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Cluster analysis of social and environment inequalities of infant mortality. A spatial study in small areas revealed by local disease mapping in France

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Abstract

Mapping spatial distributions of disease occurrence can serve as a useful tool for identifying exposures of public health concern. Infant mortality is an important indicator of the health status of a population. Recent literature suggests that neighborhood deprivation status can modify the effect of air pollution on preterm delivery, a known risk factor for infant mortality. We investigated the effect of neighborhood social deprivation on the association between exposure to ambient air NO₂ and infant mortality in the Lille and Lyon metropolitan areas, north and center of France, respectively, between 2002 and 2009. We conducted an ecological study using a neighborhood deprivation index estimated at the French census block from the 2006 census data. Infant mortality data were collected from local councils and geocoded using the address of residence. We generated maps using generalized additive models, smoothing on longitude and latitude while adjusting for covariates. We used permutation tests to examine the overall importance of location in the model and identify areas of increased and decreased risk. The average death rate was 4.2‰ and 4.6‰ live births for the Lille and Lyon metropolitan areas during the period. We found evidence of statistically significant precise clusters of elevated infant

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mortality for Lille and an east-west gradient of infant mortality risk for Lyon. Exposure to NO₂ did not explain the spatial relationship. The Lille MA, socioeconomic deprivation index explained the spatial variation observed. These techniques provide evidence of clusters of significantly elevated infant mortality risk in relation with the neighborhood socioeconomic status. This method could be used for public policy management to determine priority areas for interventions. Moreover, taking into account the relationship between social and environmental exposure may help identify areas with cumulative inequalities.

1. Introduction

Infant mortality (death less than one year of age) is recognized as a key indicator of the health status of a population (OECD-Organization for Economic Co-operation and Development, 2010). Several studies have investigated the association between air pollution and infant mortality in countries with relatively high levels, as well as in countries with lower pollution levels (Tsai et al., 2006; Woodruff et al., 2008; Vrijheid et al., 2012; Romieu et al., 2004; Ritz et al., 2006; Lin et al., 2004; Kaiser et al., 2004; Hajat et al., 2007). The recent literature has established that the neighborhood environment of mother and child has an influence on future birth outcomes independently of individual risk factors (O'Campo et al., 1997; Ponce et al., 2005; Luo et al., 2006; Génereux et al., 2008; Zeitlin et al., 2011).

The neighborhood socioeconomic status (SES) has been mentioned as an important determinant of birth outcomes, in combination with air pollution (Ponce et al., 2005; Carbajal-Arroyo et al., 2011). Low SES populations may be more susceptible to air pollution than those with higher SES, as several factors more prevalent in disadvantaged populations may modify the pollution-mortality relationship (Yi et al., 2010). Genereux et al. showed that area-level maternal education and the percent of low income families were associated with the distance between the residence and the nearest highway, which, in turn, were related to differences in exposure to air pollution and the probability of preterm birth (Génereux et al., 2008). In two studies performed in Mexico (Carbajal-Arroyo et al., 2011; Romieu et al., 2004), the risk of death was significantly higher in infants from low and/or medium-SES areas than in those from high SES areas. Most of these studies are focused in the United States, Canada (Salihu et al., 2011; Ponce et al., 2005; Génereux et al., 2008; Jerrett, Buzzelli, et al., 2005) or countries in economic transition (Carbajal-Arroyo et al., 2011; Romieu et al., 2004; Yi et al., 2010). The number of studies in Europe is very limited (Scheers et al., 2011; Vrijheid et al., 2012). To identify geographic areas with an unfavorable infant mortality risk and provide relevant data to design local health policies, ecological studies are useful. In particular when the fine resolution scale of such areas allows to take into account the specificity of the territory in terms of social and environmental characteristics. However, this type of study requires a rigorous methodology in order to minimize ecological biases and to account for the dependency of spatial units. An original statistical method applicable in spatial epidemiologic settings is a generalized additive model (GAM) which can be applied with locally weighted regression smoothers (LOESS) to account for geographic location as a possible predictor of the infant mortality rate (Vieira et al., 2005; Vieira et al., 2008; Webster et al., 2006). GAMs provide a spatial representation of health risks, which may be a useful tool to understand the distribution of

disease, identifying areas of high disease prevalence, and therefore to set up focused public health interventions (Gatrell and Bailey, 1996; Jerrett et al., 2010).

In this paper, we assess social and environmental inequalities in the spatial distribution of infant mortality in two major metropolitan areas in France. This study has several objectives: i) to detect spatial variations of infant mortality across census blocks, ii) to identify areas of significantly increased and decreased risk adjusted on known risk factors (social characteristics and air pollution, both determined at a neighborhood level), and iii) to illustrate the relevance of spatial epidemiology techniques using generalized additive models, smoothing on longitude and latitude, while adjusting for covariates.

2. Materials and methods

2.1 Study sites and study design

The study is ecological and investigates the spatial distribution of infant mortality in two major metropolitan areas (MAs) in France. The Lille metropolitan area (Nord-Pas-de Calais region, northern France), named Lille Métropole, has an approximate population of 1.1 million inhabitants divided into 85 municipalities and 506 census blocks, for a total area of 611.45 km². The Lyon metropolitan area (Rhône-Alpes region, mid-eastern France), named Grand Lyon, is subdivided into 58 municipalities and 510 census blocks for a total population of approximately 1.2 million inhabitants in an area of 527.15 km².

The statistical unit is the sub-municipal French census block (called IRIS “Îlot Regroupé pour l'Information Statistique”) defined by the National Institute of Statistics and Economic Studies (INSEE). It is the smallest administrative unit for which socioeconomic and demographic data are available in France. This geographical unit averages 2000 inhabitants and is constructed to be as homogenous as possible in terms of socio-demographic characteristics and land use. The delineations of the census blocks provided by INSEE also take into account the urban landscape and obstacles that could divide it, such as major traffic roads, green places and water bodies. These two metropolitan areas are of particular interest because they exhibit contrasts in their urban landscape and in some important demographic and socio-economic characteristics.

2.2 Health outcome

Infant mortality is defined as the number of babies who died during their first year of life per number of births that occurred during this time period. Cases were collected from death certificates in the city hall of each municipality in the MA and the parental addresses were geocoded to the census blocks. A total of 516 and 684 cases of infant deaths in Lille MA and the Lyon MA, respectively, occurred during the period 2002-2009. Figure 1.A illustrates the spatial distribution of the prevalence of infant mortality by tertiles at the census block level of Lille and Lyon MAs.

2.3 Potential cofounders

Deprivation index—For the analysis of socioeconomic disparities, a deprivation index was constructed for all census blocks of the metropolitan areas of Lille and Lyon. The

detailed methodological development of this index has been described elsewhere (Havard et al., 2008). In short, the socioeconomic data were obtained from the 2006 national census and provided counts of population, households or residences at the census block level classified by social, economic and demographic characteristics. Using these raw data, we constructed 48 indicators at the census block level according to INSEE's definitions. These variables can be divided into 5 domains: family and household, immigration status and mobility, employment and income, education, housing. Principal components analysis was used to synthesize information from these data. To construct a single numeric index for all of the blocks, we maximized the inertia of the first component by deleting all of the variables only weakly correlated with it and the variables with a contribution lower than the average. This allowed us to identify an axis, composed of 21 variables, which explained 63 percent of the inertia of the initial variables for the Lille MA and 54 for the Lyon MA.

The socioeconomic variables included in both MAs were Foreigners (%), Immigrants population (%), Single-parent families (%), Unemployed people (%), Employed workers (%), People with stable job (%), Non-owner occupied primary residence (%), Population 15 years and over without diploma (%), Population 15 years and over with post-secondary or secondary diploma (%), Individual house as a primary residence (%), Apartment building as a primary residence (%), Primary residence with a minimum surface area of 100 meters (%), Subsidized housing among all primary residences (%), Primary residence with a garage or other parking space (%), Households without a car (%), Households with 2 or more cars (%), and Median income per consumption unit. Some variables are specific to one MA, as People aged 25 years or younger (%) (Lille), People with insecure job (Lille) (%), Self-employed people (Lyon) (%), Managers workers (Lyon) (%), Blue-collar workers (Lyon) (%). Figure 1.B shows the spatial distribution of the deprivation index by tertiles on a map of the census blocks of Lille and Lyon MA.

Air pollution concentrations—Annually ambient concentrations of nitrogen dioxide (NO₂) were modeled by the local air quality monitoring network (Atmo Nord Pas-de-Calais, Air Rhône-Alpes) for each block and the entire study period (2002–2009). The two networks developed and tested a methodological approach to describe and characterize disparities in environmental exposures at a local scale for that period. They used different deterministic models: ADMS (Atmospheric Dispersion Modeling System) Urban for the Lille MA (Carruthers et al., 2000; McHugh C et al., 1997) and SIRANE for the Lyon MA (Soulhac L et al., 2011; Soulhac L et al., 2012). These models integrate meteorological data: air temperature, wind speed and direction, relative humidity, barometric pressure (supplied by Météo France, the French meteorologic service), emission sources according to their contribution to ambient air pollution and background pollution measurements as input parameters. Selected emission sources were linear sources (main roads), surface sources (diffuse road sources and residential and tertiary emissions) and important point sources: 31 for the Lille MA and 91 for the Lyon MA (the main polluting industries). The Agglomerative Hierarchical Clustering (AHC) was chosen to associate each census blocks with a measuring background permanent station, then assign daily variations. In total, 18 stations were used for the Lille MA and 31 for the Lyon MA. For Lille, in 2009 the mean concentration was modeled using the ADMS model. To reconstruct annual mean

concentrations of NO₂ from 2002-2008, the method used consists of a spatial interpolation of data stations that uses spatial concentrations of 2009 as an auxiliary variable. Kriging gives accurate results at the stations for the years 2002–2008. For Lyon, the annual mean concentrations were calculated with the SIRANE model without spatial interpolation, nor measurements assimilation. In a recent review, Jerrett et al. demonstrated the effectiveness and reliability of this type of model for assessing air quality in health effects assessment research (Jerrett et al., 2010). Figure 1.C shows the spatial distribution of the NO₂ concentrations by tertiles on a map of the census blocks of the Lille and Lyon MAs.

2.4 Statistical methods

Geocoding and descriptive data—Through the efforts to collect cases information, we obtained the parental address of residence of each case, with the authorization of the national committee on digitalized information and privacy (CNIL). Residential addresses were matched to the corresponding census blocks using map databases (Correspondance Adresses-Zones Urbaines, 2004) a software issued by INSEE. The following data were available: longitude and latitude of the centroid of each census block, reported number of cases, total births, the modeled NO₂ concentration (µg/m³) and the deprivation index reported in tertiles of the distribution. For east /west comparisons, the Lyon MA was divided using geographic boundaries: the “Rhône” river that flows north-east to south. No geographic boundary divided the Lille MA into eastern and western parts, so we used a vertical line to divide it into two equal surfaces.

Census blocks without any birth (for example, an industrial census block or a park) were excluded from the analysis. We excluded 7 census blocks without births and 2 without socioeconomic information in both Lille and Lyon MAs. We also excluded 24 census blocks (4.5%) in Lille and 13 census blocks in Lyon (2.5%) that had no information on air pollution. The final dataset for Lille included 471 census blocks and 488 census blocks for Lyon during the years 2002 to 2009.

Local disease mapping—We used generalized additive models to estimate census block infant mortality risk, a form of non-parametric or semi parametric regression with the ability to analyze area-based data adjusting for covariates.

We modeled location, a potential proxy measure of unknown exposure or uncontrolled risk factors, using a smooth (S) of longitude (X) and latitude (Y) with a Poisson link function.

$$\text{Log}[p(X, Y)] = S(X, Y) + \text{offset}(\text{pop}) + \gamma'Z \quad (\text{equation 1})$$

where the left-hand side is the logarithm of the disease risk at the census block's centroid (X,Y), according to the size of the population (offset(pop)), and γ is a vector of parameters associated with Z, the vector of covariates.

The model is semi-parametric because it includes both nonparametric and parametric components. Without the smooth function, S(X,Y), the model becomes an ordinary Poisson regression on the covariates. Omitting the covariates produces a crude (unadjusted) map. We

used a LOESS smooth which adapts to changes in population density previously used in case control studies (Vieira et al., 2008; Vieira et al., 2005; Webster et al., 2006; Kelsall and Wakefield, 2002).

The amount of smoothing depends on the percentage of the data points in the neighborhood, referred to as the span size. GAMs also allow selection of “optimal” span size. We used R software using the gam package, which is written by Trevor Hastie and is an implementation of the GAM framework of Hastie and Tibshirani 1990, to perform the generalized additive modeling and ArcView 9.3 software (ESRI, Inc., Redlands, California) to map the results of our analyses. We determined the optimal amount of smoothing for each map by minimizing the Akaike's Information Criterion (AIC). Small span sizes produce bumpier surfaces and larger span sizes produce smoother surfaces. As the span size increases, the amount of bias in the fit increases and the variance decreases.

GAMs also provide a framework for testing hypotheses. There are a number of ways to test the global null hypothesis that disease status does not depend on location, i.e., that the map is flat. Similar to analysis of variance in ordinary linear regression, we examined the overall significance of location using the difference in deviance of the complete model (equation 1) and the reduced model omitting the smoothing term. The R software provides an approximate p-value for this statistic assuming a chi square distribution. Because the latter assumption is in general not true for GAMs, we calculated the p-value using a permutation test (Vieira et al., 2002). To test the null hypothesis of no association between infant mortality rate and location, we randomly reassigned the coordinates of the census blocks while keeping the case counts, population, and covariates fixed. We sampled from the null permutation distribution 999 times in addition to the original model. For each permutation, we ran the GAM using the optimal span of the original data and computed the deviance statistic. We divided the rank of the observed value by 1000 to obtain the approximate permutation p-value. If the deviance global statistic indicated that location was significant at the 0.05 level, we then identified areas with significantly increased or decreased risk. We did this by obtaining a distribution of the log risk at every census block using the same set of permutations we used for calculating the global statistics. The areas of significantly decreased risk (“cold spots”) include all census blocks that rank in the lower 2.5% of the census blocks distributions. Areas of significantly elevated risk (“hot spots”) include all census blocks that rank in the upper 2.5% of the census block distributions. (Vieira et al., 2005; Young et al., 2010)

We first performed a spatial analysis using the crude model to determine the unadjusted geographic variation in infant mortality. Spatial patterns in the underlying crude analysis could be due to a number of factors with a geographic component. In this study, we were primarily interested by spatial patterns that can be explained by the deprivation index or the NO₂ concentrations. To assess the contribution of these factors to the underlying spatial patterns, we performed adjusted analyses with the deprivation index alone, the NO₂ concentration alone, the deprivation index and NO₂ concentration together, and with their interaction.

3. Results

3.1. Descriptive statistics

The infant mortality rate is equal to 4.2 and 4.6 per 1000 live births for the Lille and Lyon MAs, respectively, between 2002 to 2009. The classes of tertiles of the socioeconomic deprivation and the NO₂ concentration for both MAs are summarized in the Table 1. We note that the classes of tertiles of NO₂ concentrations of the Lyon MA are higher than in the Lille MA (Table 1). Figure 2 shows the temporal trends of the NO₂ concentrations during the period 2002 to 2009. In the Lille MA, the meteorology was penalizing in terms of dispersion during years 2003, 2005, which led to higher annual levels of nitrogen dioxide. The pattern is quite stable in both graphs, but the mean NO₂ in the Lyon MA is higher than 40µg/m³ which is the limit value set by the WHO European community.

Figure 3 reveals two different relationships between the deprivation index and the NO₂ concentrations. For Lille, the relationship follows a linear trend, the most deprived population living in the most exposed census blocks, whereas in Lyon, the medium class of deprivation is the most exposed. The p-values for an anova-test to compare the mean NO₂ concentrations between the classes of deprivation are significant for both MAs (p<0.0001).

3.2 Spatial analysis

The crude (unadjusted) maps show significant geographic variation based on the global statistics, with p=0.005 for the Lyon and <0.001 for the Lille MA (Table 2, Figures 4.A and 5.A). For Lille, two significant urban hotspots are visible that include the two major cities of the metropolitan area, Lille city in the center and Roubaix, a city in the north east of the metropolitan area (Figure 4A). For Lyon, Figure 5.A shows a different pattern of spatial variability as indicated by the large span (span=0.95). Rather than multiple clusters (i.e., bumpier surface) that we observe with a smaller span, there is a visible significant spatial gradient of risk from northwest to southeast (p<0.0001), with a cluster of significant elevated mortality situated in the east of the map. In the Appendix, we also note contrasts in some important demographic and socio-economic characteristics between east and west of the Lyon MA.

After adjustment for NO₂ concentrations alone, Figure 4.B shows little differences compared to the results from the crude analysis in the Lille MA: the same location pattern remains significant, suggesting that exposure to NO₂ does not explain the spatial pattern of infant mortality (Table 2-A). The same holds true in the Lyon MA (Figure 5.B and Table 2-B).

After adjusting for deprivation alone, the results differ depending on the MA. For Lille, Figure 4.C no longer shows any area of statistically significant risk and Table 2-A exhibits a borderline significant p value (p=0.07). This strongly suggests that socioeconomic status explains a great part of the spatial variability of infant mortality. Populations living in census blocks of higher deprivation have a significant greater risk of infant mortality than populations in the census blocks of the lower deprivation (p=<0.001). For Lyon, Figure 5.C shows that the magnitude of the infant mortality decreases compared to figures derived from the crude analysis (Figure 5.A and Table 2-B); however, there is little change in the

geographic pattern, and the global statistic for location remains significant ($p=0.025$), suggesting that socioeconomic status alone does not entirely explain the spatial variability.

Finally, fully adjusting with the two variables (SES and NO_2) in the models shows little change in the Lille MA (Table 2-A and Figure 4.D) and less pronounced hot and cold spots than in the crude and SES-only adjusted maps in the Lyon MA (Figures 5.A and 5.D); this speaks in favor of a joint effect of SES and SES and NO_2 . However, the area of increased risk of infant mortality is still visible (and borderline significant) in the southeast of the Lyon MA, suggesting that infant mortality is yet to be explained by other factors not accounted for in our model. No interaction is shown between the two factors in the Lille or Lyon MAs.

4. Discussion

We used generalized additive models to explore the spatial variation of infant mortality in two major French metropolitan areas. Our results highlight differences in the spatial inequality patterns of infant mortality across the two metropolitan areas.

For the Lille MA, socioeconomic deprivation explained the spatial variations of infant mortality across the different census blocks. More precisely, the two significant clusters of elevated infant mortality detected in the cities of Lille and Roubaix (a city near the Belgium border in the north east of the metropolitan area) are no longer apparent after adjustment for the census blocks socioeconomic status. In the Lyon MA, adjusting for socioeconomic status did not erase the clusters of elevated infant mortality. For both MAs, a positive trend of infant mortality from the most deprived to the less deprived census blocks was found. Several studies demonstrated that the socioeconomic status is an important risk factor for a variety of birth outcomes (Guildea et al., 2001; Krieger et al., 2003; Elo et al., 2009; Zeka et al., 2008; Blumenshine et al., 2010; Singh and Kogan, 2007; Luo et al., 2006; Arntzen et al., 2004). During pregnancy, mothers are likely to face multiple stressful life events, including lone-mother, unemployment, and little resources to deal with these conditions (Miranda et al., 2009; O'Neill et al., 2003; Larson, 2007; Nkansah-Amankra, Dhawain, et al., 2010; Nkansah-Amankra, Luchok, et al., 2010; Lu and B Chen, 2004). To improve upon the methodology employed in ecological studies of health inequalities, it would be necessary to carry out studies with individual data in which risk factors related to specific causes of infant mortality are analyzed. These parental factors include poor health status (for example, diabetes, obesity and chronic obstructive lung diseases), toxicants such as nicotine, caffeine, cocaine or alcohol (Patra et al., 2011; O'Leary et al., 2009; Crane et al., 2011) and multiple exposures to pollution (passive smoking, occupational exposure) that could act in addition to or in synergy with access to healthcare. In the conclusion of their extensive analysis of the epidemiologic literature David et al state that genetic factors fail to explain the strong disparities in birth outcomes according to race in the US, which are better explained by social determinants (David et al,2007).

In the two MAs, exposure to ambient air NO_2 did not explain the spatial distribution of infant mortality observed in the crude analysis, though the size of the areas of statistically elevated risk did change. Some authors hypothesize that air pollution contributes to creating

or accentuating the socioeconomic inequalities that exist for various illnesses, including cancer, asthma and cardiovascular diseases (Forastiere et al., 2007; Barceló et al., 2009, Jerrett 2005). It is now highly suspected to contribute to preterm births, intra-uterine growth and perinatal mortality (Weck 2008, Ponce 2005, Slama 2008, Slama 2009, Bell 2007, Woodruff 2008). In the city of Sao Paulo, Brazil, logistic regression revealed a gradient of increasing risk of an early neonatal death with higher exposure to traffic-related air pollution (De Medeiros et al., 2009). In Europe, Sheers et al. (2011) found that risk levels infant mortality increased by 4% for a $10\mu\text{g}/\text{m}^3$ increase in daily PM_{10} among European children under the age of one. In our study setting, NO_2 concentrations stand as a global indicator of air pollution associated with traffic and industrial emissions (Chaix et al., 2006; Vrijheid et al., 2012).

After the final multivariate models were constructed, we tested two-way interactions between pollution and the socioeconomic status. While our main intent was to control for confounding, some studies suggest variables such as socioeconomic status may modify the air pollution–mortality association (Barceló et al., 2009; Jerrett et al., 2005; Martins et al., 2004). Jerrett et al in 2005, in a study of Hamilton (Canada), found that high mortality was associated with exposure to air pollution (specially SO_2) in a citywide model and in intra-urban zones with lower socioeconomic characteristics. In our case, we found no significant results. This finding must be tempered with recognition that the interaction terms themselves tended to be collinear with one or more of the independent variables.

The interpretation of our findings must also consider some weaknesses, notably in exposure assessment. First, the use of atmospheric dispersion models such as the ADMS-Urban or SIRANE may be limited by the extensive amount of input data that are required. Uncertainty may come from data sources, estimation methods, or measurement tools. However, in term of validation, the models give quite acceptable results. For the Lille MA, five monitoring sites were available to evaluate the NO_2 model's results and the correlations varied between 0.63 to 0.74. For the Lyon MA, four monitoring sites were available for this comparison and high correlations between the model's predictions and the measured NO_2 values were observed (0.78-0.96). To be mentioned is that NO_2 concentrations in the Lille MA were modeled only for 2009, and used kriging for previous years, which yields some uncertainty. Models such as land-use regression, which are less complex to implement and can also provide reliable estimates of traffic-related air pollution, could have been a relevant alternative (Jerrett 2010).

This work has some notable strengths. Small area analysis allows a deeper understanding of the geographic patterns of health inequalities and is essential for revealing local-level inequalities that are often masked when health estimates are produced at large area scales (cities, counties, states). Laurent 2007 showed that several studies that had used socioeconomic characteristics measured at an aggregate level (municipality, county or region) did not find the effect of pollution to vary across different areas, whereas many studies that measured socioeconomic conditions at a more disaggregate level (district, neighbourhood or census blocks) did reveal joint effects of the two families of factors.

One other strength of our approach is that we could draw in the maps areas of significantly elevated risk (hot spots) by delineating areas that were above the 97.5% confidence interval. This was done by permutation tests, which are flexible hypothesis tests not making prior assumptions on parameters and outcome distribution. Simulation studies showed that the permutation tests behave considerably better than the corresponding classical tests if measured by the critical values attained. We modeled health risks by GAMs. Differently from classical cluster detection methods, GAMs make it possible to include a non-parametric term to account for spatial variation in the health risk, as well as to adjust for potential confounders, and consider multiple tests: a global one and a test to determine areas of significantly elevated risks. But the limitation that Gam doesn't have compare to other famous method is that the clusters are not circle or ellipses which could detect clusters of size larger than that of real clusters encompassing neighboring regions.

Finally, the procedure to model air pollution concentrations at surface areas of the size of census blocks provides unbiased estimates of exposure to ambient air pollution. Jerrett et al in 2010 demonstrated the effectiveness and reliability of this type of model for assessing air quality in health effects assessment research. Some studies on reproductive effects of air pollution used surrogate air pollution measures (e.g. average pollutant concentrations at fixed ambient monitoring stations, distance to monitoring sites, vehicular traffic emissions, proximity to highway, distance to main roads) to estimate maternal but failure to consider spatial variations can lead to exposure misclassification and subsequent bias (Jerrett, Burnett, et al., 2005).

5. Conclusion

The use of GIS and spatial analysis techniques has been shown to be useful tools to inform public policy and determine areas that warrant specific intervention. In the present setting, these techniques identified clusters of elevated infant mortality in relation with the socioeconomic status, and marginally to air pollution. Moreover, this paper illustrates an approach to take into account the combined effect, and possibly, the interaction between socioeconomic characteristics and environment exposures and to identify areas which cumulate conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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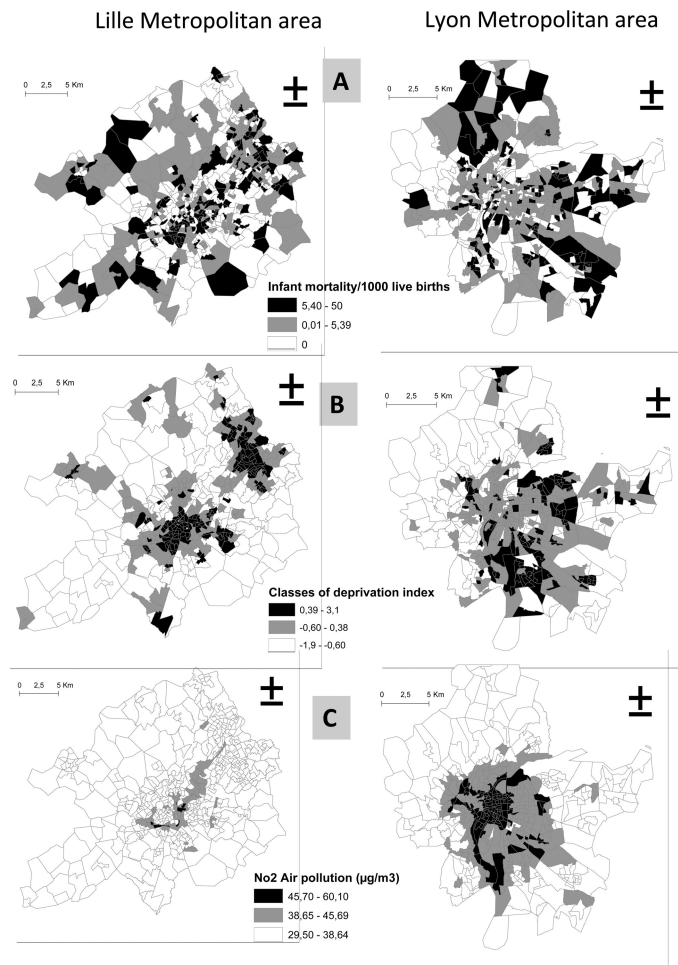


Figure 1.
 A. Spatial distribution of infant mortality by census block in the Lyon and Lille MAs during 2002-2009. B. Spatial distribution of the deprivation index by census block in Lyon and Lille MA during 2002-2009. C. Spatial distribution of the NO₂ air pollution by census block in Lyon and Lille MA during 2002-2009.

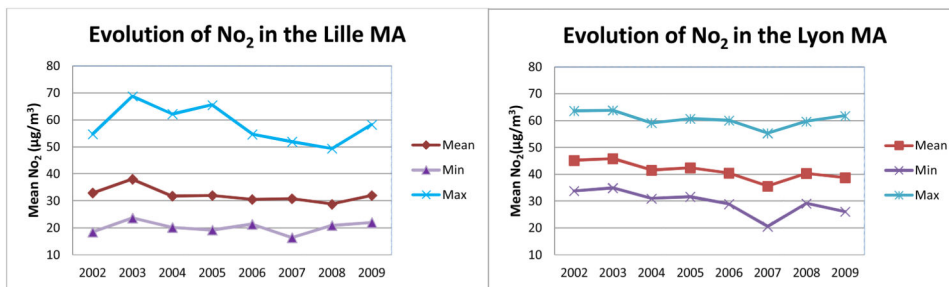


Figure 2. Yearly averages of the NO₂ ambient air concentrations during the period 2002-2009 for the Lille and Lyon MAs.

Figure 2 show the temporal trends of the NO₂ concentration during the period 2002 to 2009. In Lille MA, a meteorology penalizing in terms of dispersion, combined with majority of traffic emissions for the years 2003, 2005, led to annual levels of nitrogen dioxide higher. The pattern is quite stable in both graphs, but the mean NO₂ in Lyon MA is higher than 40µg/m³ which represents the referent limit by the WHO.

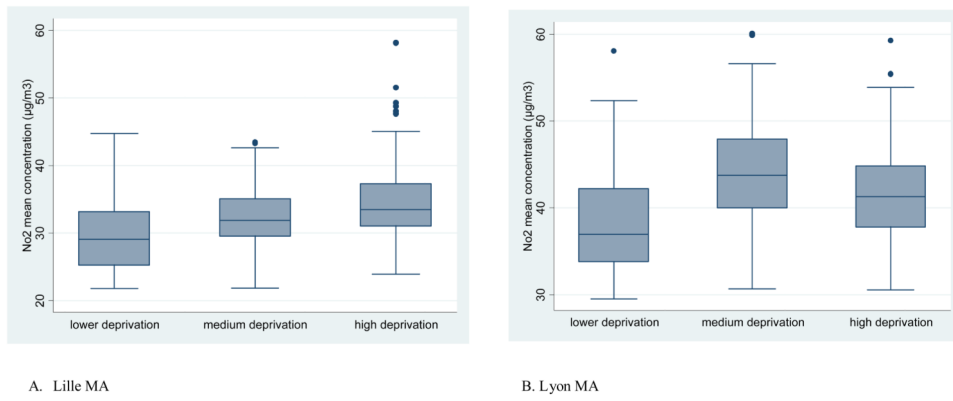


Figure 3. Comparison of the NO₂ average concentrations according to the classes of deprivation in the Lille and Lyon MAs, period 2002-2009.

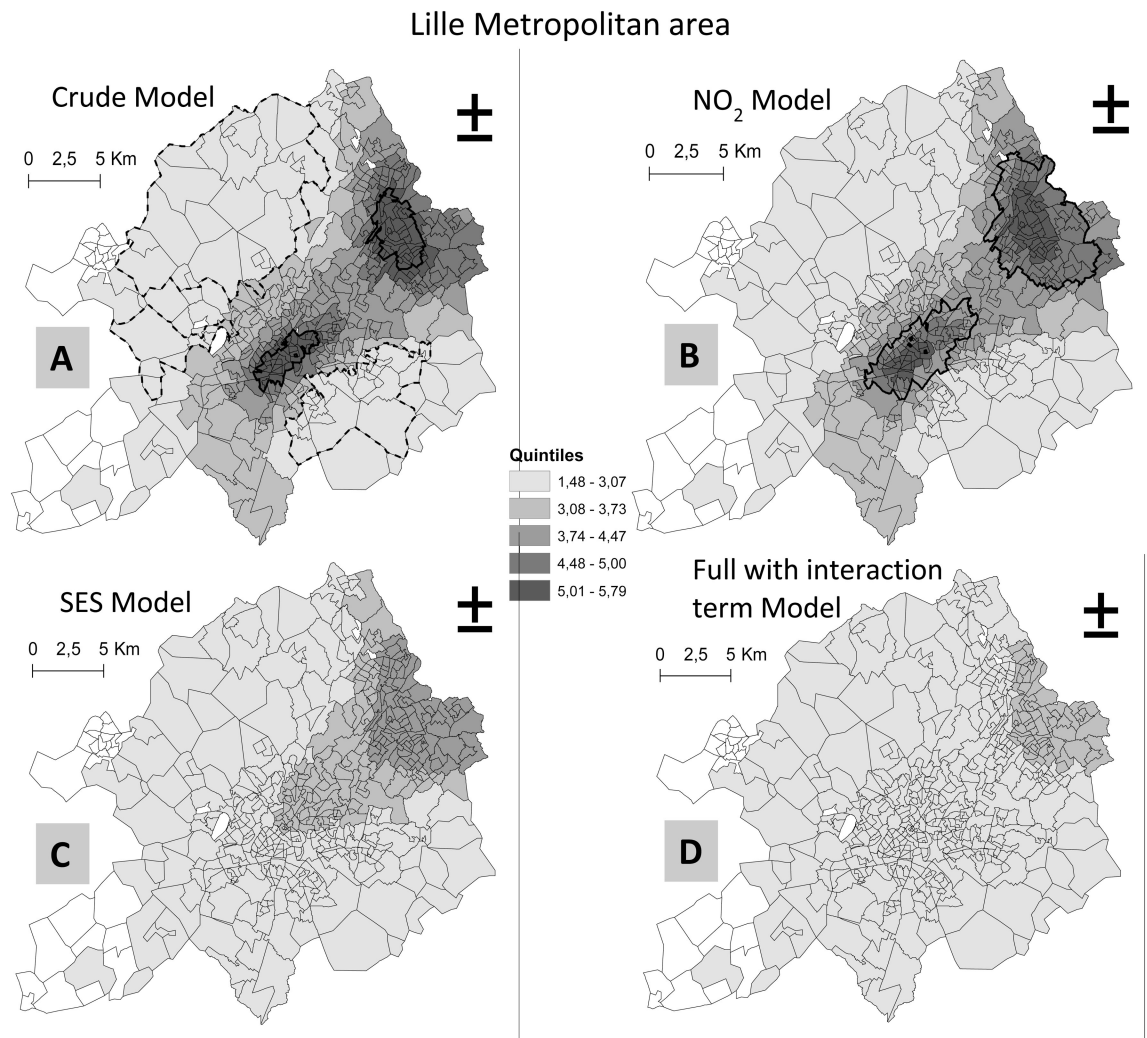


Figure 4. (A) Prevalence of infant mortality estimated by the GAMs in the Lille Metropolitan Area for crude model (A), according to (B) NO_2 air pollution exposure, (C) deprivation index and (D) with the interaction term. Light grey to dark grey shading indicates lower to higher prevalence. Solid lines identify areas with significantly increased rates (hotspots) and dashed lines identify areas with significantly decreased rates (coldspots).

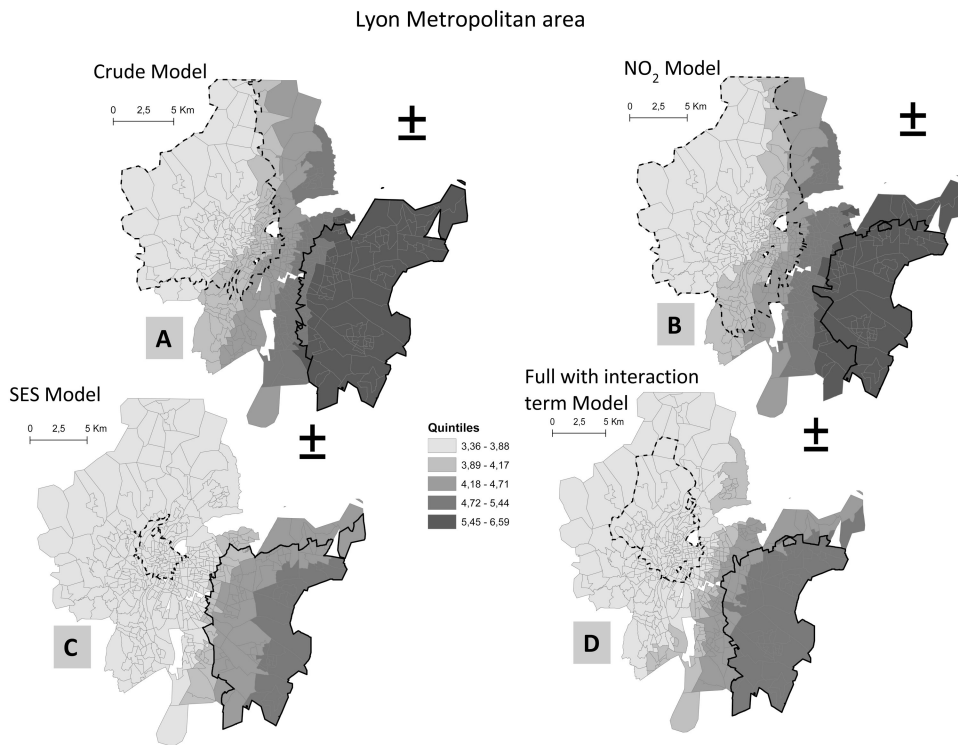


Figure 5. (A) Prevalence of infant mortality estimated by the GAMs in the Lyon Metropolitan Area for crude model (A), according to (B) NO₂ air pollution exposure, (C) deprivation index and (D). with the interaction term. Light grey to dark grey shading indicates lower to higher prevalence. Solid lines identify areas with significantly increased rates (hotspots) and dashed lines identify areas with significantly decreased rates (coldspots).

Table 1
Descriptive statistics of the main confounders, classes of deprivation and classes of NO₂ air pollution for the Lille and Lyon MAs during the period 2002-2009

	Lille MA (N=479 census blocks)		Lyon MA (N=491 census blocks)		
	mean ± SD	[min; max]	mean ± SD	[min; max]	
Classes of deprivation (tertiles)	Global	0.02± 1.01	[-1.93; 3.10]	-0.02± 0.99	[-2.04; 3.06]
	1st	-1.04± 0.28	[-1.93; -0.60]	-1.00± 0.42	[-2.04; -0.47]
	2nd	-0.12± 0.27	[-0.59; 0.38]	-0.13± 0.19	[-0.48; 0.20]
	3rd	1.19± 0.64	[0.39; 3.10]	1.06± 0.74	[0.20; 3.06]
Classes of NO ₂ air pollution (tertiles)	Global	32.06± 5.31	[21.79; 58.16]	47.78± 5.81	[29.49; 60.10]
	1st	26.53± 2.39	[21.79; 30.00]	34.88± 2.19	[29.49; 37.97]
	2nd	31.91± 1.05	[30.05; 33.82]	41.06± 1.76	[38.04; 43.73]
	3rd	37.75± 3.83	[33.84; 58.16]	47.78± 3.18	[43.73; 60.10]

Table 2
Summary of the infant mortality models in the Lille and Lyon MAs

A.

Lille MA	Span	Deviance p value Global
Crude Model	0.30	<0.001
Adjusted by NO2	0.30	0.007
Adjusted by SES	0.95	0.070
Full Adjusted	0.95	0.124
Interaction model	0.95	0.125

B.

Lyon MA	Span	Deviance p value Global
Crude Model	0.95	0.005
Adjusted by NO2	0.95	0.001
Adjusted by SES	0.95	0.025
Full Adjusted	0.95	0.085
Interaction model	0.95	0.047