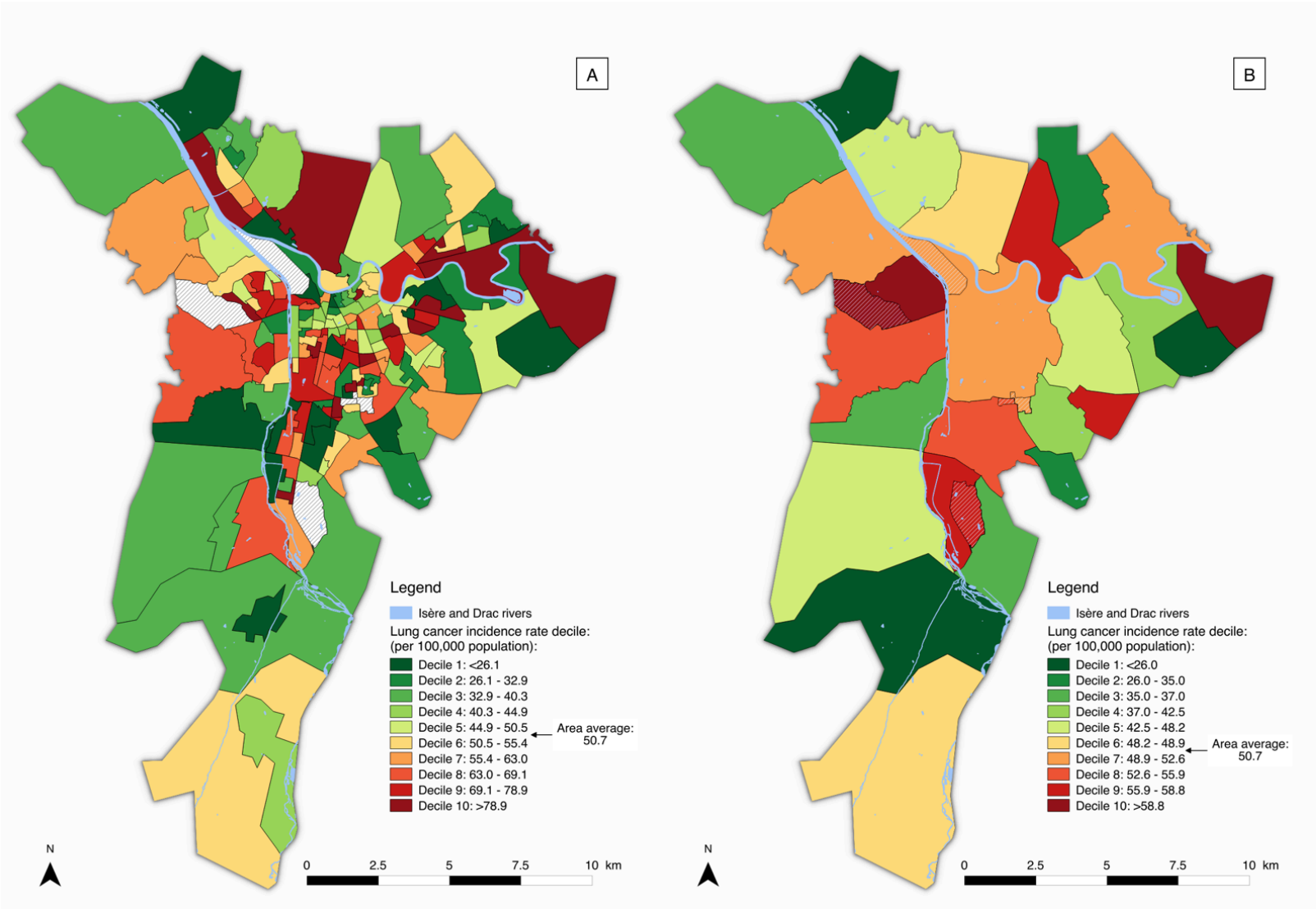


Figure 3: Lung cancer incidence in Grenoble urban area, taking into account the neighborhood (IRIS)-specific information on the distribution of cases (A) and assuming spatial homogeneity in the distribution of cases in neighborhoods (IRIS) from the same municipality (B).



IRIS: housing Blocks Regrouped for Statistical Information, or neighborhood.

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](#)).

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).

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) associated with PM_{2.5} levels^a		95% CI	(% of total)
Non-accidental mortality					
Grenoble	2,250	114	(5.1%)	71–157	(3.2–7.0%)
Lyon	8,150	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					
Pedersen et al. (2013) 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%)
Dadvand et al. (2013) 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 µg/m³)

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

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 to 5.6% compared to under *H1* (fine-scale approach), 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 to 8.6% in Grenoble, depending on the health event, and by 8.3 to 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* (station-based approach), 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 to 19.8% under *H4* (station-based approach) compared to *H1* (fine-scale approach), 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* (fine-scale approach) and *H2* (homogeneous population density) 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, Figure 3).

Table 3: Sensitivity 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: 5 th –50 th –95 th 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 [Figure 1](#)).

Table 4: Estimated 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: 5 th –50 th –95 th 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%)

^aThe neighborhood (IRIS, or housing Block Regrouped for Statistical Information) is the finest scale for which lung cancer cases were available; IRIS included on average 2,280 inhabitants (interquartile range: 1,940–2,760) and Grenoble area included a total of 169 IRIS.

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

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 [Figure 1](#)).

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](#), [Figure 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, [Figure 5](#), [Figure S1](#)).

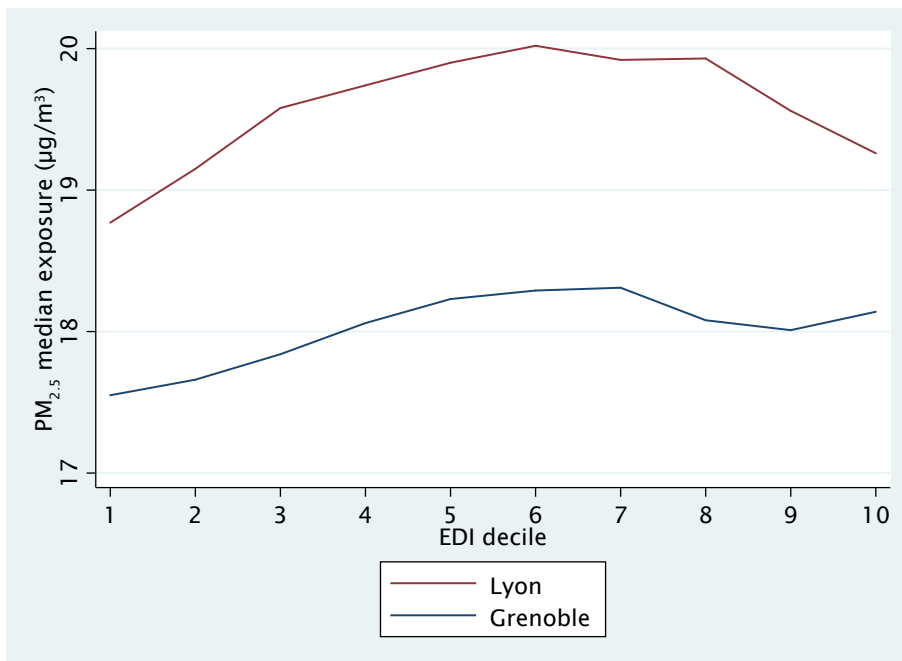
Stratification of the attributable risk of PM_{2.5} on the EDI showed similar contrasts. For mortality and term low birth weight, and depending on the social deprivation decile, the maximum between-EDI decile differences in attributable risk were in the 11.8%–12.0% and 9.8%–10.9% ranges in Grenoble and 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](#), [Figure S2](#)).

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%

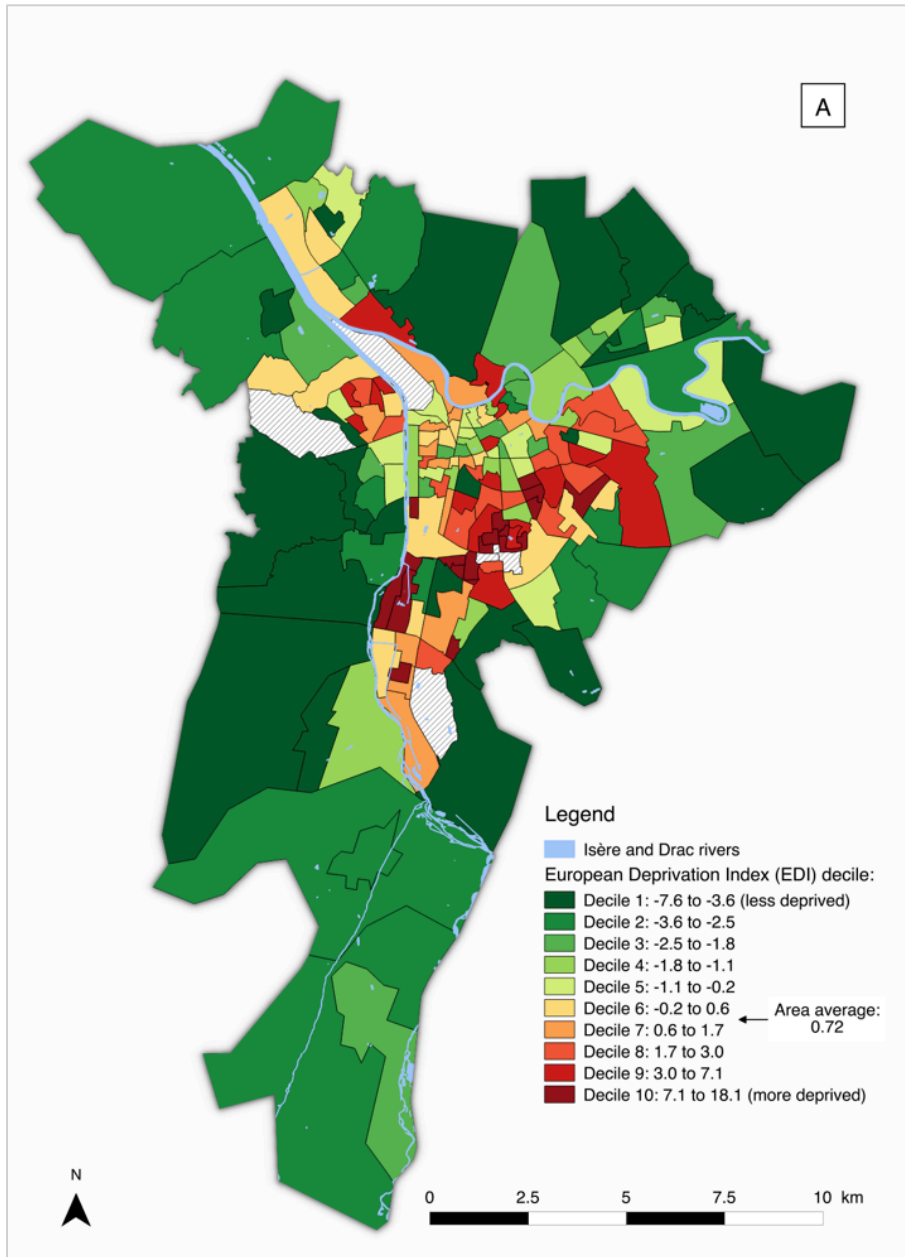
EDI: European Deprivation Index.

Figure 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).



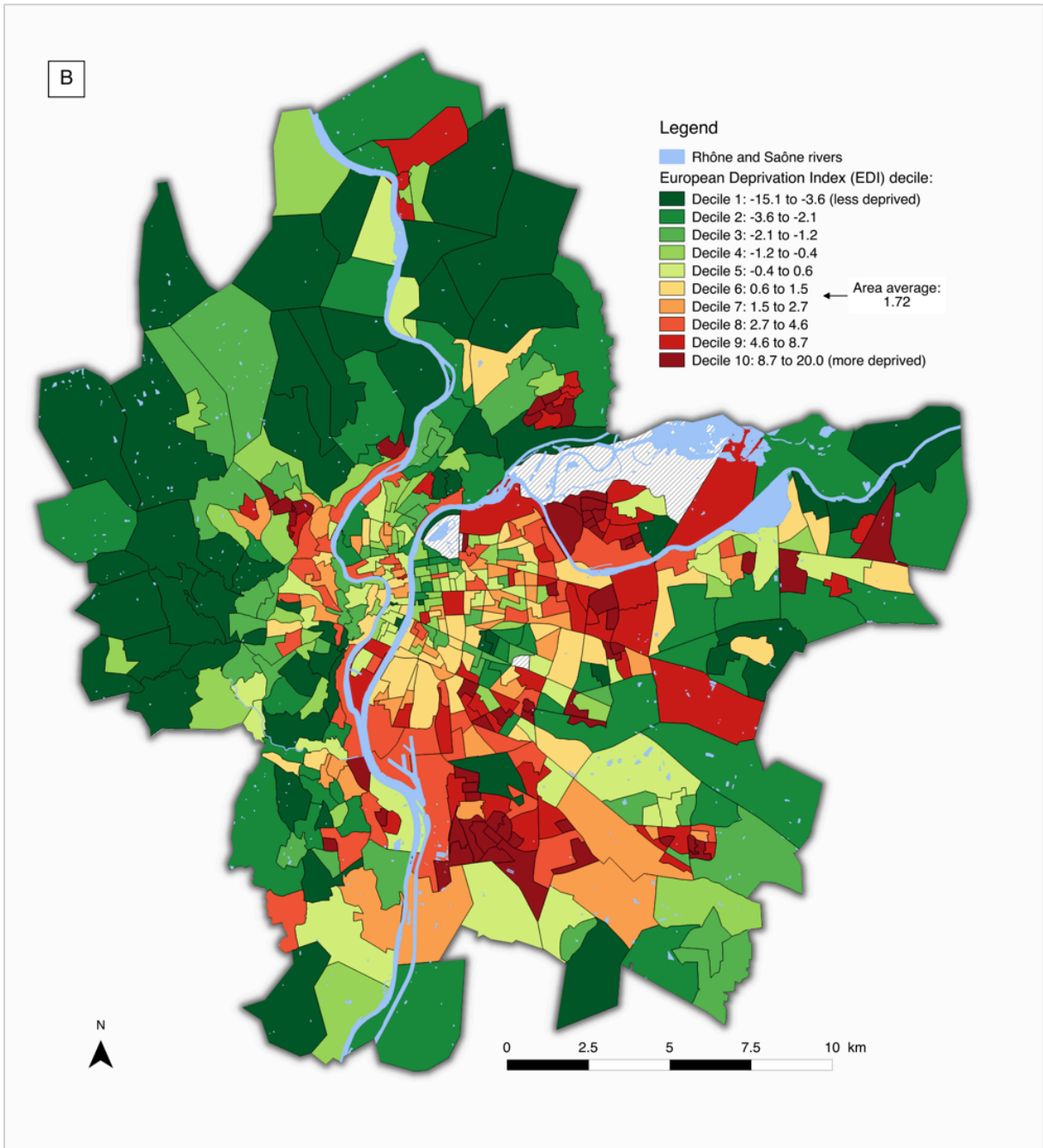
EDI: European Deprivation Index.

Figure 5A: Social deprivation status (European Deprivation Index, EDI) at the IRIS scale in Grenoble urban area.



IRIS: housing Blocks Regrouped for Statistical Information, or neighborhood.

Figure 5B: Social deprivation status (European Deprivation Index, EDI) at the IRIS scale in Lyon urban area.



IRIS: housing Blocks Regrouped for Statistical Information, or neighborhood.

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 fine-scale dispersion model with a 10-meter 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 to 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 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}). 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 ([Figure S2B](#)).

Results of risk assessment studies such as ours are generally highly sensitive to case ascertainment and 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) 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 except for confidence interval, 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, 2011). 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 µg/m³ 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 area 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 (Ortu 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 (Perez 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 to 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 to 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 (lowest, intermediate and highest quintiles). 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 2014). 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.

Acknowledgements

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Supplemental material

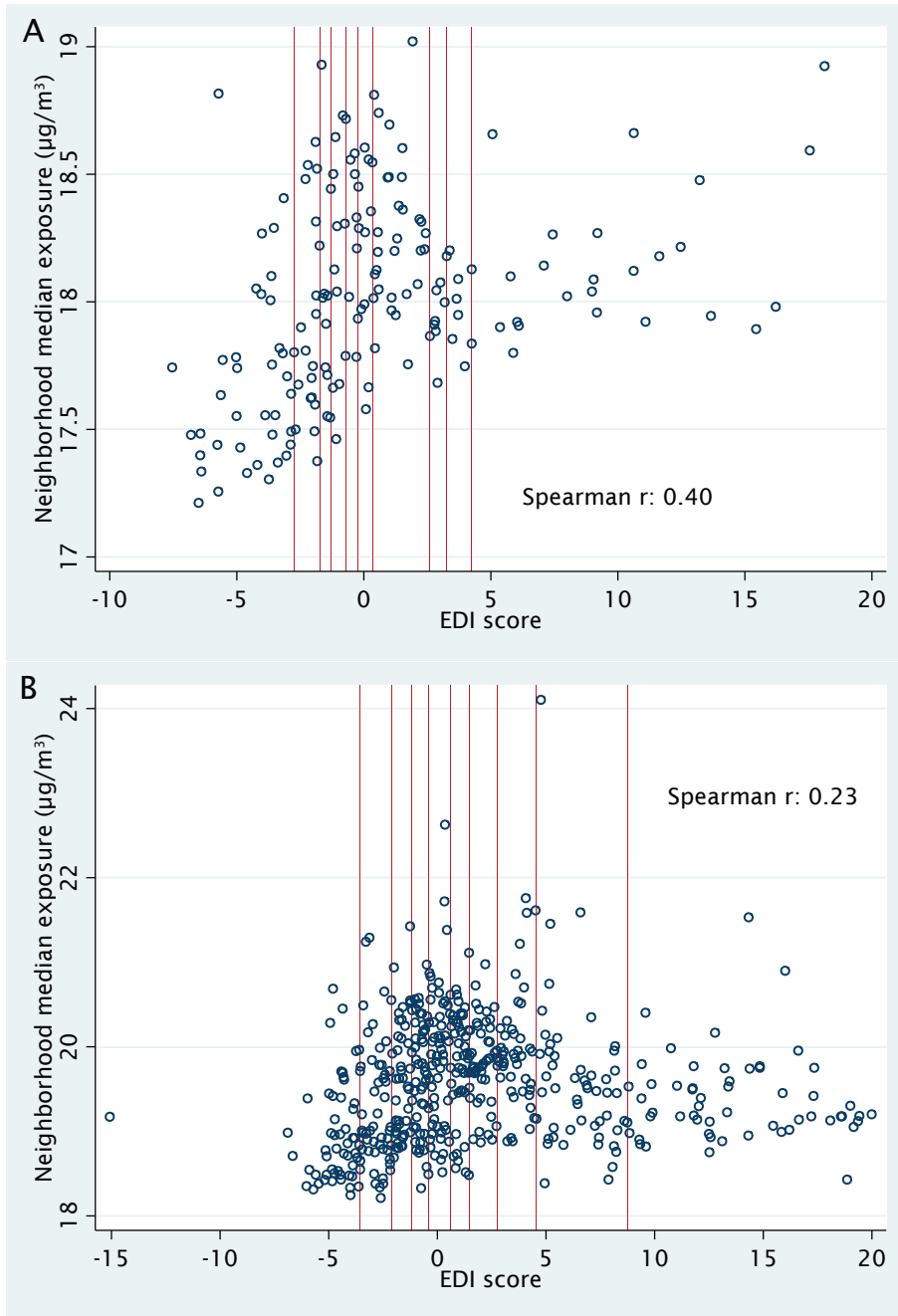
Table S1: Sensitivity analyses of the risk assessment of fine particulate matter (PM_{2.5}) exposure under three different alternative hypotheses, restricted to the main municipality in each of the two areas.

Health event and hypothesis	Number of attributable cases (NAC)			
	NAC	(% of total)	95% CI	(% of total)
Non-accidental mortality				
Grenoble municipality (n=157,000)				
H1 (reference)	53.8	(5.2%)	33.4–74.1	(3.2–7.2%)
H2	55.1	(5.4%)	34.2–75.9	(3.3–7.4%)
H3	53.2	(5.2%)	33.0–73.3	(3.2–7.1%)
H4	48.2	(4.7%) ^a	29.8–66.4	(2.9–6.4%) ^a
Lyon municipality (n=470,000)				
H1 (reference)	206	(6.4%)	128–283	(4.0–8.8%)
H2	209	(6.5%)	130–287	(4.1–9.0%)
H3	200	(6.2%)	125–275	(3.9–8.6%)
H4	161	(5.0%) ^a	100–222	(3.1–6.9%) ^a
Lung cancer incidence				
Grenoble municipality (n=157,000)				
H1 (reference)	5.8	(7.0%)	2.7–8.6	(3.3–10.4%)
H2	5.9	(7.2%)	2.7–8.8	(3.3–10.7%)
H3	5.7	(6.9%)	2.6–8.5	(3.2–10.3%)
H4	5.2	(6.3%) ^a	2.4–7.7	(2.9–9.4%) ^a
Term low birth weight cases				
Grenoble municipality (n=157,000)				
H1 (reference)	14.3	(24.4%)	5.5–22.4	(9.4–38.2%)
H2	14.6	(24.9%)	5.6–22.7	(9.5–38.7%)
H3	14.1	(24.0%)	5.4–22.2	(9.2–37.8%)
H4	12.9	(22.1%) ^a	4.9–20.5	(8.4–35.0%) ^a
Lyon municipality (n=470,000)				
H1 (reference)	53.8	(29.0%)	21.1–82.7	(11.4–44.6%)
H2	54.4	(29.3%)	21.4–83.3	(11.5–44.9%)
H3	52.7	(28.4%)	20.6–81.2	(11.1–43.8%)
H4	43.5	(23.4%) ^a	16.7–68.4	(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: H1 assuming spatial homogeneity of population density; H3: H2 assuming spatially homogeneous air pollution levels (area-specific median level of dispersion model estimate); H4: H2 assuming spatially homogeneous air pollution levels, as estimated by the area-specific background air quality monitoring stations (1 station in Grenoble: *Villeneuve Les Frênes*, and 3 stations in Lyon: *Vaulx en Velin*, *Lyon Centre* and *Villefranche Village*; see Figure 1).

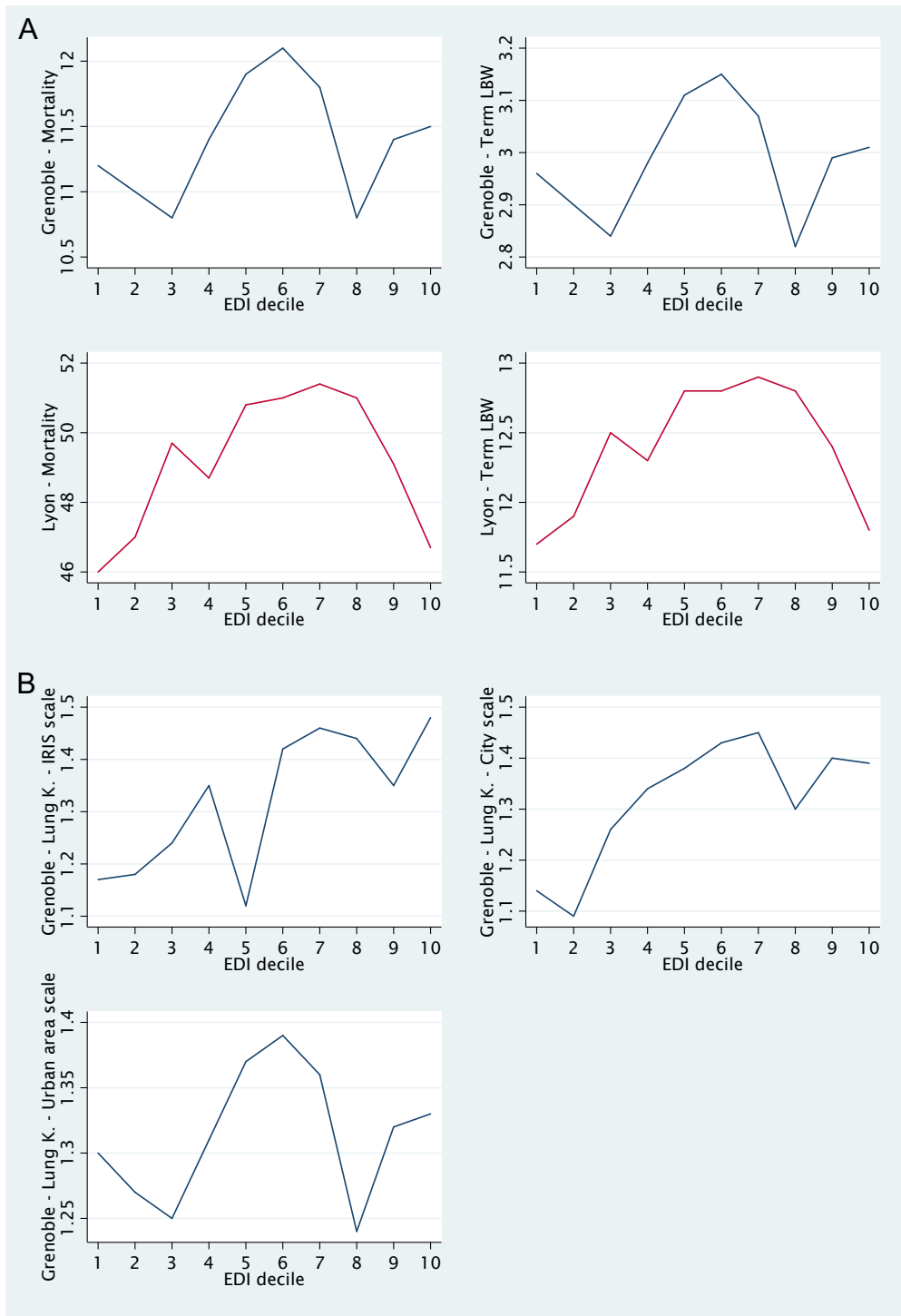
^a H4 relies on the monitoring station(s), which provide identical exposure estimates regardless of the study area.

Figure S1: Scatter plots of the ranked median fine particulate matter (PM_{2.5}) concentrations and the EDI score at the IRIS scale in the Grenoble (A) and Lyon (B) urban areas (higher EDI values represent more deprived neighborhoods).



EDI: European Deprivation Index.

Figure S2: Stratification of the number of cases attributable to the exposure to PM_{2.5} on the EDI decile, for non-accidental mortality and term low birth weight in Grenoble and Lyon (A) and lung cancer incidence with different levels of spatial distribution of cases (B) (see Table 5 for exact values).



Note: in the figure B above, the upper-left and upper-right curves correspond to the spatial distribution of lung cancer cases represented in Figure 3A and 2B, respectively.

EDI: European Deprivation Index.

Chapter III: Estimating the health benefits of hypothetical scenarios on the health of the population in urban areas

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Unsubmitted manuscript.

Résumé du Chapitre III

Dans les pays industrialisés, la plupart des émissions locales en zone urbaine proviennent de sources mobiles telles le trafic routier, de sources fixes comme le chauffage individuel ou urbain, et dans une moindre mesure de l'industrie. Pour les émissions liées au trafic routier, une solution pour réduire le trafic et accélérer le renouvellement du parc consiste à mettre en place des zones à faibles émissions, ou zones à trafic limité (*low emission zones*, LEZ). Plusieurs pays européens ont implémenté des LEZ depuis le milieu des années 1990, à l'exception de la France. Un certain nombre de LEZ sont basées sur le standard d'émission Euro (véhicules légers et poids lourds), mais il existe de fortes variations dans le degré de limitation du trafic d'une LEZ à l'autre. En outre, la plupart des LEZ ont été mises en place récemment ou sans étude conjointe pour évaluer leurs effets. Des études basées sur des scénarios théoriques pourraient compléter les investigations sur les effets de mesures réelles, et aider à planifier des politiques publiques efficaces en terme de gains sanitaires. En Europe, la valeur limite relative à la qualité de l'air est de $25 \mu\text{g}/\text{m}^3$ en moyenne annuelle pour les particules fines ($\text{PM}_{2.5}$; Journal Officiel de l'Union Européenne, 2008). Cette valeur est nettement supérieure à la recommandation de l'Organisation Mondiale de la Santé (OMS) en matière de qualité de l'air; pour les $\text{PM}_{2.5}$, cette valeur est de $10 \mu\text{g}/\text{m}^3$ en moyenne annuelle (WHO, 2006). Plusieurs études ont quantifié les bénéfices sanitaires théoriques d'une mise en conformité avec des normes de qualité de l'air (Ballester et al., 2008). Quelques études ont considéré d'autres scénarios de réduction de la pollution atmosphérique (Boldo et al., 2011), par exemple le remplacement des trajets en véhicule par un usage plus fréquent du vélo et des transports publics (Rojas-Rueda et al., 2012).

L'objectif principal de ce chapitre était d'étudier les effets de différents scénarios théoriques de réduction des niveaux de pollution atmosphérique sur l'exposition de la population dans deux zones urbaines, et de traduire ces changements de concentration en polluants en bénéfices sanitaires.

Dans les agglomérations de Grenoble et Lyon (respectivement 0,4 et 1,2 millions d'habitants), 10 scénarios théoriques de réduction des niveaux de particules fines ($\text{PM}_{2.5}$) ont été élaborés. Certains scénarios portaient sur des réductions homogènes des niveaux de pollution de l'air, tandis que d'autres scénarios se limitaient à certaines zones (plus polluées). L'exposition aux $\text{PM}_{2.5}$ a été estimée à l'aide d'un modèle de dispersion atmosphérique à la résolution spatiale fine ($10 \times 10 \text{ m}$), couplé à des données de densité de population. Les événements de santé retenus

étaient la mortalité non accidentelle ainsi que l'incidence du cancer du poumon (Grenoble) et des petits poids des naissances à terme (voir Chap. II). Les nombres de cas attribuables à la pollution de l'air étaient estimés avant (en 2012) et après l'implémentation de chaque scénario. Le scénario basé sur la valeur recommandée par l'OMS s'est montré le plus efficace en terme de nombre de cas attribuables à la pollution évités, avec des réductions de l'impact sanitaire de la pollution de l'air sur les décès non accidentels variant de 5,1% (Grenoble) à 6,0% (Lyon) du total des cas. Du fait de la valeur limite réglementaire élevée de l'UE, aucun bénéfice sanitaire ne pouvait être attendu selon ce scénario. Un scénario inspiré d'une directive européenne de 2008 (retirée depuis) a entraîné les gains sanitaires les plus importants, avec 2 à 2,4% de décès évités selon l'agglomération. Ce résultat représente environ 40% du total des bénéfices sanitaires qui seraient observées si les niveaux moyens de $PM_{2,5}$ étaient ramenés à la valeur guide de l'OMS. Pour atteindre 10% de l'effet obtenu par le scénario respectant la valeur guide de l'OMS, une diminution à l'échelle de l'agglomération des concentrations annuelles en $PM_{2,5}$ de l'ordre de 5% serait nécessaire.

Ce chapitre a évalué les bénéfices sanitaires de différents scénarios visant à réduire la pollution atmosphérique en zone urbaine. Ces résultats indiquent un ordre de grandeur de l'amélioration de la qualité de l'air requise pour améliorer significativement la santé publique. Des réductions d'au moins 5% des niveaux de pollution auxquels la population est exposée entraînerait une bénéfice sanitaire substantiel. Nous avons montré que dans les deux agglomérations considérées, aucun bénéfice sanitaire ne pouvait être tiré du respect de la valeur limite instaurée par l'UE. Ce point soulève la question de la législation européenne en matière de qualité de l'air (Brunekreef et al., 2015). Une révision des objectifs actuellement prévus pour 2020-2030 apparaît cruciale, au regard du fardeau actuel de maladie généré par la pollution atmosphérique, et considérant les avancées d'autres pays développés sur ce sujet.

Abstract

Air pollutants such as fine particulate matter have a large effect on health, in particular in urban areas. Various types of measures can be implemented to limit air pollution levels, but knowledge on the amount of reduction to target in order to obtain a significant reduction in the public health burden is very limited.

Our objective was to investigate the health benefits expected from several types of scenarios of PM_{2.5} reduction, defined by their amplitude and the targeted area.

In Grenoble and Lyon areas (0.4 and 1.2 million inhabitants, respectively), we defined 10 hypothetical scenarios of reduction of PM_{2.5} concentrations. Scenarios differed in terms of spatial homogeneity of the decrease in PM levels and amplitude of the PM change. PM_{2.5} exposure was estimated on a 10×10 m grid by coupling a dispersion model to population density. The numbers of mortality, lung cancer and term low birth weight cases attributable to PM_{2.5} were estimated before (in 2012) and after the implementation of each scenario.

Median PM_{2.5} exposures in 2012, before the hypothetical implementation of scenarios, were 18.1 in Grenoble and 19.6 µg/m³ in Lyon urban areas. The scenarios of reduction of air pollution exhibited contrasted results. The scenario restricted to bringing areas above the yearly EU regulatory limit to this value did not entail a reduction of the health burden, while a reduction to the WHO air quality guideline yielded the most important number of avoided cases, ranging from a decrease by 5.1 to 27.6% of the total number of cases, depending on the outcome and urban area. A decrease by 5% in PM_{2.5} levels in the whole area were required to reach 10% of the health benefit obtained with the WHO guidelines scenario.

Ambitious measures improving air quality far below the EU PM_{2.5} regulation are required to significantly improve health in these European urban areas.

Keywords

Air pollution; air quality improvement; attributable risk; burden of disease; dispersion model; health impact assessment; low emission zone; lung cancer; mortality; particulate matter (PM); scenarios

1. Introduction

Atmospheric pollution exposure leads to an increase in mortality rates as well as cardiovascular and respiratory morbidity, including lung cancer (Raaschou-Nielsen et al., 2013). An effect on low birth weight risk is also plausible (Wilhelm et al., 2012; Pedersen et al., 2012; WHO, 2013). In industrialized countries, the health impact of atmospheric pollutants such as particulate matter (PM) tends to be larger in urban areas, where pollution levels and population density are higher. In a previous study (Morelli et al., in revision), we estimated that in Grenoble and Lyon urban areas, two middle- to large-size French urban areas, 114 and 491 deaths were attributable to PM_{2.5} exposure in 2012, corresponding to 5.1 and 6.0% of the total, respectively. These large proportions make of atmospheric pollution one of the main factors on which it is possible to act at the population level to improve public health.

In Europe, the current air quality limit values in annual averages are 40 µg/m³ for nitrogen dioxide (NO₂) and 25 µg/m³ for the fine particulate matter (PM_{2.5}; European Union (Official Journal), 2008). The values for PM_{2.5} are much higher than the air quality guidelines issued by the World Health Organization (WHO). The current WHO guidelines are 40 µg/m³ for NO₂ and 10 µg/m³ for PM_{2.5} (WHO, 2006).

In the urban areas of western countries, most of the local emissions of air pollutants come from mobile sources such as road traffic and stationary sources such as heating and, to a lesser extent, the industry. Several policies are targeted towards reducing traffic-related emissions. These include regulating emission limits for new vehicles (the *Euro* standard in the EU), developing public transportation, supporting bikes and walks as transportation means as well as low emission zoning. Several countries across Europe have implemented low emission zones (LEZ) since the mid-1990s, France being an exception. LEZs most often consist in limiting access to motor vehicles in specific areas based on the Euro standard (vehicles with the highest emissions undergoing circulation restrictions), with strong variations in the degree of traffic limitation

between LEZs (ADEME, 2014). Sweden was first to experiment a LEZ in 1996, followed by Italy, Germany and Great Britain with the London congestion charge. Other measures targeting heating system, isolation or industrial emissions can also be planned.

Since many of the measures aiming at reducing air pollution levels have been implemented recently or without accompanying evaluation studies, and since measures are being considered in many areas of the world, studies based on hypothetical scenarios could complement the investigations of real measurements and help plan policies efficient for public health.

Several studies quantified the effects of compliance to air quality guidelines in term of health impact. In the Aphis project, Ballester et al. (2008) conducted a health impact assessment (HIA) of PM_{2.5} depending on the fulfillment of 4 different limit values (25, 20, 15 and 10 µg/m³). Another study conducted in Barcelona by Pérez et al. (2009) estimated the health benefits attained if the PM₁₀ annual averages were lowered to either the WHO (20 µg/m³) or EU (40 µg/m³) limit value. In Mexico, a HIA study of PM₁₀ evaluated the Mexican limit value (50 µg/m³) in addition to the WHO and EU standards (Riojas-Rodriguez et al., 2014). Some studies considered other reduction scenarios; Boldo et al. (2011) estimated the health benefits of a local, specific air quality policy by comparing a 2011 scenario assuming various measures aiming at reducing air pollution levels (resulting in a reduction of 10.7% of the PM_{2.5} in 2011 compared to 2004) to a baseline scenario in 2004. Rojas-Rueda et al. (2012) compared 8 scenarios involving the replacement of car use by bicycle and public transportation in Barcelona.

The main aim of this work was to consider a variety of hypothetical scenarios of reduction of air pollutants levels in two urban areas, and translate these hypothetical changes in air pollution levels into health benefits.

2. Materials and Methods

2.1 Study areas and assessment of fine particulate matter exposure

The study consists of Grenoble and Lyon urban areas in the South-East of France, which are respectively the 11th and 2nd largest in France in term of population, with 0.7 and 2.1 million inhabitants (INSEE, 2013). The study areas corresponded to the coverage of the air pollution model. Population exposure to air pollution was assessed with a fine-scale spatial resolution, and is fully described in another study (Morelli et al., in revision). Briefly, the PM_{2.5} levels were estimated by the Sirane dispersion model, covering at a 10-meter spatial resolution the study areas (Soulhac et al., 2011, 2012). PM_{2.5} data were coupled with information on population density at the same spatial resolution, based on data from INSEE and the National Institute of Geographic and Forestry Information (IGN, 2007; INSEE, 2010).

2.2 Scenarios of reduction of air pollution levels

In each urban area, the baseline (reference) air pollution situation in 2012 was hypothetically modified according to 10 scenarios, which are described in [Table 1](#). Scenarios S1 and S2 corresponded to the achievement at the urban area scale of the WHO guideline (S1) and the EU limit value (S2) for PM_{2.5}. Four scenarios consisted in absolute (S3, S4) or relative (S5, S6) spatially homogeneous decreases in PM_{2.5} levels with various amplitudes. Four other scenarios (S7 to S10) assumed decreases limited to selected areas: S7 consisted in decreasing the PM_{2.5} concentrations down to a “low” level, corresponding to the 10th percentile of area-specific exposure (while levels already below this value remained unchanged). S8 and S9 scenarios corresponded to reductions by 2 and 5% in the PM_{2.5} levels, but only for the population exposed above the 90th percentile. We finally considered a scenario inspired by the 2008 EU directive transposed in French law in 2010 (French Republic (Official Journal), 2010), and targeting

relative decreases in PM_{2.5} yearly averages up to 20% to be attained by 2020 (S10, or Scenario 2020).

Table 1: Hypothetical scenarios of reduction of air pollution (PM_{2.5}).

Population involved	Amount of reduction (2012 yearly average)	Scenario name
Whole study area	Decrease to WHO limit	S1
	Decrease to EU limit	S2
	-1 µg/m ³ (homogeneous)	S3
	-2 µg/m ³ (homogeneous)	S4
	-2% (homogeneous)	S5
	-5% (homogeneous)	S6
Population with an exposure exceeding the level of a quiet neighborhood	Down to the 10 th percentile of exposure	S7
Restricted to the population exposed above the 90 th centile	-2%	S8
	-5%	S9
Population exposed above several thresholds inspired by the 2008 EU directive ("2020 target") ^a	-20% if C ^b ≥ 18 µg/m ³	S10
	-15% if C ^b < 18 µg/m ³	

^a Inspired by the Decree no. 2010-1250 specifying target decreases of PM_{2.5} yearly averages, in µg/m³, to be obtained by 2020. The post-scenario value depended on concentration (L) observed in 2012: -20% if L ≥ 18 µg/m³, -15% if L < 18 µg/m³.

^b C: Site-specific concentration before the implementation of the scenario.

2.3 Characterization of the attributable risk

We quantified the possible health benefits of each hypothetical scenario as the difference in the number of attributable disease cases (NAC) attributable to PM_{2.5} exposure between before and after the implementation of each scenario. The long-term health effects considered were the all-cause non-accidental mortality (ICD10: A00-R99), the lung cancer (ICD10: C33-34) and the term low birth weight incidences. For each health outcome, we selected a dose-response function from the literature, aiming at robust studies such as meta-analyses and studies with limited potential for confounding (Table 2). The NAC were estimated at the street level, namely with a 10-m spatial resolution and based on the observed and hypothetical PM_{2.5} annual

average, the population density, the dose-response function and the number of disease subjects. The sum of the NAC for each grid point provided an attributable risk estimate at the urban area scale. Further details regarding the calculation of the attributable risk in a given situation have been previously described (Morelli et al., in revision).

Table 2: 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/m³ increase in exposure	
Non-accidental mortality	WHO 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

^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).

3. Results

3.1 Study population and baseline air pollution exposure

Grenoble and Lyon study areas had a surface of 245 km² and 480 km², with population sizes of 385,000 and 1.2 million, respectively ([Figure 1](#)). In Grenoble, each of the 169 IRIS –or neighborhoods– included an average population of 2,280 (interquartile range, IQR: 1,940–2,760), while in Lyon the average population by IRIS was 2,470 (IQR 1,970–2,990).

Before the implementation of any hypothetical scenario, the population density-weighted median PM_{2.5} level was 18.1 µg/m³ (5th–95th percentiles: 17.4–19.0 µg/m³) in Grenoble and 19.6 µg/m³ (5th–95th percentiles: 17.4–19.0 µg/m³) in Lyon urban area ([Figure 2](#)). An illustration of the spatial contrasts in exposure is given by two 10-m large cross-sections of Grenoble and Lyon urban areas in [Figure S1](#).

Figure 1: Study areas, showing the selected neighborhood in Grenoble and Lyon with a low $PM_{2.5}$ median exposure corresponding to the 10th percentile (scenario S7), and the population exposed above the 90th percentile of the average $PM_{2.5}$ concentration in 2012 (scenarios S8 and S9).

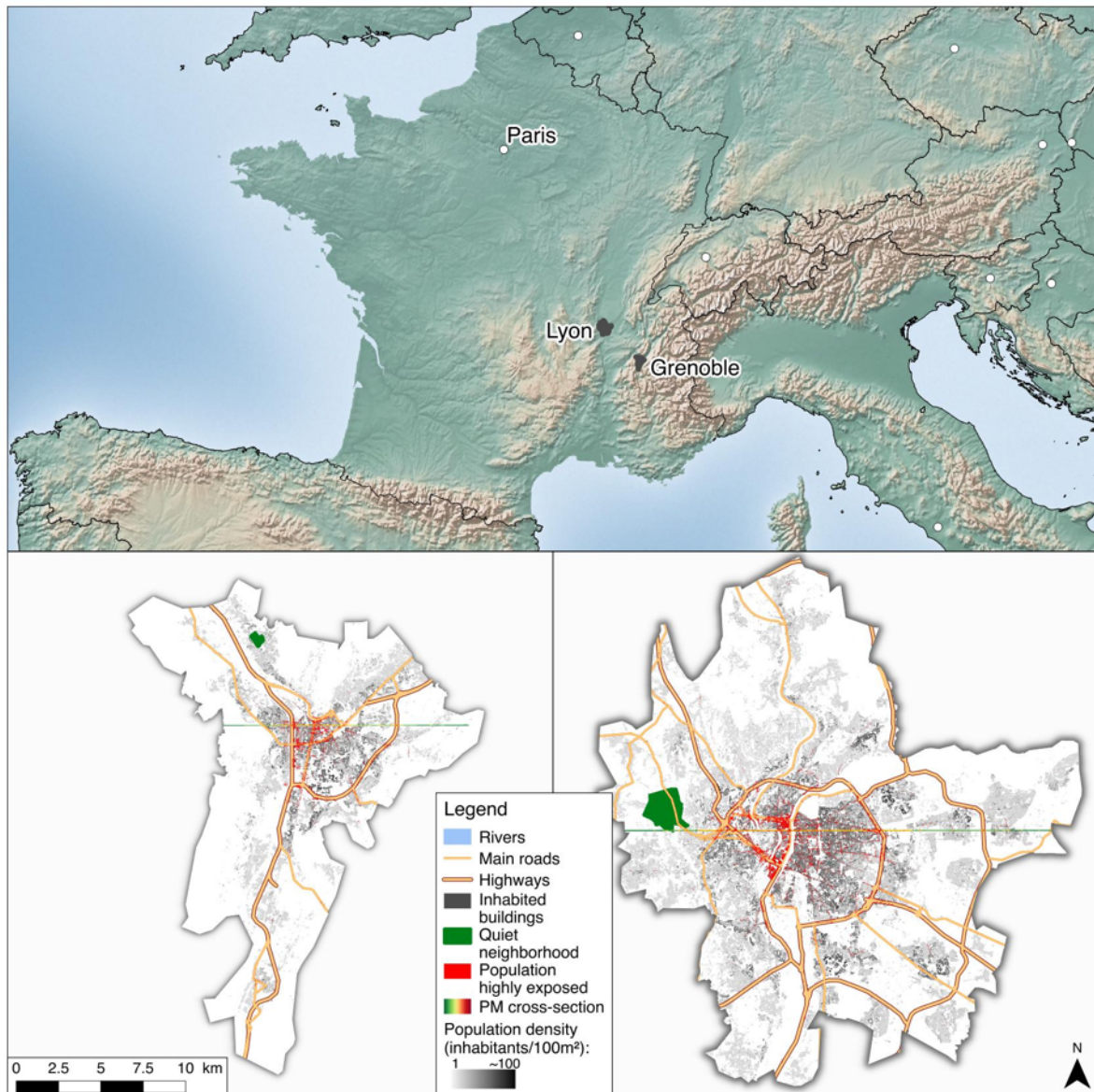
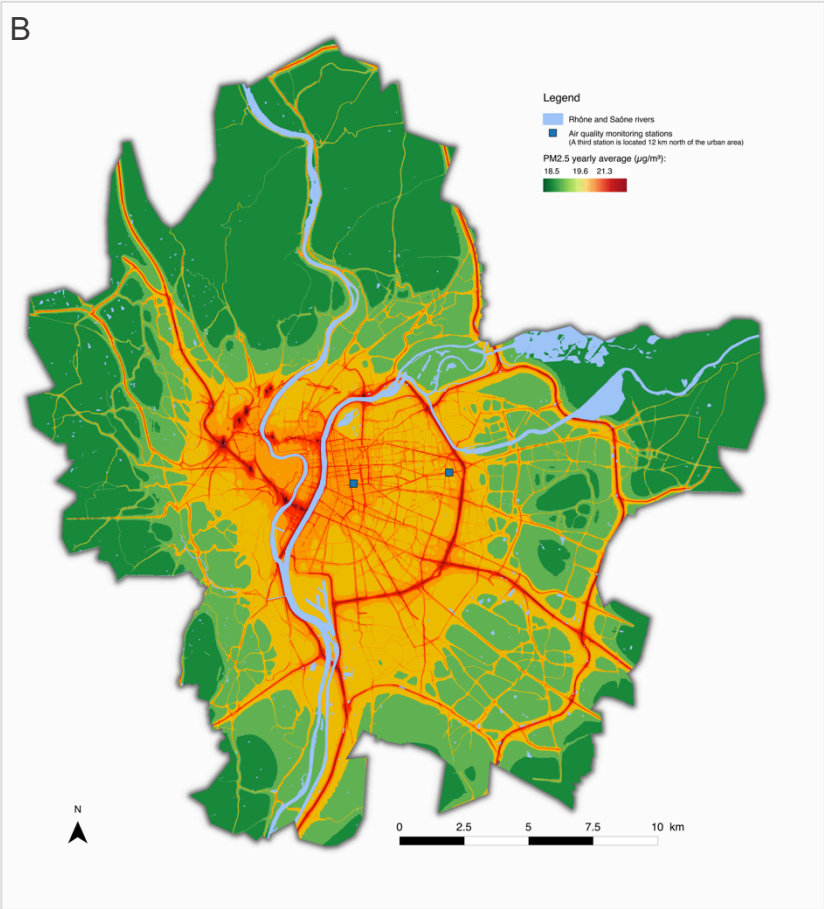
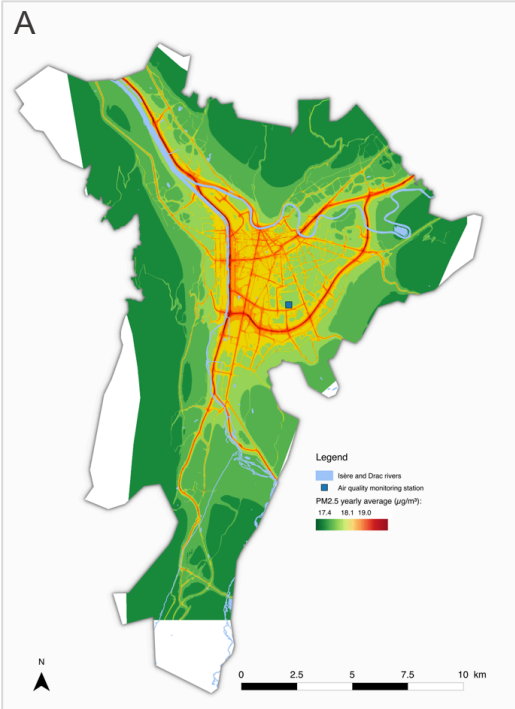


Figure 2: Air pollution models in Grenoble (A) et Lyon (B) urban areas, and population exposure (PM_{2.5} yearly averages for the year 2012).

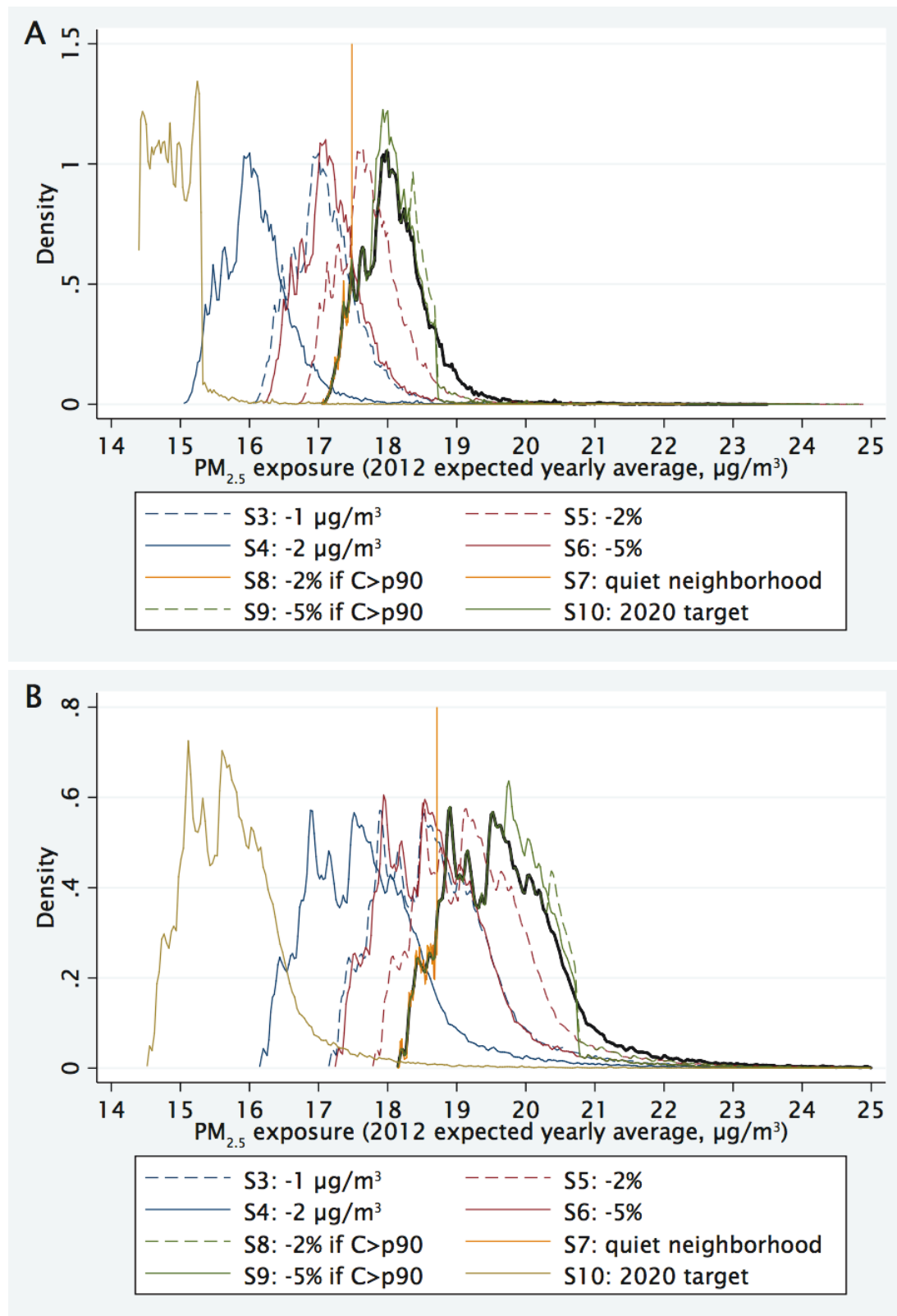


3.2 Changes in air pollution and expected health benefits of the scenarios

The expected distributions of population exposures under each scenario are displayed in [Figure 3](#) and [Table 3](#). Decreases in median PM_{2.5} levels were strongest for the WHO (S1) scenario followed by the S10 scenario (“2020 target”), while it did not vary for S2 (compliance with the current EU yearly limit) and S8 (decrease by 2% for the 10% most exposed subjects) scenarios.

The predicted health benefits associated with each air pollution reduction scenario are shown in [Table 3](#). The WHO scenario (S1) entailed the largest number of prevented disease cases, with a burden of disease reduced on the long-term by 5.1% (Grenoble urban area) to 6.0% (Lyon urban area) for mortality, 6.8% for lung cancer (Grenoble only) and 23.6 (Grenoble) to 27.6% (Lyon) for term low birth weight incidence. The scenario inspired by the 2008 EU directive (S10, or “2020 target”) was the second scenario in terms of amplitude of the reduction in exposure levels, and hence in health benefits, with 2.0–2.4% of avoided cases for mortality, depending on the urban area, which corresponds to approximately 40% of the WHO (S1) scenario. Since only a marginal fraction of the population was exposed above the EU yearly limit, no health benefits were expected under the scenario (S2) in which all the population above the yearly regulatory limit was brought down to an exposure equal to this limit. To reach 10% of the health benefit of the WHO scenario, PM_{2.5} yearly averages had to be decreased by at least 5%, which corresponded to S4 scenario ([Table 3](#)).

Figure 3: Population exposure for each scenario of reduction of PM_{2.5} concentration in the Grenoble (A) and Lyon (B) urban areas. The black curve indicates the distribution observed (modeled) for 2012 (reference year).



In the legend, *C* represents the concentration threshold, namely the 90th percentile of the exposure, above which the air pollution levels are decreased. The *quiet neighborhood* is the neighborhood with a median exposure level ranked as the 10th percentile the least exposed (illustrated by the orange curves attaining infinite density at the PM_{2.5} exposure level corresponding to the quiet neighborhood median exposure).

Table 3: Estimated effects of the scenarios in terms of population exposure to fine particulate matter (PM_{2.5}) and health benefit.

Health event and scenario	PM _{2.5} exposure (µg/m ³): 5 th –50 th –95 th percentile	Health benefit in number of avoided cases (NAC)											
		Non-accidental mortality				Lung cancer incidence				Term low birth weight			
		NAC	(% of total)	95% CI	(% of total)	NAC	(% of total)	95% CI	(% of total)	NAC	(% of total)	95% CI	(% of total)
Grenoble area (n=385,000)	17.4–18.1–19.0												
S1 “WHO” ^a	10.0–10.0–10.0	114	5.1%	71–157	3.2–7%	13.2	6.8%	6.1–19.7	3.1–10.1%	31.4	23.6%	12–49.4	9–37.1%
S2 “EU” ^b	17.4–18.1–19.0	0	0	0–0	0–0%	0	0	0–0	0–0%	0	0	0–0	0–0%
S3 “-1 µg/m ³ ”	16.4–17.1–18.0	14	0.6%	9–19	0.4–0.8%	1.6	0.8%	0.7–2.3	0.4–1.2%	3.4	0.2%	1.4–5	1–3.7%
S4 “-2 µg/m ³ ”	15.4–16.1–17.0	28	1.2%	18–38	0.8–1.7%	3.2	1.6%	1.5–4.6	0.8–2.4%	7	0.3%	2.8–10.2	2.1–7.6%
S5 “-2%”	17.0–17.7–18.6	5	0.2%	4–7	0.2–0.3%	0.3	0.2%	0.2–0.8	0.1–0.4%	1.2	0.1%	0.5–1.8	0.4–1.3%
S6 “-5%”	16.5–17.2–18.0	13	0.6%	8–17	0.4–0.8%	1.4	0.7%	0.7–2.1	0.4–1.1%	3.1	0.1%	1.3–4.5	1–3.4%
S7 “quiet neighborhood”	17.4–17.5–17.5	9	0.4%	6–12	0.3–0.5%	1	0.5%	0.5–1.5	0.3–0.8%	2.2	0.1%	0.9–3.1	0.7–2.3%
S8 “-2% p90”	17.4–18.1–18.7	1	0.0%	1–1	0–0%	0.1	0.1%	0–0.1	0–0.1%	0.1	0.0%	0–0.2	0–0.1%
S9 “-5% p90”	17.4–18.0–18.6	1	0.0%	1–2	0–0.1%	0.1	0.1%	0–0.2	0–0.1%	0.3	0.0%	0.1–0.5	0.1–0.4%
S10 “2020 target”	14.4–14.9–15.3	45	2.0%	28–61	1.2–2.7%	5.2	2.7%	2.4–7.6	1.2–3.9%	11.5	8.6%	4.6–17	3.4–12.8%
Lyon area (n=1,220,000)	18.5–19.6–21.3												
S1 “WHO” ^a	10.0–10.0–10.0	491	6.0%	305–675	3.7–8.3%					131	27.6%	51–202	10.8–42.6%
S2 “EU” ^b	18.5–19.6–21.3	0	0	0–0	0–0%					0	0	0–0	0–0%
S3 “-1 µg/m ³ ”	17.5–18.6–20.3	49	0.6%	31–66	0.4–0.8%					12	2.5%	5–16	1.1–3.4%
S4 “-2 µg/m ³ ”	16.5–17.6–19.3	98	1.2%	62–134	0.8–1.6%					24	5.0%	10–33	2.1–7.0%
S5 “-2%”	18.2–19.2–20.9	19	0.2%	12–26	0.2–0.3%					5	1.1%	2–6	0.4–1.3%
S6 “-5%”	17.6–18.6–20.3	48	0.6%	30–65	0.4–0.8%					12	2.5%	5–16	1.1–3.4%
S7 “quiet neighborhood”	18.5–18.7–18.7	51	0.6%	32–69	0.4–0.9%					12	2.5%	5–16	1.1–3.4%
S8 “-2% p90”	18.5–19.6–20.9	2	0.0%	1–2	0.0–0.0%					1	0.2%	0–1	0.0–0.2%
S9 “-5% p90”	18.5–19.6–20.6	5	0.1%	3–7	0.0–0.1%					2	0.4%	1–2	0.2–0.4%
S10 “2020 target”	14.8–15.7–17.1	195	2.4%	122–266	1.5–3.3%					48	10.1%	20–69	4.2–14.6%

^a 10 µg/m³ for PM_{2.5} (yearly averages). ^b 25 µg/m³ for PM_{2.5} (yearly averages).

4. Discussion

4.1 Summary

We investigated the health impact of hypothetical reductions in fine particulate matter air pollution in two urban areas. We considered ten hypothetical scenarios of reductions of the $PM_{2.5}$ concentrations. We relied on a fine-scale dispersion model estimating concentrations with a 10 m resolution, coupled to knowledge of the population density at the same scale. A decrease down to the World Health Organization (WHO) air quality guideline level would entail a decrease in mortality by 5.1 to 6.0%, according to the area. A urban area wide reduction of at least 5% of the $PM_{2.5}$ levels would be needed to reach 10% of the effects that a decrease down to the World Health Organization (WHO) air quality guideline levels would have.

4.2 Challenges in the assessment of the efficacy of interventions aiming at improving air quality

Fensterer et al. (2014) reported that the expected decrease of PM_{10} levels following the LEZ enforcement was uneasy to estimate given the lack of monitoring stations covering both time periods “before–after”. Furthermore, Cesaroni et al. (2012) acknowledged underestimated health benefits of the LEZ since only the population living next to high-traffic roads was considered in the “before–after” comparison, while background decreases of air pollutants concentrations may have led to larger health benefits.

A recent review by Holman et al. (2015) investigated the efficacy of the European LEZ. The authors highlighted the role of confounding factors in the evaluation of the difference of concentration in air pollutants at different times, such as weather, selected sampling days or the car park renewal by incentive measures, which cannot always be taken into account. The question of the pollutant is also raised by the authors, who suggest that relying on more traffic-component specific pollutants such as carbonaceous particles (BC, EC, Abs.) may emphasize

the effect of the LEZ. For these reasons, an approach based on theoretical scenarios like ours is a useful complement to the monitoring of the efficiency of real measures. Generally, such theoretical scenarios allow focusing on the specific effect of the measure implemented, assuming that all other factors (e.g., meteorological conditions) remain similar. Such an approach can provide an order of magnitude in the reduction of air pollution for planned policy measures to be efficient from a public health point of view.

4.3 Can specific interventions lead to strong benefits?

In a review not limited to low emission zones, Henschel et al. (2012) reported the health impact of various interventions that led to decreases in air pollution (also considering measures that were not planned as a way to reduce air pollution, such as a strike in factory). The interventions considered resulted in significant decreases of adverse health events, such as the 1986 Utah Valley strike, the 1990 Irish coal ban or the 1996 and 2008 Summer Olympic Games (OG). The amplitude of the decreases in air pollutants levels ranged from 16.3% less PM_{10} in Atlanta one month after the OG compared to one month before (Friedman et al., 2001), to a 50% decrease of winter PM_{10} levels in Utah Valley after closure of the steel mill (Pope, 1989), and also up to to a 70% decrease in black smoke (BS) concentrations after the Dublin coal ban (Clancy et al., 2002). In the case of the Beijing 2008 Olympic games, PM_{10} concentrations in the period from August, 8th to September, 24th (the period of the 2008 Olympic Games) decreased from about 130 down to about 60 $\mu\text{g}/\text{m}^3$ (Rich et al., 2015). For $PM_{2.5}$, a report suggested that new regulations on residential wood burning in two urban areas of California led to a decrease in $PM_{2.5}$ concentrations in the 13–14% range (Lighthall et al., 2009). In addition, a study conducted in Japan reported a decrease in $PM_{2.5}$ concentrations of 49.8% between 2010 and 2001, when a new traffic-related regulation policy had been introduced (Hara et al., 2013).

This illustrates that specific measures, sometimes targeted on several sources of pollution simultaneously, can allow achieving a significant reduction of air pollutants, on the short or long term. By comparison, it seems that some of the LEZ implemented in Europe have led to more modest improvements in air quality, despite the difficulty to observe global reductions of the concentrations in air pollutants for which road traffic is not the only source. For example, the London LEZ –or congestion charging scheme– led to a decrease in PM₁₀ concentrations of 0.8% inside the LEZ perimeter and 0.1% outside (Tonne et al., 2008, 2010), although another study based on a single monitoring station could not conclude on an effect of the LEZ on air pollution levels (Atkinson et al., 2009). In Germany, a study adjusting for several confounding factors showed that the LEZ and truck transit ban in Munich led to a decrease of 5 to 13% in PM₁₀ concentrations depending on the traffic proximity of the monitoring stations (Fensterer et al., 2014). In addition, traffic generates both air pollution and noise. A reduction of traffic-related air pollution could also reduce road traffic noise. No joint air pollution and noise dose-response function exists to date, but one could say that traffic-related regulations may lead to decrease in noise levels, and hence its associated health burden.

4.4 Impact of air pollution interventions on environmental justice

In a previous study (Morelli et al., in revision), we relied on the same fine-scale approach to stratify the exposure to fine particulate matter and attributable risk depending on a social deprivation index. Social deprivation was assessed with the European Deprivation Index (Pornet et al., 2012), for which data are available at the IRIS –or neighborhood–, which is the finest geographical census unit. In the present study, most of the hypothetical intervention scenarios consisted in absolute or relative decreases which would not change the distribution of the exposure facing social deprivation. However, two of our scenarios could lead to a substantial distortion of this distribution by social deprivation, namely the “quiet

neighborhood” and the “2020 target” scenarios. Further investigations are needed to assess the impact of these hypothetical interventions on the social deprivation facing air pollution.

To our knowledge, few studies investigated the impact of air pollution intervention policies on social deprivation or socioeconomic status, and none considered the future impact of hypothetical scenarios on environmental justice. Tonne et al. (2008) estimated the health benefits expected from the London low emission zone (LEZ) with a dispersion model, and stratified the exposure according to socioeconomic data. Inside the LEZ perimeter, the authors found an increase of years of life gained, while the impact at the urban area scale was rather limited. The most deprived areas were exposed to higher NO₂ and PM₁₀ levels but benefited more of the reductions of air pollution and hence of the associated increase in years of life. The results of the Health Impact Assessment (HIA) conducted by Cesaroni et al. (2012) in Rome were opposite in terms of social deprivation, the population less deprived being exposed to higher concentrations of NO₂ and PM₁₀, and benefiting the most from the LEZ. The authors reported similar figures in terms of years of life gained at the city scale compared to the within-LEZ perimeter. To our knowledge, no other studies investigated the socioeconomic inequalities following an enforced low emission zone.

4.5 Conclusion

This study evaluated the health benefits of scenarios aiming at reducing air pollution in urban areas. Such results can provide indications of the air quality improvement to target in order to significantly improve public health. Reductions of at least 5% for all citizens would allow a substantial public health gain. We showed that in the two French urban areas considered, no health benefits could be expected by complying to the EU air quality limit value. In that regard, Brunekreef et al. (2015) raise the issue of air quality regulation in Europe. The authors remind that the European current limit value for PM_{2.5} of 25 µg/m³ was set in 2008, which is three

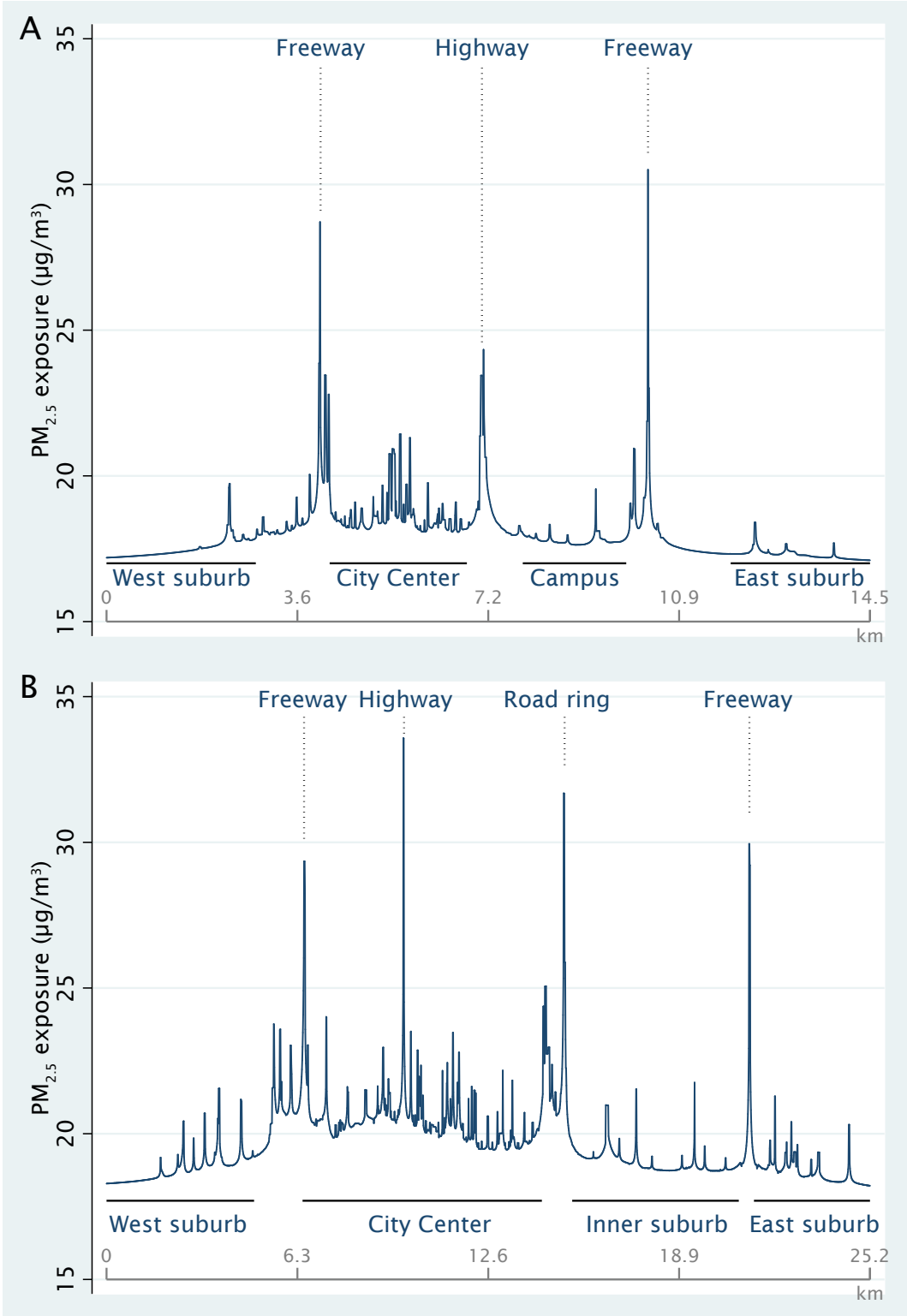
years after the 2005 WHO Global Update providing a guideline value of $10 \mu\text{g}/\text{m}^3$. In addition, the $25 \mu\text{g}/\text{m}^3$ limit value from the 2008 EU directive was supposed to be amended in 2013 with the introduction of more severe $\text{PM}_{2.5}$ limit values to be attained by 2020, but such disposition was eventually withdrawn. Our last scenario, “2020 target”, corresponded to these measures, and showed the most prominent health benefits considering the difficulty to achieve $\text{PM}_{2.5}$ yearly averages corresponding to the WHO air quality guideline. Revision of European air quality limit values before 2020-2030 –or implementation of measures far more ambitious than the EU regulation– appears as crucial in regard to the current burden of disease due to outdoor air pollution and the advances of other developed countries in that matter.

Acknowledgements

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Supplemental material

Figure S1: Cross-section in a horizontal west-east axis of the dispersion model in Grenoble (A) and in Lyon (B; PM_{2.5} 2012 yearly averages).



General discussion

1. Summary

There were three main objectives in this thesis. The first aim was to study the short-term measurements of traffic noise, ultrafine particles concentrations and traffic flows, by considering the correlations of these measurements at different periods (repeatability over time), and between simultaneous measurements. We showed that in three European cities, very brief (20 min) measurements of noise and traffic flows were stable over time, but this was not the case for 20-min measurements of ultrafine particles concentrations. Simultaneous measurements of noise and ultrafine particles concentrations were moderately correlated, while those of noise and traffic flows were better correlated; the simultaneous measurements of ultrafine particles concentrations and traffic flows exhibited the lowest correlations. These results emphasize the challenge of modeling short-term exposure to ultrafine particles in epidemiological studies, and to develop models of long-term exposures on the basis of a small number of brief UFP measurements. Conversely, the stability of short measurements of noise opens the way for developing longer-term models on the basis of short noise measurements.

The second aim of this thesis consisted mainly in a risk assessment study of fine particulate matter (PM_{2.5}) on the health of the citizens in two French urban areas, by relying on a spatially resolved air pollution and population density modeling approach. We quantified the attributable risk of PM_{2.5} on all-cause mortality, lung cancer and term low birth weight incidence in terms of number of cases attributable to air pollution exposure. Our fine-scale estimation of the exposure allowed catching the street-scale spatial contrasts; the approach relying on background air quality monitoring stations is likely to underestimate the number of disease cases attributable to air pollution, a result of practical importance given that most risk assessment studies at the city-scale rely on this approach. Regarding the spatial resolution of

cases, representing the lung cancer incident cases at the neighborhood, the finest spatial scale available, did not change the estimated number of cases attributable to PM_{2.5}. We also investigated the possible social gradients in the exposure to air pollution and its attributable risk, at the neighborhood scale. Although the two study areas had different spatial distributions of the social deprivation across the urban area, the neighborhoods with an intermediate level of social deprivation, corresponding to the 5th to 7th decile of the index, were exposed to highest PM_{2.5} concentrations in both areas. The least deprived neighborhoods, and to a lesser extent the most deprived neighborhoods, were less exposed to fine PM. Stratification of the attributable risk on the social deprivation showed similar figures, excepted for the incident lung cancer cases attributable to air pollution, since the distribution of these cases varied depending on the neighborhood.

The third aim was to perform a health impact assessment of different hypothetical scenarios of air pollution reductions in the two areas considered in Chapter II. The health benefits varied significantly depending on the scenario. The WHO guideline value for PM_{2.5} was not respected in both urban areas, indicating that more severe regulations should be enforced. A reduction of 5% of fine particulate matter concentrations in the whole urban area would correspond to approximately 10% of the health benefits expected from a reduction to the 10 µg/m³ air quality guideline proposed by the WHO. Achieving the 2020 “target” values once proposed by a 2008 EU directive –for which the enforcement has been removed from schedule– could allow reaching 40% of the health benefits of a compliance with WHO air quality guideline.

2. Disentangling the health effects of noise and ultrafine particles

2.1 Modeling ultrafine particles levels

We described and investigated the relationships between 20-min short-term measurements of noise, traffic flows and ultrafine particles (Chapter I). We showed that short-duration measures of ultrafine particles concentrations (UFP) have very high temporal variations. A large part of this temporal variability is probably explained by meteorological factors. For etiologic studies, UFP appear as an interesting marker of urban air pollution exposure, as it can represent 90% of the number of outdoor particulate matter while excluding the coarse particles, less relevant for the study of traffic-related exposures (Geiser et al., 2005). However, exposure assessment of UFP is a methodological challenge. On the one hand, monitoring stations are probably not appropriate to assess the population exposure in urban areas because of the very strong spatial contrasts in UFP levels, which quickly decrease as one gets further from sources (Sioutas et al., 2005). Land-Use Regression (LUR) modeling may be an alternative for modeling of UFP concentrations, theoretically allowing to capture spatial contrasts. Our results indicate that very short measurements have strong temporal variability, indicating that (possibly) many repeated measures (over possibly longer durations than ours) would be required to build a LUR model, which requires a good estimate of the yearly level at each location.

Several LURs have already been used to model concentrations in NO₂, PM₁₀ or PM_{2.5}, volatile organic compounds (VOC) and sometimes others pollutants (Hoek et al., 2008; Eeftens et al., 2012). For UFP, LUR models have been first proposed in Amsterdam (Hoek et al., 2011) and Vancouver (Abernethy et al., 2013). In this last study, the authors relied on 80 mobile sampling sites, 4 fixed stations with a continuous monitoring for temporal correction purposes, 135 predictor variables and other meteorological variables. The leave-one-out cross validation (LOOCV) R² of the model was 0.32, which is not satisfying, and tends to confirm that developing LUR models for UFP is challenging, at least in some areas. In the Amsterdam and

Rotterdam areas, Montagne et al. (2015) relied on short-term (30 min) monitoring campaigns in three different seasons and at 81 and 80 sites to develop a LUR model for UFP, with a R^2 in the 0.33–0.42 range. By comparison, for $PM_{2.5}$, R^2 in the 0.6–0.8 range are often obtained (Eeftens et al., 2012). Moreover, Basagana et al. (2012) have warned against the optimism of cross-validation R^2 with a limited number of measurement sites. Although authors considered that “short-term monitoring campaigns may be an efficient tool to develop LUR models” (Montagne et al., 2015), a LOOCV R^2 as low as 0.3–0.4 may entail a large amount of exposure misclassification in epidemiological studies. The impact on dose-response functions may be limited if the error structure is assumed to be of Berkson-type, but it is unclear whether the assumption of a purely Berkson-type error holds.

2.2 Modeling the road traffic noise

Short-term noise measurements were much more stable over time than the UFP measurements, implying that a small number of short-term noise measurements could allow providing an accurate estimate of the yearly outdoor noise estimate in a given location. This paves the way for LUR noise models, a development that we have considered in the context of the Tri-Tabs project upon which Chapter I is based. While many LUR models have been developed in the past to assess exposure to air pollution, and used in epidemiological studies, LUR models have very little been considered as a relevant tool to assess noise exposure. In Europe, strategic maps of the long-term noise levels are enforced by the European Noise Directive (2002/49/EC). However, such maps are not always available depending on the city size –which must have more than 100,000 inhabitants; also, the model quality may vary. In a study conducted as part of the Tri-tabs research project, Aguilera et al. (2015) developed a LUR model for noise in three cities; such a model had been only developed once before, in China (Xie et al., 2011). Aguilera et al. (2015) showed that short-term measurements of noise were correlated to long-term

estimates of the regulatory maps, and that a land-use regression model based on land characteristics alone was able to model noise levels accurately compared to the long-term estimates of noise generated by the strategic maps. When it comes to etiologic studies of noise effects, one should however keep in mind that outdoor noise levels may strongly differ from personal noise exposure. In a study in Girona, Spain, Foraster et al. (2014) considered NO₂, outdoor and an estimate of indoor noise, and their potential effects on blood pressure. Associations of noise with blood pressure adjusted for NO₂ levels strongly differed according to whether outdoor or indoor (night) noise levels were considered, which implies that developing good quality models for outdoor noise is possibly not enough for etiologic studies. Alternatives include indoor models derived from outdoor models and information on isolation and window opening habits (Foraster et al., 2014), as well as reliance on noise-meters.

2.3 Combination of air pollution and noise, and effects on health

Based on a cohort study, Foraster et al. (2014) investigated the associations between long-term, annual average exposure to nitrogen dioxide (NO₂) and blood pressure as well as hypertension, while adjusting for traffic noise. Associations between noise and hypertension as well as high blood pressure have been found in past studies, however noise could act as a confounder in the association between NO₂ and these cardiovascular disease markers. Nonetheless, results showed that outdoor traffic noise levels did not impact the relationship between NO₂ and the cardiovascular markers. Several hypotheses could be drawn to explain such a result, which might be due to the specific noise conditions in the Spanish city and its consequences in term of personal behaviors at the home addresses, to both measures of NO₂ and indoor noise suffering from exposure misclassification, or each corresponding to a proxy of an unmeasured exposure such as UFP exposure.

Other adverse health events may be affected by both air pollution and noise. For example, Gehring et al. (2014) investigated the relationship on these two markers with five pregnancy outcomes (small size for gestational age birth weight, preterm birth, very preterm birth, term low birth weight and crude birth weight). In a previous study with a similar setup, the authors found that traffic-related air pollution was associated with three birth outcomes (small size for gestational age, very preterm birth and term low birth weight); in the currently described study considering traffic-related noise, the authors found associations with three birth outcomes (small size for gestational age, term low birth weight, crude birth weight, but not very preterm birth). In another model combining noise and air pollution exposure, the authors found an association of these joint exposures with small size for gestational age; in addition, the association between noise and birth weight was unchanged after adjustment for air pollution exposure, while the association between air pollution and birth weight was attenuated by adjustment on noise. These results indicate that air pollution alone may not be a sufficient marker to address the effects of traffic-related exposures on birth outcomes, and that simultaneously considering noise in studies on pregnancy outcomes appears crucial.

2.4 Beyond the traffic-related bivariate exposure: the Exposome

The concept of exposome consists in a new paradigm for the study of the impact of environment on health (Wild, 2005; Vrijheid, 2014). The Exposome encompasses all environmental exposures, from conception and forward through lifetime, and thus complementing the genome. An example of early-life project related to the exposome is the Helix research framework. This project aims at improving the exposure assessment techniques in order to gather environmental exposure data as well as biomarkers samples in order to investigate its effects on child health outcomes (Vrijheid et al., 2014). The exposome concept requires to move forward in some fields of the epidemiological research, which includes a challenging assessment of various

environmental exposures. One could say that this –large– step flows logically from the efforts described above regarding the exposure to both traffic noise and traffic-related air pollution, the –big– difference residing in the much larger number of additional factors to be taken into account.

An example of approach related to the spirit of the exposome concept is a study that was conducted by Dadvand et al. (2014) on term low birth weight. Starting from the body of evidence in the literature suggesting an impact of the proximity of the pregnant woman home to major roads on term low birth weight, the authors investigated the possible role of air pollution, heat, noise and green space in this association. Exposure to each of these factors was assessed, as well as their possible effect on the risk of term low birth weight (LBW). The authors found an association between term LBW and maternal residential proximity to major roads, but also with heat and air pollution exposure (during the third trimester). An estimated upper limit of approximately 33% of the association between proximity to major roads and term low birth weight could be explained by the exposure to heat and particulate matter (PM_{10} , $PM_{2.5}$, $PM_{2.5-10}$). No buffer effect could be attributed to green space –or road-adjacent tree coverage– on the main association between major roads and term LBW. Moreover, the authors suggest that future studies related to the predicted changes in climate may need to address methodological challenges such as a fine-scale assessment of temperature.

Once a clearer picture of the respective contributions of specific air pollutants, noise, temperature, green space exposure is available, risk assessment studies simultaneously considering these factors altogether could be envisaged. Since there is to our knowledge no clear estimate of the simultaneous effects of noise and $PM_{2.5}$ on mortality, we chose to restrict our risk assessment study (Chapter II) to $PM_{2.5}$.

3. Relevance of fine-scale models for risk assessment

3.1 Impact of the methodological improvements

One of the key aims of our study (Chapter II) was to attempt translating the benefits of fine-scale air pollution models to risk assessment studies. We relied on a fine-scale exposure modeling approach with a spatial resolution corresponding to the street scale, while previous studies had a 100-m resolution, or less fine (e.g. a 50×50 km grid for the CAFE study, with a few exceptions for some areas where finer models were available). Until recently, most risk assessment and health impact assessment studies in urban areas relied on a station-based modeling approach. Such an approach is known to suffer from exposure misclassification as it assumes that all people from a given area are exposed to the same air pollutants levels monitored by the air quality monitoring stations (Jerrett et al., 2005). Larger scale studies rely also on satellite-based data, such as the global burden of disease study (Lim et al., 2012), for which the worldwide particulate matter concentrations were estimated on a 0.1×0.1° grid, which corresponds roughly to a 11×11 km grid at equator (and a slightly better spatial resolution when moving towards the poles).

We confirmed the existence of this bias and showed, in two French urban areas, that the underestimation of the attributable risk is in the 10–20% range. Health impact assessment studies conducted in large areas, from the country scale to the worldwide scale, cannot rely yet on advanced, fine-scale modeling techniques for technical reasons (data availability, computing time, database management). Therefore, the (global) burden of disease could be considered underestimated, in particular in urban areas, as discussed by Cohen et al. (2005) in a short paper about the global burden of disease (GBD) study of outdoor air pollution, and by Brauer et al. (2012) in a study of the exposure assessment for estimating the GBD attributable to outdoor air pollution. In this case, the underestimation of the attributable risk would probably not be in 10–20% range since the worldwide study setup is not comparable to the urban setting of Grenoble

and Lyon urban areas. However, for urban settings similar to our study areas, our tool could be used in the future to assess the attributable risk of other health outcomes, and also the health impact of air pollution interventions. Some authors argue that risk assessment studies should keep on relying on background monitoring station measures because effect estimates (relative risks or odds-ratios) have been estimated in studies relying on such exposure assessment strategies. We tend to consider that this choice is not justified, for two reasons: first, more and more etiologic studies have relied on fine scale air pollution models, so that ORs and RRs available from fine scale models are now available (Jerrett et al., 2009; Raaschou-Nielsen et al., 2013; Beelen et al., 2014). Second, even for a study relying on background station(s), the reliance on stations is expected to induce Berkson-type error (Nieuwenhuijsen, 2015). Berkson-type error is expected not to bias dose-response functions, so that the dose-response function is expected to be similar to that would be obtained from a finer-scale model such as a LUR model; in this case, there is no objection to translating the effect estimate into an attributable risk by assessing exposure through a fine-scale exposure model.

3.2 Air pollution interventions: public health perspectives

Some pollutants are exogenous and come from other regions or countries, hence no particular action at the urban area scale can be taken to limit this pollution. Emissions from local sources such as road traffic can be limited through the implementation of local actions. A first important tool consists in imposing limitations to the pollutants emissions for the newly produced vehicles (which corresponds to the Euro norm in the EU). Regulation on the content of diesel and gasoline is also an important line of action, as shown for example by the ban of lead in gasoline in the USA and Europe, effective in France around the year 2000. The executive power can also accelerate the truck and car park renewal through breaker's yard bonus or adjusted taxations favoring vehicles emitting less pollution. Another possibility consists in reducing the

traffic flows through promoting a less car-dependent mobility (public transport, bike, walking, carpools), acting on the transport of merchandises (development of logistic platforms, railroute) or generating less travel needs by means of a more efficient town planning.

In 2009, the European Commission (EC) initiated a first litigation against France and several countries across Europe for not respecting the air quality limit values for different atmospheric pollutants which exceeded the annual averages stated in the Directive 2008/50/EC (European Union (Official Journal), 2008). In France, most of the urban areas were concerned by this litigation, which targeted the nitrogen dioxide (NO₂) and particulate matter with an aerodynamic diameter of less than 10 µm (PM₁₀). A reasoned opinion was addressed in late 2010 by the EC, followed in mid-2011 by a seizure of the Court of Justice of the European Union (CJEU). The seizure was eventually dismissed, while the French government was initiating in the mean time an ambitious draft law, or *Loi Grenelle II* (French Republic (Official Journal), 2010), instigating serious actions against air pollution, namely the low emission zones (LEZ), or *Zones d'Actions Prioritaires pour l'Air (ZAPA)*. Eight urban areas participated in the experiment, including Grenoble and Lyon urban areas¹. However, the 2015 expected NO₂ and PM_{2.5} levels, calculated by *Air Rhône-Alpes* in 2013 for 2 LEZ scenarios plus a baseline, “no action” scenario, showed that the air pollutants concentrations were barely, if at all, affected by the LEZ. The question remains also as to the feasibility of implementing several LEZs across France without national framework, in opposition to other countries such as Germany, Sweden or the Netherlands. The LEZ provision of the *Grenelle II* law was ultimately cancelled in late 2012, partly due to suspected socio-economic disparities facing the enforcement of LEZs. Our study shows that the association between socioeconomic status and the health risk attributable to air pollution exhibits a complex pattern, and that detailed studies considering both the costs

¹ List of experimenting urban areas: Paris, Plaine Commune (north of Paris), Grand Lyon, Grenoble-Alpes Metropole, Pays d'Aix, Clermont Communauté, Nice Côte d'Azur and Communauté Urbaine de Bordeaux.

of the implementation of LEZ in each social class, and the expected benefit, would be required to analyze LEZ projects in terms of environmental justice. In 2013, the European Commission reinitiated its litigation against France for not respecting air pollution limit values, in addition to lacking implementing air pollution interventions. LEZ projects may be developed in the future, based on new powers given to mayors and urban areas to restrict traffic based on emission levels, in the context of the law on energetic transition (French Republic (Official Journal), 2015). To date, and considering the intense media coverage, the public debate regarding the nature of future scenarios of air pollution interventions is actively maintained.

At the beginning of this PhD (2012), no local air pollution interventions policies aiming at reducing the air pollution levels, such as low emission zones, were enforced in France, and none is currently considered at a stage as advanced as was the “ZAPA” experiment before its termination. The only exception relates to the short-term air pollution events (i.e. peaks) and consists in different levels of public information and action, depending on which threshold of concentration in air pollutant is reached. Such measures include, but are not limited to, free access to public transportations, reductions of the speed limits around urban areas (130, 110 or 90 km/h speed limits reduced to 70 km/h), or, during the most severe peaks of air pollution like in Paris during spring, a light vehicles circulation limited to approximately half the total car park, depending on the parity of the license plate number. These actions are enforced by each regional administration (*Préfecture*) and have been harmonized at the country scale in 2014 by a ministerial order (French Republic (Official Journal), 2014). To our knowledge, very few studies have investigated the effects of such measures on short-term peaks of air pollution; their impact is expected to be limited (HCSP, 2012). In addition, several methodological issues (e.g. confounding factors such as the weather or the emission level of the circulating car park) may limit the assessment of the effectiveness of the public interventions in term of reduction of long term air pollution, and hence the health impact, attributable to the intervention. The difficulty

to assess the effects of enforced low emission zones strengthen this observation, as described in a recent review of LEZs across Europe (Holman et al., 2015).

Another issue relates to future air pollution regulations in Europe. As discussed by Brunekreef et al. (2015), the European Commission showed rather unambitious figures of particulate matter concentrations to be targeted by 2020. Since no threshold exists below which the health effects of air pollution cease to exist, such lack of political will may, without doubt, delay public interventions aiming at reducing the population exposure.

References

Abernethy RC, Allen RW, McKendry IG, Brauer M. A land use regression model for ultrafine particles in Vancouver, Canada. *Environ Sci Technol*. 2013 May 21;47(10):5217–25.

ADEME. Les zones à faibles émissions (Low Emission Zones) à travers l'Europe : Déploiement, retours d'expériences, évaluation d'impacts et efficacité du système. [Internet]. 2014 [cited 2015 Oct 16]. Available from: <http://www.ademe.fr/sites/default/files/assets/documents/zones-faibles-emissions-low-emission-zones-lez-travers-europe-2014.pdf>

Aguilera I, Foraster M, Basagaña X, Corradi E, Deltell A, Morelli X, et al. Application of land use regression modelling to assess the spatial distribution of road traffic noise in three European cities. *J Expo Sci Environ Epidemiol*. 2015 Jan;25(1):97–105.

Allen RW, Davies H, Cohen MA, Mallach G, Kaufman JD, Adar SD. The spatial relationship between traffic-generated air pollution and noise in 2 US cities. *Environ Res*. 2009 Apr;109(3):334–42.

Atkinson RW, Barratt B, Armstrong B, Anderson HR, Beevers SD, Mudway IS, et al. The impact of the congestion charging scheme on ambient air pollution concentrations in London. *Atmospheric Environment*. 2009 Nov;43(34):5493–500.

Babisch W. Cardiovascular effects of noise. *Noise Health*. 2011 May-Jun;13(52):201–4.

Babisch W. Exposure to environmental noise: risks for health and the environment. Workshop on “sound level of motor vehicles”. Directorate General for Internal Policies of the European Parliament, Brussels. [Internet]. 2012 [cited 2015 Oct 16]. Available from: <http://www.europarl.europa.eu/document/activities/cont/201205/20120524ATT45762/20120524ATT45762EN.pdf>

Baccini M, Biggeri A, Grillo P, Consonni D, Bertazzi PA. Health impact assessment of fine particle pollution at the regional level. *Am J Epidemiol*. 2011 Dec 15;174(12):1396–405.

Ballester F, Medina S, Boldo E, Goodman P, Neuberger M, Iñiguez C, et al. Reducing ambient levels of fine particulates could substantially improve health: a mortality impact assessment for 26 European cities. *J Epidemiol Community Health*. 2008 Feb;62(2):98–105.

Basagaña X, Rivera M, Aguilera I, Agis D, Bouso L, Elosua R, et al. Effect of the number of measurement sites on land use regression models in estimating local air pollution. *Atmospheric Environment*. 2012 Jul;54:634–42.

Basner M, Babisch W, Davis A, Brink M, Clark C, Janssen S, et al. Auditory and non-auditory effects of noise on health. *Lancet*. 2014 Apr 12;383(9925):1325–32.

Beelen R, Raaschou-Nielsen O, Stafoggia M, Andersen ZJ, Weinmayr G, Hoffmann B, et al. Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. *Lancet*. 2014 Mar 1;383(9919):785–95.

- Bell ML, Davis DL. Reassessment of the lethal London fog of 1952: novel indicators of acute and chronic consequences of acute exposure to air pollution. *Environ Health Perspect*. 2001 Jun;109(Suppl 3):389–94.
- Benbrahim-Tallaa L, Baan RA, Grosse Y, Lauby-Secretan B, Ghissassi F El, Bouvard V, et al. Carcinogenicity of diesel-engine and gasoline-engine exhausts and some nitroarenes. *The Lancet Oncology*. 2012 Jul;13(7):663–4.
- Boldo E, Linares C, Lumbreras J, Borge R, Narros A, García-Pérez J, et al. Health impact assessment of a reduction in ambient PM(2.5) levels in Spain. *Environ Int*. 2011 Feb;37(2):342–8.
- Brauer M, Hoek G, van Vliet P, Meliefste K, Fischer P, Gehring U, et al. Estimating long-term average particulate air pollution concentrations: application of traffic indicators and geographic information systems. *Epidemiology*. 2003 Mar;14(2):228–39.
- Brauer M, Amann M, Burnett RT, Cohen A, Dentener F, Ezzati M, et al. Exposure assessment for estimation of the global burden of disease attributable to outdoor air pollution. *Environ Sci Technol*. 2012 Jan 17;46(2):652–60.
- Brochu PJ, Yanosky JD, Paciorek CJ, Schwartz J, Chen JT, Herrick RF, et al. Particulate Air Pollution and Socioeconomic Position in Rural and Urban Areas of the Northeastern United States. *Am J Public Health*. 2011 Nov 28;101(S1):S224–30.
- Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A, Siscovick D, Smith SC Jr, Whitsel L, Kaufman JD; American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, and Council on Nutrition, Physical Activity and Metabolism. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation*. 2010 Jun 1;121(21):2331-78.
- Brunekreef B, Künzli N, Pekkanen J, Annesi-Maesano I, Forsberg B, Sigsgaard T, et al. Clean air in Europe: beyond the horizon? *Eur Respir J*. 2015 Jan;45(1):7–10.
- Can A, Rademaker M, Van Renterghem T, Mishra V, Van Poppel M, Touhafi A, Theunis J, De Baets B, Botteldooren D. Correlation analysis of noise and ultrafine particle counts in a street canyon. *Sci Total Environ*. 2011 Jan 1;409(3):564-72.
- Cesaroni G, Boogaard H, Jonkers S, Porta D, Badaloni C, Cattani G, et al. Health benefits of traffic-related air pollution reduction in different socioeconomic groups: the effect of low-emission zoning in Rome. *Occup Environ Med*. 2012 Feb;69(2):133–9.
- CIRE. Evaluation de l'impact sanitaire de la pollution atmosphérique urbaine sur l'agglomération de Lyon. Impact à court et long terme. Cellule interrégionale d'épidémiologie Rhône-Alpes. 58 pages. [Internet]. 2006 [cited 2015 Nov 3]. Available from: http://www.invs.sante.fr/publications/2006/pollution_lyon/rapport_pollution_lyon.pdf
- CIRE. Impact sanitaire de la pollution atmosphérique sur l'agglomération de Grenoble. Cellule interrégionale d'épidémiologie Rhône-Alpes. 53 pages. [Internet]. 2006 [cited 2015 Nov 3]. Available from: http://www.invs.sante.fr/publications/2006/pollution_grenoble/rapport_pollution_grenoble.pdf

Clancy L, Goodman P, Sinclair H, Dockery DW. Effect of air-pollution control on death rates in Dublin, Ireland: an intervention study. *The Lancet*. 2002 Oct 19;360(9341):1210–4.

Cohen AJ, Ross Anderson H, Ostro B, Pandey KD, Krzyzanowski M, Künzli N, et al. The global burden of disease due to outdoor air pollution. *J Toxicol Environ Health Part A*. 2005 Jul 9;68(13-14):1301–7.

Cui P, Huang Y, Han J, Song F, Chen K. Ambient particulate matter and lung cancer incidence and mortality: a meta-analysis of prospective studies. *Eur J Public Health*. 2015 Apr;25(2):324–9.

de Klerk NH, English DR, Armstrong BK. A review of the effects of random measurement error on relative risk estimates in epidemiological studies. *Int J Epidemiol*. 1989 Sep;18(3):705–12.

Dadvand P, Parker J, Bell ML, Bonzini M, Brauer M, Darrow LA, et al. Maternal exposure to particulate air pollution and term birth weight: a multi-country evaluation of effect and heterogeneity. *Environ Health Perspect*. 2013 Mar;121(3):267–373.

Dadvand P, Ostro B, Figueras F, Foraster M, Basagaña X, Valentín A, et al. Residential proximity to major roads and term low birth weight: the roles of air pollution, heat, noise, and road-adjacent trees. *Epidemiology*. 2014 Jul;25(4):518–25.

Davies HW, Vlaanderen JJ, Henderson SB, Brauer M. Correlation between co-exposures to noise and air pollution from traffic sources. *Occup Environ Med*. 2009 May;66(5):347-50.

Deguen S, Zmirou-Navier D. Social inequalities resulting from health risks related to ambient air quality—A European review. *The European Journal of Public Health*. 2010 Feb 1;20(1):27–35.

Eeftens M, Beelen R, de Hoogh K, Bellander T, Cesaroni G, Cirach M, Declercq C, Dèdelè A, Dons E, de Nazelle A, Dimakopoulou K, Eriksen K, Falq G, Fischer P et al. Development of Land Use Regression models for PM_{2.5}, PM_{2.5} absorbance, PM₁₀ and PM_{coarse} in 20 European study areas; results of the ESCAPE project. *Environ Sci Technol*. 2012 Oct 16;46(20):11195-205.

European Union (Official Journal). Directive 2008/50/EC of the European Parliament and of the Council of 21 May 2008 on ambient air quality and cleaner air for Europe. [Internet]. 2008 [cited 2015 Oct 16]. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:152:0001:0044:EN:PDF>

Fattore E, Paiano V, Borgini A, Tittarelli A, Bertoldi M, Crosignani P, et al. Human health risk in relation to air quality in two municipalities in an industrialized area of Northern Italy. *Environ Res*. 2011 Nov;111(8):1321–7.

Fensterer V, Küchenhoff H, Maier V, Wichmann H-E, Breitner S, Peters A, et al. Evaluation of the impact of low emission zone and heavy traffic ban in Munich (Germany) on the reduction of PM₁₀ in ambient air. *Int J Environ Res Public Health*. 2014 May;11(5):5094–112.

Foraster M, Deltell A, Basagaña X, Medina-Ramón M, Aguilera I, Bouso L, Grau M, Phuleria HC, Rivera M, Slama R, Sunyer J, Targa J, Künzli N. Local determinants of road traffic noise

levels versus determinants of air pollution levels in a Mediterranean city. *Environ Res.* 2011 Jan;111(1):177-83.

Foraster M. Is it traffic-related air pollution or road traffic noise, or both? Key questions not yet settled! *Int J Public Health.* 2013 Oct;58(5):647-8.

Foraster M, Basagaña X, Aguilera I, Rivera M, Agis D, Bouso L, et al. Association of Long-Term Exposure to Traffic-Related Air Pollution with Blood Pressure and Hypertension in an Adult Population-Based Cohort in Spain (the REGICOR Study). *Environmental Health Perspectives* [Internet]. 2014 Feb 14 [cited 2015 Oct 16]; Available from: <http://ehp.niehs.nih.gov/1306497/>

Forastiere F, Stafoggia M, Tasco C, Picciotto S, Agabiti N, Cesaroni G, et al. Socioeconomic status, particulate air pollution, and daily mortality: differential exposure or differential susceptibility. *Am J Ind Med.* 2007 Mar;50(3):208–16.

Forastiere F, Badaloni C, de Hoogh K, von Kraus MK, Martuzzi M, Mitis F, et al. Health impact assessment of waste management facilities in three European countries. *Environ Health.* 2011;10:53.

Freire C, Ramos R, Puertas R, Lopez-Espinosa M-J, Julvez J, Aguilera I, et al. Association of traffic-related air pollution with cognitive development in children. *J Epidemiol Community Health.* 2010 Mar;64(3):223–8.

French Republic (Official Journal). French Republic (Official Journal). Expérimentation de zones d'actions prioritaires pour l'air. Code de l'environnement (Art. L228-3, abrogé au 19 août 2015). [Internet]. 2010 [cited 2015 Oct 16]. Available from: <http://www.legifrance.gouv.fr/affichCode.do?cidTexte=LEGITEXT000006074220&idSectionTA=LEGISCTA000022494840&dateTexte=20100714>

French Republic (Official Journal). Ministère de l'écologie, du développement durable et de l'énergie. Arrêté du 26 mars 2014 relatif au déclenchement des procédures préfectorales en cas d'épisodes de pollution de l'air ambiant. [Internet]. 2014 [cited 2015 Oct 16]. Available from: http://www.legifrance.gouv.fr/jopdf/common/jo_pdf.jsp?numJO=0&dateJO=20140329&numTexte=30&pageDebut=06139&pageFin=06142

French Republic (Official Journal). Loi n°2015-992 du 17 août 2015 relative à la transition énergétique pour la croissance verte. Chapitre III : Réduction des émissions de gaz à effet de serre et de polluants atmosphériques et qualité de l'air dans les transports. Art. 48, 49. [Internet]. 2015 [cited 2015 Nov 2]. Available from: <http://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000031044385>

Friedman MS, Powell KE, Hutwagner L, Graham LM, Teague WG. Impact of changes in transportation and commuting behaviors during the 1996 Summer Olympic Games in Atlanta on air quality and childhood asthma. *JAMA.* 2001 Feb 21;285(7):897–905.

Frumkin H. Urban sprawl and public health. *Public Health Rep.* 2002 Jun;117(3):201–17.

Gehring U, Tamburic L, Sbihi H, Davies HW, Brauer M. Impact of noise and air pollution on pregnancy outcomes. *Epidemiology.* 2014 May;25(3):351–8.

Geiser M, Rothen-Rutishauser B, Kapp N, Schürch S, Kreyling W, Schulz H, et al. Ultrafine Particles Cross Cellular Membranes by Nonphagocytic Mechanisms in Lungs and in Cultured Cells. *Environ Health Perspect.* 2005 Nov;113(11):1555–60.

Hajat A, Hsia C, O'Neill MS. Socioeconomic Disparities and Air Pollution Exposure: a Global Review. *Curr Environ Health Rep.* 2015 Dec;2(4):440–50.

Hamra GB, Guha N, Cohen A, Laden F, Raaschou-Nielsen O, Samet JM, et al. Outdoor particulate matter exposure and lung cancer: a systematic review and meta-analysis. *Environ Health Perspect.* 2014 Sep;122(9):906–11.

Hänninen O, Knol AB, Jantunen M, Lim T-A, Conrad A, Rappolder M, et al. Environmental burden of disease in Europe: assessing nine risk factors in six countries. *Environ Health Perspect.* 2014 May;122(5):439–46.

Hara K, Homma J, Tamura K, Inoue M, Karita K, Yano E. Decreasing trends of suspended particulate matter and PM_{2.5} concentrations in Tokyo, 1990–2010. *J Air Waste Manag Assoc.* 2013 Jun;63(6):737–48.

Havard S, Deguen S, Zmirou-Navier D, Schillinger C, Bard D. Traffic-related air pollution and socioeconomic status: a spatial autocorrelation study to assess environmental equity on a small-area scale. *Epidemiology.* 2009 Mar;20(2):223–30.

HCSP. Pollution par les particules dans l'air ambiant. Recommandations pour protéger la santé. Haut Conseil de la Santé Publique. Pages 96–111. [Internet]. 2012 [cited 2015 Nov 4]. Available from: http://www.hcsp.fr/Explore.cgi/Telecharger?NomFichier=hcspr20120413_ppaa.pdf

Health Effects Institute, 2013. Understanding the health effects of ambient ultrafine particles. HEI Review Panel on Ultrafine Particles. [Internet]. 2013 [cited 2014 Mar 19]. Available from: <http://pubs.healtheffects.org/getfile.php?u=893>

Henschel S, Atkinson R, Zeka A, Le Tertre A, Analitis A, Katsouyanni K, et al. Air pollution interventions and their impact on public health. *Int J Public Health.* 2012 Oct;57(5):757–68.

Hoek G, Beelen R, de Hoogh K, Vienneau D, Gulliver J, Fischer P, et al. A review of land-use regression models to assess spatial variation of outdoor air pollution. *Atmospheric Environment.* 2008 Oct;42(33):7561–78.

Hoek G, Beelen R, Kos G, Dijkema M, van der Zee SC, Fischer PH, et al. Land Use Regression Model for Ultrafine Particles in Amsterdam. *Environ Sci Technol.* 2011 Jan 15;45(2):622–8.

Holman C, Harrison R, Querol X. Review of the efficacy of low emission zones to improve urban air quality in European cities. *Atmospheric Environment.* 2015 Jun;111:161–9.

Huang J, Deng F, Wu S, Lu H, Hao Y, Guo X. The impacts of short-term exposure to noise and traffic-related air pollution on heart rate variability in young healthy adults. *J Expo Sci Environ Epidemiol.* 2013 Sep-Oct;23(5):559–64.

Hystad P, Demers PA, Johnson KC, Carpiano RM, Brauer M. Long-term residential exposure to air pollution and lung cancer risk. *Epidemiology.* 2013 Sep;24(5):762–72.

IGN. BD TOPO® [Internet]. 2007 [cited 2015 Mar 24]. Available from: <http://pro.ign.fr/bdtopo>

INPES (Guignard et al.). Le tabagisme en France : analyse de l'enquête Baromètre santé 2010 [Internet]. 2014 [cited 2015 Mar 24]. Available from: <http://www.inpes.sante.fr/Barometres/barometre-sante-2010/index.asp#tabac>

INSEE. IRIS - Définition [Internet]. 2008 [cited 2015 Mar 24]. Available from: <http://www.insee.fr/fr/methodes/default.asp?page=definitions/iris.htm>

INSEE. Populations légales 2007 [Internet]. 2010 [cited 2015 Mar 24]. Available from: <http://www.insee.fr/fr/ppp/bases-de-donnees/recensement/populations-legales/default.asp?annee=2007>

INSEE. Naissances par commune, département et région de 2003 à 2013 [Internet]. 2013 [cited 2015 Mar 24]. Available from: http://www.insee.fr/fr/themes/detail.asp?reg_id=99&ref_id=etat-civil-naissances

INSEE. Populations légales 2011 des départements et des collectivités d'outre-mer [Internet]. 2013 [cited 2015 Mar 24]. Available from: <http://www.insee.fr/fr/ppp/bases-de-donnees/recensement/populations-legales/france-departements.asp?annee=2011>

INSERM. Enquête nationale périnatale 2010 [Internet]. 2011 [cited 2015 Mar 24]. Available from: <http://www.sante.gouv.fr/enquete-nationale-perinatale-2010.html>

International Agency for Research on Cancer. IARC: Diesel engine exhaust carcinogenic. Press Release no. 213 [Internet]. 2012 [cited 2015 Oct 16]. Available from: http://www.iarc.fr/en/media-centre/pr/2012/pdfs/pr213_E.pdf

International Agency for Research on Cancer. IARC: Outdoor air pollution a leading environmental cause of cancer deaths. Press Release no. 221 [Internet]. 2013 [cited 2015 Oct 16]. Available from: http://www.iarc.fr/en/media-centre/iarcnews/pdf/pr221_E.pdf

INVS, Ung A, Pascal M, Corso M, Chanel O, Declercq C. How to perform a health impact assessment of air pollution in urban areas? Methodological guide. Saint-Maurice: Institut de veille sanitaire [Internet]. 2013 [cited 2015 Oct 1]. Available from: <http://www.invs.sante.fr>

Jerrett M, Arain A, Kanaroglou P, Beckerman B, Potoglou D, Sahuvaroglu T, et al. A review and evaluation of intraurban air pollution exposure models. *J Expo Anal Environ Epidemiol*. 2005 Mar;15(2):185–204.

Jerrett M, Finkelstein MM, Brook JR, Arain MA, Kanaroglou P, Stieb DM, et al. A cohort study of traffic-related air pollution and mortality in Toronto, Ontario, Canada. *Environ Health Perspect*. 2009 May;117(5):772–7.

Johansson C, Burman L, Forsberg B. The effects of congestions tax on air quality and health. *Atmospheric Environment*. 2009 Oct;43(31):4843–54.

Kovats RS, Hajat S. Heat stress and public health: a critical review. *Annu Rev Public Health*. 2008;29:41–55.

- Kruize H, Driessen PPJ, Glasbergen P, van Egmond KND. Environmental equity and the role of public policy: experiences in the Rijnmond region. *Environ Manage*. 2007 Oct;40(4):578–95.
- Künzli N, Kaiser R, Medina S, Studnicka M, Chanel O, Filliger P, et al. Public-health impact of outdoor and traffic-related air pollution: a European assessment. *Lancet*. 2000 Sep 2;356(9232):795–801.
- Künzli N, Jerrett M, Garcia-Esteban R, Basagaña X, Beckermann B, Gilliland F, et al. Ambient air pollution and the progression of atherosclerosis in adults. *PLoS ONE*. 2010;5(2):e9096.
- Lepeule J, Laden F, Dockery D, Schwartz J. Chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. *Environ Health Perspect*. 2012 Jul;120(7):965–70.
- Lestel Laurence. La production de céruse en France au XIXe siècle : évolution d'une industrie dangereuse. [Internet]. 2002 [cited 2015 Oct 16]. Available from: <https://tc.revues.org/1067>
- Lighthall, D, Nunes D, Tyner T. Environmental Health Evaluation of Rule 4901: Domestic Wood Burning. A Case Study of the Fresno/Clovis and Bakersfield Metropolitan Areas. [Internet]. 2009 [cited 2015 Nov 4]. Available from: <https://www.fresnostate.edu/chhs/cvhipi/documents/wood-burning-report.pdf>
- Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012 Dec 15;380(9859):2224–60.
- Loomis D, Grosse Y, Lauby-Secretan B, Ghissassi FE, Bouvard V, Benbrahim-Tallaa L, et al. The carcinogenicity of outdoor air pollution. *The Lancet Oncology*. 2013 Dec;14(13):1262–3.
- MacIntyre EA, Karr CJ, Koehoorn M, Demers PA, Tamburic L, Lencar C, et al. Residential air pollution and otitis media during the first two years of life. *Epidemiology*. 2011 Jan;22(1):81–9.
- Madrigano J, Jack D, Anderson GB, Bell ML, Kinney PL. Temperature, ozone, and mortality in urban and non-urban counties in the northeastern United States. *Environ Health*. 2015;14:3.
- Maas J, Verheij RA, Groenewegen PP, de Vries S, Spreeuwenberg P. Green space, urbanity, and health: how strong is the relation? *J Epidemiol Community Health*. 2006 Jul;60(7):587–92.
- McGraw, Kenneth O.; Wong, S. P. Forming inferences about some intraclass correlation coefficients. *Psychological Methods*, Vol 1(1), Mar 1996, 30-46.
- Medina S, Plasencia A, Ballester F, Mücke HG, Schwartz J, Apeis group. Apeis: public health impact of PM10 in 19 European cities. *J Epidemiol Community Health*. 2004 Oct;58(10):831–6.
- Mishra VK, Kumar P, Van Poppel M, Bleux N, Frijns E, Reggente M, Berghmans P, Int Panis L, Samson R. Wintertime spatio-temporal variation of ultrafine particles in a Belgian city. *Sci Total Environ*. 2012 Aug 1;431:307-13.

Montagne DR, Hoek G, Klompmaker JO, Wang M, Meliefste K, Brunekreef B. Land Use Regression Models for Ultrafine Particles and Black Carbon Based on Short-Term Monitoring Predict Past Spatial Variation. *Environ Sci Technol*. 2015 Jul 21;49(14):8712–20.

Nafstad P, Håheim LL, Oftedal B, Gram F, Holme I, Hjermmann I, et al. Lung cancer and air pollution: a 27 year follow up of 16 209 Norwegian men. *Thorax*. 2003 Dec;58(12):1071–6.

Namdeo A, Stringer C. Investigating the relationship between air pollution, health and social deprivation in Leeds, UK. *Environ Int*. 2008 Jul;34(5):585–91.

Nemery B, Hoet PH, Nemmar A. The Meuse Valley fog of 1930: an air pollution disaster. *The Lancet*. 2001 Mar 3;357(9257):704–8.

Nieuwenhuijsen M, Paustenbach D, Duarte-Davidson R. New developments in exposure assessment: the impact on the practice of health risk assessment and epidemiological studies. *Environ Int*. 2006 Dec;32(8):996–1009.

Nieuwenhuijsen MJ, Kruize H, Gidlow C, Andrusaityte S, Antó JM, Basagaña X, et al. Positive health effects of the natural outdoor environment in typical populations in different regions in Europe (PHENOTYPE): a study programme protocol. *BMJ Open*. 2014;4(4):e004951.

Nieuwenhuijsen MJ, Donaire-Gonzalez D, Foraster M, Martinez D, Cisneros A. Using personal sensors to assess the exposome and acute health effects. *Int J Environ Res Public Health*. 2014 Aug;11(8):7805–19.

Nieuwenhuijsen Mark. *Exposure Assessment in Environmental Epidemiology*. Second Edition. ISBN 9780199378784. Oxford University Press; 2015.

NRC (National Research Council). *Risk assessment in the federal government: Managing the process*. National Academies Press, Washington, D.C.; 1983.

Orru H, Teinemaa E, Lai T, Tamm T, Kaasik M, Kimmel V, et al. Health impact assessment of particulate pollution in Tallinn using fine spatial resolution and modeling techniques. *Environ Health*. 2009;8:7.

Padilla CM, Kihal-Talantikite W, Vieira VM, Rossello P, Nir GL, Zmirou-Navier D, et al. Air quality and social deprivation in four French metropolitan areas—A localized spatio-temporal environmental inequality analysis. *Environmental Research*. 2014 Oct;134:315–24.

Pascal M, Corso M, Chanel O, Declercq C, Badaloni C, Cesaroni G, et al. Assessing the public health impacts of urban air pollution in 25 European cities: results of the Aphekom project. *Sci Total Environ*. 2013 Apr 1;449:390–400.

Pedersen M, Giorgis-Allemand L, Bernard C, Aguilera I, Andersen A-MN, Ballester F, et al. Ambient air pollution and low birthweight: a European cohort study (ESCAPE). *Lancet Respir Med*. 2013 Nov;1(9):695–704.

Pedersen M, Stayner L, Slama R, Sørensen M, Figueras F, Nieuwenhuijsen MJ, et al. Ambient air pollution and pregnancy-induced hypertensive disorders: a systematic review and meta-analysis. *Hypertension*. 2014 Sep;64(3):494–500.

- Pérez L, Sunyer J, Künzli N. Estimating the health and economic benefits associated with reducing air pollution in the Barcelona metropolitan area (Spain). *Gac Sanit.* 2009 Aug;23(4):287–94.
- Perez L, Declercq C, Iñiguez C, Aguilera I, Badaloni C, Ballester F, et al. Chronic burden of near-roadway traffic pollution in 10 European cities (APHEKOM network). *Eur Respir J.* 2013 Sep;42(3):594–605.
- Peters A, von Klot S, Heier M, Trentinaglia I, Hörmann A, Wichmann HE, Löwel H; Cooperative Health Research in the Region of Augsburg Study Group. Exposure to traffic and the onset of myocardial infarction. *N Engl J Med.* 2004 Oct 21;351(17):1721–30.
- Peters A. Ambient particulate matter and the risk for cardiovascular disease. *Prog Cardiovasc Dis.* 2011 Apr;53(5):327–33.
- Pieters N, Koppen G, Van Poppel M, De Prins S, Cox B, Dons E, et al. Blood Pressure and Same-Day Exposure to Air Pollution at School: Associations with Nano-Sized to Coarse PM in Children. *Environ Health Perspect.* 2015 Jul;123(7):737–42.
- Pope CA. Respiratory disease associated with community air pollution and a steel mill, Utah Valley. *Am J Public Health.* 1989 May;79(5):623–8.
- Pope CA, Dockery DW. Health effects of fine particulate air pollution: lines that connect. *J Air Waste Manag Assoc.* 2006 Jun;56(6):709–42.
- Pornet C, Delpierre C, Dejardin O, Grosclaude P, Launay L, Guittet L, et al. Construction of an adaptable European transnational ecological deprivation index: the French version. *J Epidemiol Community Health.* 2012 Nov;66(11):982–9.
- Raaschou-Nielsen O, Sørensen M, Ketzel M, Hertel O, Loft S, Tjønneland A, et al. Long-term exposure to traffic-related air pollution and diabetes-associated mortality: a cohort study. *Diabetologia.* 2013 Jan;56(1):36–46.
- Raaschou-Nielsen O, Andersen ZJ, Beelen R, Samoli E, Stafoggia M, Weinmayr G, et al. Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE). *Lancet Oncol.* 2013 Aug;14(9):813–22.
- Ranft U, Schikowski T, Sugiri D, Krutmann J, Krämer U. Long-term exposure to traffic-related particulate matter impairs cognitive function in the elderly. *Environ Res.* 2009 Nov;109(8):1004–11.
- Raz R, Roberts AL, Lyall K, Hart JE, Just AC, Laden F, et al. Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: a nested case-control analysis within the Nurses' Health Study II Cohort. *Environ Health Perspect.* 2015 Mar;123(3):264–70.
- Reche C, Viana M, Rivas I, Bouso L, Álvarez-Pedrerol M, Alastuey A, Sunyer J, Querol X. Outdoor and indoor UFP in primary schools across Barcelona. *Sci Total Environ.* 2014 Sep 15;493:943–53.

Rich DQ, Liu K, Zhang J, Thurston SW, Stevens TP, Pan Y, et al. Differences in Birth Weight Associated with the 2008 Beijing Olympics Air Pollution Reduction: Results from a Natural Experiment. *Environ Health Perspect.* 2015 Sep;123(9):880–7.

Riojas-Rodríguez H, Álamo-Hernández U, Texcalac-Sangrador JL, Romieu I. Health impact assessment of decreases in PM10 and ozone concentrations in the Mexico City Metropolitan Area: a basis for a new air quality management program. *Salud Publica Mex.* 2014 Dec;56(6):579–91.

Rojas-Rueda D, de Nazelle A, Tainio M, Nieuwenhuijsen MJ. The health risks and benefits of cycling in urban environments compared with car use: health impact assessment study. *BMJ.* 2011;343:d4521.

Rojas-Rueda D, de Nazelle A, Teixidó O, Nieuwenhuijsen MJ. Replacing car trips by increasing bike and public transport in the greater Barcelona metropolitan area: a health impact assessment study. *Environ Int.* 2012 Nov 15;49:100–9.

Rojas-Rueda D, de Nazelle A, Teixidó O, Nieuwenhuijsen MJ. Health impact assessment of increasing public transport and cycling use in Barcelona: a morbidity and burden of disease approach. *Prev Med.* 2013 Nov;57(5):573–9.

Rückerl R, Schneider A, Breitner S, Cyrys J, Peters A. Health effects of particulate air pollution: A review of epidemiological evidence. *Inhal Toxicol.* 2011 Aug;23(10):555–92.

Sartini C, Zauli Sajani S, Ricciardelli I, Delgado-Saborit JM, Scotto F, Trentini A, Ferrari S, Poluzzi V. Ultrafine particle concentrations in the surroundings of an urban area: comparing downwind to upwind conditions using Generalized Additive Models (GAMs). *Environ Sci Process Impacts.* 2013 Oct;15(11):2087–95.

Sellier Y, Galineau J, Hulin A, Caini F, Marquis N, Navel V, et al. Health effects of ambient air pollution: do different methods for estimating exposure lead to different results? *Environ Int.* 2014 May;66:165–73.

Shah PS, Balkhair T, Knowledge Synthesis Group on Determinants of Preterm/LBW births. Air pollution and birth outcomes: a systematic review. *Environ Int.* 2011 Feb;37(2):498–516.

Sioutas C, Delfino RJ, Singh M. Exposure Assessment for Atmospheric Ultrafine Particles (UFPs) and Implications in Epidemiologic Research. *Environ Health Perspect.* 2005 Aug;113(8):947–55.

Snijders, Tom A.B., and Bosker, Roel J. *Multilevel Analysis: An Introduction to Basic and Advanced Multilevel Modeling* London etc.: Sage Publishers, 1999 (ISBN 0-7619-5889-4)

Sørensen M, Andersen ZJ, Nordsborg RB, Jensen SS, Lillelund KG, Beelen R, et al. Road Traffic Noise and Incident Myocardial Infarction: A Prospective Cohort Study. *PLoS ONE.* 2012 Jun 20;7(6):e39283.

Sørensen M, Hvidberg M, Andersen ZJ, Nordsborg RB, Lillelund KG, Jakobsen J, et al. Road traffic noise and stroke: a prospective cohort study. *European Heart Journal.* 2011 Mar 1;32(6):737–44.

- Soulhac L, Salizzoni P, Mejean P, Didier D, Rios I. The model SIRANE for atmospheric urban pollutant dispersion; PART II, validation of the model on a real case study. *Atmospheric Environment*. 2012 Mar;49:320–37.
- Soulhac L, Salizzoni P, Cierco F-X, Perkins R. The model SIRANE for atmospheric urban pollutant dispersion; part I, presentation of the model. *Atmospheric Environment*. 2011 Dec;45(39):7379–95.
- Sousa SIV, Pires JCM, Martins EM, Fortes JDN, Alvim-Ferraz MCM, Martins FG. Short-term effects of air pollution on respiratory morbidity at Rio de Janeiro--Part II: health assessment. *Environ Int*. 2012 Aug;43:1–5.
- Strand LB, Barnett AG, Tong S. The influence of season and ambient temperature on birth outcomes: a review of the epidemiological literature. *Environ Res*. 2011 Apr;111(3):451–62.
- Tan J, Zheng Y, Tang X, Guo C, Li L, Song G, et al. The urban heat island and its impact on heat waves and human health in Shanghai. *Int J Biometeorol*. 2010 Jan;54(1):75–84.
- Tétreault LF, Perron S, Smargiassi A. Cardiovascular health, traffic-related air pollution and noise: are associations mutually confounded? A systematic review. *Int J Public Health*. 2013 Oct;58(5):649-66.
- Thomas D, Stram D, Dwyer J. Exposure measurement error: influence on exposure-disease. Relationships and methods of correction. *Annu Rev Public Health*. 1993;14:69–93.
- Tonne C, Beevers S, Armstrong B, Kelly F, Wilkinson P. Air pollution and mortality benefits of the London Congestion Charge: spatial and socioeconomic inequalities. *Occup Environ Med*. 2008 Sep;65(9):620–7.
- Tonne C, Beevers S, Kelly FJ, Jarup L, Wilkinson P, Armstrong B. An approach for estimating the health effects of changes over time in air pollution: an illustration using cardio-respiratory hospital admissions in London. *Occup Environ Med*. 2010 Jun;67(6):422–7.
- van Kempen E, Babisch W. The quantitative relationship between road traffic noise and hypertension: a meta-analysis. *J Hypertens*. 2012 Jun;30(6):1075-86.
- Villanueva CM, Cantor KP, Grimalt JO, Malats N, Silverman D, Tardon A, et al. Bladder cancer and exposure to water disinfection by-products through ingestion, bathing, showering, and swimming in pools. *Am J Epidemiol*. 2007 Jan 15;165(2):148–56.
- Vrijheid M, Slama R, Robinson O, Chatzi L, Coen M, van den Hazel P, et al. The human early-life exposome (HELIX): project rationale and design. *Environ Health Perspect*. 2014 Jun;122(6):535–44.
- Vrijheid M. The exposome: a new paradigm to study the impact of environment on health. *Thorax*. 2014 Sep;69(9):876–8.
- Weber N, Haase D, Franck U. Assessing traffic-induced noise and air pollution in urban structures using the concept of landscape metrics. *Landscape and Urban Planning* 125 (2014) 105–116.

Wild CP. Complementing the genome with an “exposome”: the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiol Biomarkers Prev.* 2005 Aug;14(8):1847–50.

Wilhelm M, Ghosh JK, Su J, Cockburn M, Jerrett M, Ritz B. Traffic-related air toxics and term low birth weight in Los Angeles County, California. *Environ Health Perspect.* 2012 Jan;120(1):132–8.

World Health Organization. Health and Environment in Sustainable Development: Five Years after the Earth Summit. Executive summary. [Internet]. 1997 [cited 2015 Oct 16]. Available from: http://apps.who.int/iris/bitstream/10665/63708/1/WHO_EHG_97.12_eng.pdf

World Health Organization. The World health report : 2002 : Reducing the risks, promoting healthy life. Rapport sur la santé dans le monde : 2002 : réduire les risques et promouvoir une vie saine [Internet]. 2002 [cited 2016 Jan 1]; Available from: http://apps.who.int/iris/bitstream/10665/42510/1/WHR_2002.pdf

World Health Organization. Guidelines for Drinking-water Quality. Vol. 1: third edition. ISBN 92 4 154638 7. [Internet]. 2004 [cited 2015 Nov 1]. Available from: http://www.who.int/water_sanitation_health/dwq/gdwq3rev/en/

World Health Organization. WHO Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide. Global update 2005. Summary of risk assessment. [Internet]. 2006 [cited 2015 Oct 16]. Available from: http://apps.who.int/iris/bitstream/10665/69477/1/WHO_SDE_PHE_OEH_06.02_eng.pdf

World Health Organization. Burden of disease from environmental noise. [Internet]. 2011 [cited 2015 Oct 16]. Available from: http://www.euro.who.int/__data/assets/pdf_file/0008/136466/e94888.pdf

World Health Organization. Review of evidence on health aspects of air pollution – REVIHAAP project: final technical report [Internet]. 2013 [cited 2015 Mar 24]. Available from: <http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2013/review-of-evidence-on-health-aspects-of-air-pollution-revihaap-project-final-technical-report>

World Health Organization. WHO Expert Meeting: Methods and tools for assessing the health risks of air pollution local, national and international level. Meeting report. [Internet]. 2014 [cited 2015 Mar 24]. Available from: <http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2014/who-expert-meeting-methods-and-tools-for-assessing-the-health-risks-of-air-pollution-at-local,-national-and-international-level>

Xie D, Liu Y, Chen J. Mapping Urban Environmental Noise: A Land Use Regression Method. *Environ Sci Technol.* 2011 Sep 1;45(17):7358–64.

Résumé général

En zone urbaine, la pollution atmosphérique représente un enjeu majeur de santé publique. La caractérisation du risque associé dépend fortement de la qualité de l'estimation des expositions. Si les études étiologiques s'appuient maintenant souvent sur des modèles ayant une résolution spatiale fine, les *études d'impact sanitaire* (EIS) reposent encore généralement sur des approches avec une faible résolution spatiale. Ces contrastes spatiaux pourraient entraîner des inégalités sociales dans la distribution de l'impact sanitaire des polluants atmosphériques. D'autres facteurs, et en particulier le bruit, partagent les mêmes sources et ont potentiellement des effets sur la santé, et devraient aussi être pris en compte dans les études épidémiologiques. Du point de vue de la gestion du risque, les décideurs pourraient bénéficier d'une estimation des gains de pollution atmosphérique à viser pour permettre une amélioration quantitativement significative de la santé.

Les objectifs de la thèse étaient : 1. D'étudier la possibilité de modéliser la distribution des particules ultrafines (UFP) en milieu urbain, et d'évaluer la corrélation entre UFP et bruit ; 2. De réaliser une EIS des particules fines avec une résolution spatiale fine, et d'investiguer les inégalités socio-économiques dans le fardeau de maladie généré par les particules ; 3. D'estimer les bénéfices sanitaires de scénarios théoriques de réduction de la pollution de l'air à l'échelle urbaine.

Le premier objectif fait partie du projet *Tri-tabs*, conduit dans les villes de Bâle, Gêrone et Grenoble. Des mesures de 20 min du bruit routier et du trafic, mais pas des UFP, étaient fortement reproductibles sur plusieurs mois. Sur des mesures simultanées, la corrélation entre le bruit et les UFP était modérée, ce qui ouvre la possibilité d'un ajustement réciproque pour de futures études épidémiologiques, permettant ainsi de démêler leurs potentiels effets court terme.

Le second objectif se focalise sur le long terme. La plupart du temps, les études d'impact sanitaire ne prennent pas en compte les variations spatiales des concentrations en polluants en zone urbaine. Dans les agglomérations de Grenoble et Lyon en 2012, l'exposition aux PM_{2.5} a été estimée à une échelle de 10×10 m en combinant un modèle de dispersion à des données de densité de population. Les événements de santé retenus étaient la mortalité ainsi que l'incidence du cancer du poumon (Grenoble) et des petits poids des naissances à terme. Les estimations de l'impact sanitaire ont été répétées en considérant les concentrations en polluants de façon homogène au sein de chaque agglomération. La proportion de cas attribuables à la pollution de l'air était de 3–8% pour la mortalité et 9–43% pour les petits poids de naissances à terme. A Grenoble, 6,8% (intervalle de confiance à 95% : 3,1–10,1%) des nouveaux cas de cancer du poumon étaient attribuables à la pollution de l'air. L'impact était sous-estimé de 8 à 20% lorsque les stations de mesure de fond étaient utilisées. Le risque attribuable était plus important dans les quartiers dont le niveau de défaveur sociale était intermédiaire ou légèrement au-delà.

Nous avons estimé l'impact de scénarios de réduction des niveaux de particules fines. Les scénarios visant une réduction de ces niveaux de 5% permettraient une réduction d'environ 10% des décès attribuables aux particules, tandis que les actions visant à réduire uniquement la pollution chez les 10% d'habitants les plus exposés ne procureraient qu'un gain sanitaire marginal (environ 1%).

En conclusion, nous avons montré que les mesures à court terme ne peuvent pas être utilisées pour modéliser les UFP en zone urbaine ; nous avons été parmi les premiers à réaliser une EIS s'appuyant sur un modèle de dispersion à résolution spatiale fine, et à avoir intégré les petits poids de naissances dans une EIS. Nos estimations ont montré que les stations de fond utilisées couramment en France pour les EIS tendent à sous-estimer les expositions, comparées à un modèle de dispersion. Notre estimation de la réduction des niveaux de particules fines nécessaire pour atteindre une réduction significative de l'impact sanitaire de la pollution de l'air en zone urbaine pourrait servir de guide à des politiques publiques.

Thesis abstract

In urban areas, atmospheric pollution represents a major threat to human health. The accurate characterization of this threat relies centrally on the quality of exposure assessment. It also requires assessment of other factors sharing the same sources and also possibly impacting health, such as noise. Fine-scale exposure assessment of air pollution levels may allow identifying spatial contrasts. Such spatial variations may lead to social differences in the distribution of the health impact of these pollutants.

The general aims of the PhD were: 1. To study the possibility to model ultrafine particles distribution in urban areas and assess the correlation of ultrafine particles levels with road traffic noise; 2. To assess the risk incurred by air pollution exposure with a fine-scale modeling approach and investigate the potential socio-economic disparities in health burden induced by particulate matter; 3. To investigate the health benefits expected from hypothetical scenarios of reduction of air pollution levels at the urban scale.

The first aim relies on *Tri-tabs* project, conducted in three European cities (Basel, Girona, Grenoble) in order to study the short-term associations between traffic-related noise, ultrafine particle number concentrations (UFP) and traffic flows, as well as the temporal variability of these factors. Measurements during 20 minutes of outdoor noise and traffic, but not of UFP, were strongly reproducible over durations of a couple of days or months. In these areas, on the short-term, noise levels and UFP concentrations exhibited relatively moderate correlations, which may allow adjustment for mutual confounding in epidemiological studies, thus allowing to disentangle their possible short-term health effects.

The second aim introduces health effects, and focuses on the longer term. Risk assessment studies often ignore within-city spatial variations of air pollutants. 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 fine-scale data on population density. Outcomes were mortality, lung cancer and term low birth weight incidences. The numbers of cases attributable to air pollution were estimated overall and stratifying areas according to the European Deprivation Index, a measure of social deprivation. Estimations were repeated assuming spatial homogeneity of air pollutants within city. The proportion of cases attributable to air pollution was in the 3-8% range for mortality and 9-43% range for term low birth weight. In Grenoble, 6.8% (95% CI: 3.1-10.1%) of incident lung cancer cases were attributable to air pollution. The impact was underestimated by 8 to 20% when background monitoring stations were used to assess exposure, compared to fine-scale dispersion modeling. Health impact was highest in neighborhoods with intermediate to higher social deprivation.

Several countries across Europe have implemented air pollution regulation policies, or *low emission zones*, France being an exception. We estimated the health impact of air pollution under different scenarios of reduction of fine particulate matter concentrations. Scenarios targeting a reduction in the PM_{2.5} annual averages by 5% led to a 10% decrease of the health burden, while actions aiming at only reducing the exposure of the population exposed above the 90th percentile did not yield a significant reduction of the health burden (around 1%).

In conclusion, we have shown that short-term measurements cannot be used to model ultrafine particles levels in urban areas; we were among the first to rely on a fine-scale exposure model for estimating the health impact of air pollution, and quantify its impact on term low birth weight. Our estimations showed that background air quality monitoring stations used classically in France for health impact assessment studies tend to underestimate exposure, compared to a spatially-resolved dispersion model. We have provided an estimate of the air pollution decrease required to obtain a significant reduction of the health impact of air pollutants in urban areas.