Master of Public Health

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Neighborhood risk factors of low birthweight in Paris-city

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LIST OF ABBREVIATIONS

EU	European Union
GIS	Geographic information systems
INSEE	National Institute of Statistics and Economic Studies
IRIS	Îlot Regroupé pour l'Information Statistique (French census block unit)
LBW	Low birth weight
LLr	Log likelihood ratio
LUR	Land use regression model
Term LBW	Full term low birth weight
NO_2	Nitrogen dioxide
OR	Odds ratio
$PM_{2.5}$	Particulate matter with an aerodynamic diameter of less than 2.5□g
PM_{10}	Particulate matter with an aerodynamic diameter of less than 10□g
RR	Relative risk
SES	Socioeconomic Status
SGA	Small for gestational age

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1. Introduction

1.1 Public Health Context

Low birth weight (LBW) is an adverse pregnancy outcome that has recently been given great attention due to its relative higher frequency among adverse birth outcomes[1] and increased incidence in the past two decades. Based on epidemiological observations, LBW is defined by the World Health Organization as an infant weighing less than 2,500 grams (5.5 pounds) at birth and is an international, standardized threshold regarding measuring infant increased risk of death[2]. Despite programs and policies in a number of countries designed to lower the incidence of adverse birth outcomes in the past 10 to 15 years, LBW has not decreased[3]. On the contrary, in France, 6.4% of newborns were born with LBW in 2010, having increased by 23% since 1980[2]. LBW is a major public health burden with subsequent and long term adverse consequences in childhood health and associated increased costs.

As an indicator of fetal growth restriction, LBW is a condition associated with increased mortality during the first year of life[4] and with adverse health outcomes that could extend well into adulthood. Long term sequelae include the development of coronary heart disease[5,6] hypertension[7], non-insulin-dependent diabetes[8], and is also linked to increase incidence of stroke[5], such outcomes that are considered as top causes of death in developed countries[9]. In addition, LBW is associated with a greater risk of subsequent morbidity and higher healthcare expenditure. Subsequent complications for infants born with low birth weight include respiratory failures shortly after birth, and childhood asthma.[10,11] Although, no national study has been conducted to date in France with regards to socio-economic costs due to LBW in the country,[12] a US study found that the mean length of hospital stay for LBW is 12.9 days approximately costing $15,100 compared to an uncomplicated birth with an average 1.9 hospital days costing approximately $600.[13] Furthermore, US national research estimated that the per-child cost of a LBW birth, throughout the child's life, is about $51,000.[14]

As one of the single most important factors determining child survival with straining emotional and economic costs, low birth weight is a critical child and maternal health issue. Addressing this challenge requires greater epidemiological investigation to design more effective interventions.

1.2 Socioeconomic individual risk factors

There is a strong causal relationship between individual risk factors associated with maternal socioeconomic status (SES) to LBW. The fundamental causation theory, according to social epidemiologists, outlines the causal chain of adverse health outcomes with social factors such as socioeconomic status being the distal, fundamental cause of disease anteceding the mediate, proximal individual risk factors that directly affect health such as lifestyle and behavior[15] (figure 1).

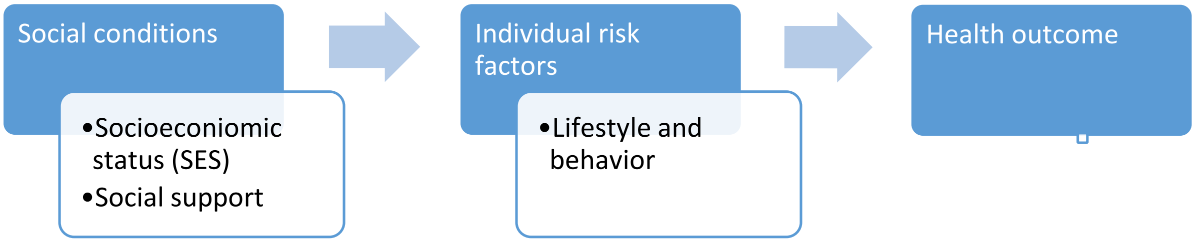

Figure 1. Fundamental theory causal chain

While it is not definitively known how socially disadvantaged situations influence the risk of LBW, associated lower SES proximal effects, ultimately affecting maternal health include limited access to health care, poor health-seeking behaviors, unhealthy lifestyles, poor nutrition, increased risk of infections, and greater physical and psychological stress.[16-18] Maternal health can be considerably related to deviation of infant genetic growth potential. LBW predictors and proximal related maternal risk indicators include education level, [19,20] age,[1,21] marital status, parity, [1,20-22] previous adverse birth outcomes, active/passive smoking, alcohol consumption, and gestational chronic diabetes or hypertension.[2,21]

Social-based programs are the most common developed interventions aimed at reducing the incidence of LBW. [23] During the 1980's in the US, reductions of LBW were observed after expansion of federally funded prenatal and pediatric care to extremely impoverished women with an annual income that was 185% below the poverty line.[17] Federal services and programs included food vouchers, nutritional education, income supports, and referrals to health and social services. However, there was no association with decreased rates of LBW after later expanding coverage to less impoverished women with no health insurance, but with greater resources.

Studies assessing the hypothesis that social support has a mediating effect on the relationship between socially disadvantaged situations and adverse birth outcomes have been inconsistent. While some studies have found reductions in low birthweight after prenatal care programs incorporate nutrition, health education, and psychosocial assessments and services for high risk women,[24,25] others have not. A review of 17 randomized control trials assessing the effects of comprehensive and intensive social support over a significant length of time to high risk pregnant women of giving birth to an infant of LBW, found no statistically significant reduction in the outcome (11 trials; 8681; RR 0.92, 95% CI 0.83–1.03). Trials had been conducted in developed countries including Australia, France, the UK and USA, while social support had been defined as advice and counselling (on health-related behaviors, such as nutrition, stress management, alcohol and recreational drug use), tangible help (transportation for clinical appointments and household help) and emotional support.[26] The same review explained that the lack of effect concluded maybe due to the studies failure to identify women at true high risk of having LBW babies.

In addition to individual risk factors, SES also encompasses neighborhood risk factors that both, directly affect health and/or indirectly shape individual risk of developing an adverse health outcome. Therefore, studies need to conceptually expand on the observing set of exposures linked to LBW, such as the environmental context associated with social conditions to identify true at risk mothers (figure 2).

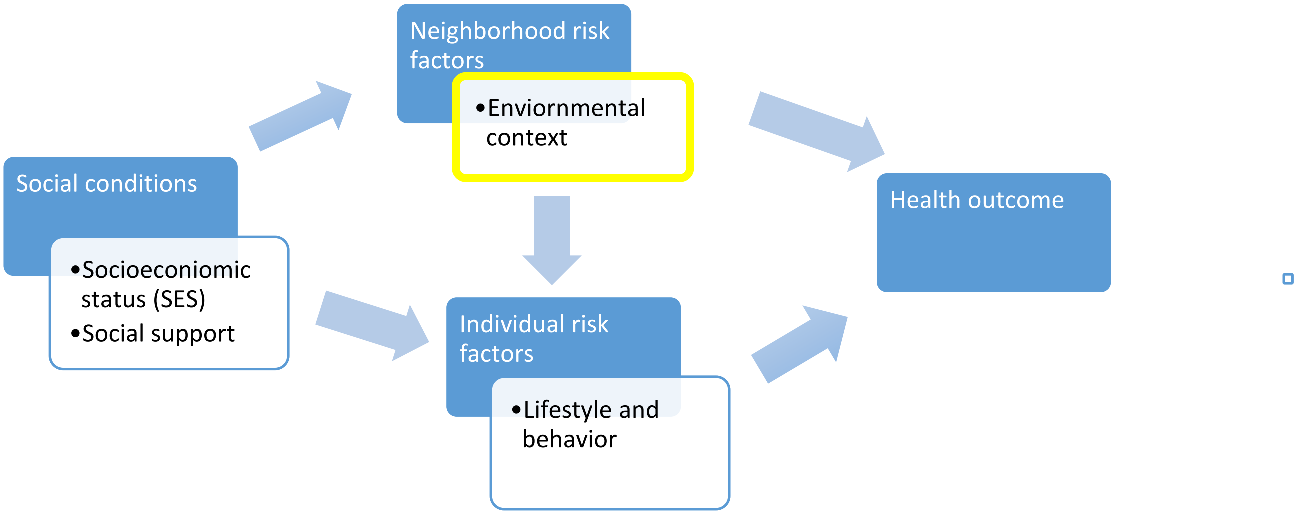

Figure 2. Conceptual causal chain of LBW hierarchical risks

1.3 Contextual environmental risk factors

Interest in focusing on environmental determinants of adverse birth outcomes has been increasing in the field of pediatric health in recent years. Prenatal development constitutes a window of high susceptibility to the impact of environmental toxins including ambient air pollution which is gaining concern due to its widespread exposure. Although the biological mechanism identifying how air pollutants affect fetal development still remains largely unknown, it has been suggested that air pollutants can invade the body through direct diffusion or active transport. More specifically, suggested main mechanisms involve placental inflammation linked to oxidative stress, changes in hemodynamic and rheological factors, endocrine disruption, and genetic and epigenetic changes.[27-31] These highlighted changes are believed to impede with the maternal-fetal exchange of nutrients and oxygen, ultimately inhibiting full fetal growth potential. Granted it is suggested air pollution may have an impact on adverse birth outcomes,[32-37] results vary widely, both quantitatively and qualitatively, provided by the different study settings and methodologies used.

1.3.1 Particulate Matter ($PM_{2.5}$ & PM_{10})

Despite methodological and effect heterogeneity across studies, a meta-analyses[35-37] and a literature review[34] have indicated that increased risk of an infant born at term (> 36 gestational weeks) with LBW is shown to be most consistently associated to particulate matter with an aerodynamic diameter of less than 2.5µg/m^3 ($PM_{2.5}$). In addition, a European cohort study using pooled data from 12 countries, have found significant increased risks to LBW among mothers exposed to mean $PM_{2.5}$ concentrations of less than 25μg/m^3 (OR 1.21, 95% CI 1.06–1.38), 20μg/m^3 (OR 1.41, 95% CI 1.20-1.65), and 15μg/m^3 (OR 1.79, 95% CI 1.29-2.48) during pregnancy, such exposure mean concentrations that are even lower than the present European Union (EU) annual limit of 25μg/m^3. [20] With regards to maternal exposure to particulate matter with an aerodynamic diameter of less than 10μg/m^3 (PM_{10}), a meta-analysis[39] found no association to term LBW (OR 1.02, 95% CI 0.90–1.32), while another meta-analysis[35] found an association to term LBW from maternal exposure throughout the entire pregnancy (OR 1.03, 95% CI 1.01-1.05), consistent to other studies.[39,40] The annual EU exposure mean concentration limit for PM_{10} is 40 μg/m3[76].

1.3.1 Nitrogen Dioxide (NO_2)

Recent findings on the association between nitrogen dioxide (NO_2) and term LBW have been inconsistent estimated by land use regression models (LUR) observing a positive association,[20] negative associations,[9,41] and no associations.[42-44] The varying results could possibly be due to low spatial variability in the LUR models with poor distribution heterogeneity of monitoring stations (general and roadside stations) from which the data had been extracted,[41,45] thus consistency may be hindered by exposure misclassification.[42] Such inconsistencies among research findings have set back policy implementation due to exposure measurement uncertainties.[35] The EU exposure mean concentration limit for NO_2 per year is 40 μg/m3[76].

1.4 Policy limitations

Exposure assessments on the relationship between air pollution and adverse birth outcomes are often challenged by obtaining spatially resolved estimates of exposure in large, population-based studies. Most exposure assessments rely on regulatory monitoring networks for air pollution data, often assigning maternal concentration levels according to the nearest, continuous monitor. Although such monitors can provide high temporal resolution (daily and hourly data), spatial coverage is usually poor as few urban monitoring networks collect pollutant concentration data at more than 20 locations.[46-49] As air pollution geographically varies within a city, there is a critical need to characterize variation in exposure associated with the spatial location of maternal residences to identify true risk.

Among other study inconsistencies, a major drawback for policymakers is the lack of adequate control for confounders[20] including the interacting examination of individual and neighborhood level socioeconomic indicators either alone or in combination, on the effect of air pollution on birth outcomes. [18] Given that air pollution levels are often highest in the most socioeconomically deprived areas, greater exposure spatial resolution and adjustment for major SES indicators are needed to capture the intra-urban differences at both, the individual and neighborhood level to identify the attributable variability explained.[50,51] While many studies have adjusted effect estimates of air pollutants on term LBW for major risk factors indicative of growth restriction (i.e. socioeconomic factors), only a few have looked at the potential confounding and interacting effects of individual and neighborhood socioeconomic related variables.[52,53] However, these studies have only used one level models, thus neighborhood contextual variables were assessed as individual risk factors.

1.5 Improved modeling approach

1.5.1 Multilevel modeling

Multilevel modeling is indicated to be a useful way to analyze the relationships between community level environmental data, individual risk factors, and birth outcomes.[54] Studies using multilevel hierarchical models, of which only a few have done, have observed differed risks by neighborhood stratified SES. One study observed a greater risk of adverse birth outcomes in the most deprived areas (-1.7g, 95% CI -4.6-1.3) and no significant association in high SES neighborhoods (0.6g 95% CI -1.3-2.5) after adjusting for both individual characteristics and air pollution exposure on reduced birth weight,[18] consistent with other studies.[54,55] However, two studies used proxy measures such as distance to highways to measure air pollution exposure,[18] of which one also focused on preterm births.[55] Multilevel modeling is warranted as these authors have highlighted the interaction of which a mother's individual susceptibility to adverse birth outcomes can be altered by not only social and economic conditions, but also further exacerbated by the physical environment in which she resides in. However, these studies have been done in the US, where major cofounders explaining the disparity include individual risk factors such as maternal race/ethnicity, lack of prenatal care and access to health insurance, all of which are most strongly prevalent in the most socially deprived neighborhoods.

Although a European meta-analysis didn't observe a significant change on the effect of air pollution on term LBW after adjusting for individual SES indicators based on educational level,[20] area level deprivation on adverse birth outcomes has still been poorly examined in Europe. Adjusting for neighborhood level deprivation may yield different effects in Europe, particularly in France, due to full national coverage of health insurance and free pre-natal care in comparison to other countries like the US where health coverage is limited, but nonetheless, isn't deemed any less relevant. On the contrary, a multi-level study in Spain, although air pollution was not measured, found that term LBW varied among the different socioeconomically stratified neighborhoods (unemployment by census tract) with greater risks in poorer neighborhoods (OR 1.56, 95% CI 1.37–1.78) after adjustment for individual risk factors.[56] Other independent variables measured at the contextual neighborhood level included educational attainment and maternal ethnic origin, also having found similar findings.

1.5.2 Spatial Analysis

Exploratory spatial data analysis is a common spatial technique used to support ongoing epidemiological investigations of health-related events. Only a few studies have assessed the effect of the geospatial distribution of air pollution on adverse birth outcomes, although not looking at term LBW as an outcome specifically.[44,49,57,58] Geographic information systems (GIS) is suggested to be an improved exposure assessment approach in conjunction with improved spatial data such as census data versus regional, to take into account small-area variations and minimize exposure misclassification. In addition, other known contextual, predictive risk factors (i.e. SES) can be accounted for in the geospatial exposure assessment. With the exception of infant mortality studies,[49,57,58] to our knowledge, there has been no such birth outcome study conducted in France on reduced birth weight. By characterizing and geographically identifying maternal areas of vulnerability to reduced birthweight from both environmental and social factors, such findings could aid policy decision making in designing effective regulation.

As such, the aim of our study is to assess the role of environmental exposures and social characteristics on the risk of LBW at both the individual and neighborhood levels in Paris-city. Two methodological objectives are included in this study: i) a spatial analysis to assess the correlation between the distributions of the contextual exposures with adjusted covariates in relation to LBW and term LBW ii) a multilevel analysis to analyze the effect of social and environmental determinants on the risk of LBW at the individual and contextual level.

2. Methods and Material

2.1 Study setting

The study takes place in Paris metropolitan area, the most populous city in France and the most populous urban area in the European Union. The City of Paris is one out of Ile-de-France’s eight departments (Northern region) with an area of 105.4 km² (40.7 mi²) and a population of approximately 2.2 million inhabitants in 2009. The city is subdivided into 20 administrative districts (arrondissments) and 992 census blocks.[59]

2.2 Neighborhood characteristics

2.2.1 IRIS

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) is the statistical unit used. It is the smallest administrative unit with available socioeconomic data in France and is constructed to be as homogenous as possible in terms of socio-demographic characteristics and land use. Each geographical unit is home to approximately 2000 inhabitants. We did not have data from 46 IRIS’s, thus our analysis included a total of 946 census blocks.

2.1.2 Social deprivation index

Socioeconomic and demographical data were obtained from the 2006 national census provided by INSEE at census block level to create the index. The index is used to characterize neighborhood deprivation encompassing a total of 48 census block variables from different socioeconomic domains including household demographics, immigration, income, education, and housing characteristics.

The methodology and contextual variables used to construct the index is described elsewhere.[60] In short, successive principal-component analysis were used to maximize the inertia of the first component and eliminate the poorly correlated variables. A final 20 variables were included in the index explaining 59% of the inertia for the first component. In addition, these variables alone are assessed on the effect of term LBW at the census tract level in the multi-level analysis. These variables include foreigners (%), Immigrant population (%), Single-parent families (%), Unemployed people (%), Employed workers (%), People with stable job (%), Non-owner occupying 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 m (%), 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 (%), Self-employed people (%), Managers workers (%), Blue-collar workers (%) and Median income per consumption unit. Refer to Figure 8 for the spatial distribution of the index distribution by tertiles at the census blocks level in Paris-city.

2.2.4 Air pollution data

Annual ambient air concentrations of NO_2, $PM_{2.5}$ and PM_{10} were modeled by the local air quality monitoring networks (AirPARIF and 'petite couronne') for each census block within Paris metropolitan area during the study period (2007-2010). The air quality monitoring networks in Paris uses the ESMERALDA deterministic methodology to describe and characterize environmental exposure disparities at a local scale.[61] This modeling method was tested for effectiveness and reliability for assessing air quality in health assessment research,[62] integrating meteorological data (air temperature, wind speed and direction, relative humidity, barometric pressure, supplied by Météo France, the French meteorological service), emission sources of air pollutants, and background pollution measurements, as input parameters. Selected emission sources included linear sources (main sources), surface sources (diffuse road sources, residential and tertiary emissions) and important point sources.

The total mean of each annual mean concentration level for each air pollutant type during the study period (2007-2009) was used in the analysis. Refer to figure 5, 6 and 7 for the spatial distribution of NO_2, $PM_{2.5}$, and PM_{10}, respectively, by tertiles at the census block level in Paris-city.

2.3 Individual data

2.3.1 Study population

The study population include all live births in Paris- city metropolitan area between the years of 2007 to 2009 obtained from ”Certifcat de santé du 8ème jour” (translated: health certificate of infant aged 8 days) provided by l'agence Centre de Protection Infantile et maternelle (translated: Central agency of infant and maternal protection) agency, or PMI of Paris. A total sample of 79,876 births were used in the spatial analysis. Due to missing maternal socio-economic information, our sample size for the multilevel analysis had been reduced to 35,314 births. All births were geocoded according to the postal address of maternal residence by the Geocible institution.

Individual characteristics obtained with the certificates that were used in the multilevel analysis include the following set of variables: infant sex and maternal related variables such as level of education, occupation, activity, age, parity, and number of deliveries. Paternal variables such as level of education, occupation, and activity, were not used in the analysis due to collinearity issues with the maternal variables.

2.3.2 Health outcome

To investigate the incidence of reduced birth weight, our outcome measures include both LBW and term LBW (dichotomous variables). LBW is defined as an infant weighing less than 2,500 grams (5.5 pounds) at birth, and term LBW is defined as an infant born full term with a gestational age ranging between 37 – 41 weeks, weighing less than 2,500 grams. In our final dataset for the spatial analysis, there are a total of 5499 cases of LBW (6.9 percent) and 3340 cases of term LBW (4.18 percent) between the time period of 2007-2009. Refer to Fig. 3 and 4 for the spatial distribution of the prevalence of LBW and term LBW by tertiles at the census blocks level in Paris-city. However, the prevalence of term LBW drops to a total of 862 cases (1.84 percent) for our final dataset used in the multilevel analysis. LBW was not assessed due to the conclusion of its distribution obtained in the spatial analysis.

2.4 Statistical methods

2.4.1 Spatial methodology

The spatial analysis uses census data and generated spatial models to identify geographical areas of susceptibility of mothers to give birth to an infant with reduced birth weight in Paris-City. The spatial analysis carried out by the SaTScan software[63] is comprised of two major components including the descriptive and the clustering analysis. The descriptive analysis aims to give us a visualization of the spatial display of both LBW and term LBW, in addition to the exposures: atmospheric air pollutants NO_2, $PM_{2.5}$ and PM_{10}, and social deprivation. The identification of a spatial pattern for the rate of LBW and term LBW is facilitated by the clustering

analysis, and the inclusive multivariate analysis aims to measure spatial relationships with the corresponding exposures to reveal risk factors.
All explanatory data extracted from Paris-City's 946 census blocks, including social deprivation index and the concentration of atmospheric air pollutants NO_2, $PM_{2.5}$ and PM_{10} are categorized into tertiles for both the descriptive and multivariate analysis. However, we did not have social deprivation scores for a total of 11 census blocks, thus the descriptive analysis for social deprivation alone and the multivariate analysis including social deprivation (alone and with covariates NO_2, $PM_{2.5}$ and PM_{10}) were reduced to 935 census blocks. The rates for both LBW and term LBW are also categorized into tertiles for the descriptive analysis, but left continous for the multivariate analysis.

The number of cases for both LBW and term LBW in each census block is assumed to follow a Poisson distribution (rare outcome). The procedure used by SaTScan works as follows: a circle or window of variable radius (from zero up to 50% of the population size) is placed at the longitude and latitude of every census block centroid and moves across the whole study area to compare the incidence rate in the windows with what would be expected under a random distribution. The identification of the most likely clusters is based on a likelihood ratio test with an associated p-value (0.05) obtained using Monte Carlo replications. The ArcGis 10.1 software (ESRI, Inc., Redlands, California) was used to map the results.

2.4.2 Logistic multilevel methodology

The multilevel mixed-effects logistic regression was carried out to produce a two level model for the binomial data. Using the STATA 12.0 software[64] with reference to the model form for the binary outcome term LBW,

$$\text{Logit}(\Pr Y_{ij} = 1|X_{ij}, u_j) = H(x_{ij}\beta + z_{ij} u_j)$$

Yij is the outcome in the ith subject in the jth census tract, where uj is the random census tract intercept. This model form is an example of a generalized linear mixed model, generalizing the linear mixed-effects model to non-Gaussian responses. On the left side of the equation, the covariates of interest in our study are noted by the group i subject level which includes all individual characteristics (maternal agei, infant genderi, etc.) and the group j census tract level includes all contextual, longitudinal variables (NO_2j, SES indexj, etc.). The random effects uj are group realizations, thus summarizes the variance components at the census tract level (IRIS). This is to assume that the random effects shared within the individual level are unique to the IRIS level groups, concluding if a spatial structure exists.

On the right side of the equation, H() is the logistic cumulative distribution function, which maps the linear predictor to the probability that yij = 1. Vector xij are the covariates for the fixed effects, similar to the covariates one would find in a classical regression model with regression coefficients β. Vector zij are the covariates corresponding to the random effects and can be used to represent both random intercepts and random coefficients.

3. Results

3.1 Descriptive Analysis

3.1.1 Spatial distribution of LBW and term LBW rate

LBW rate: The lowest level of the LBW rate (<4 cases) is concentrated in the west-central part of Paris, as well as in the eastern and western census blocks that extend outside the Paris island. Meanwhile the highest level (8 – 27 cases) is concentrated in the north eastern part of the city. The medium level (5 – 7 cases) with the highest level almost encircle the west-central part of the city (Figure 3).

Term LBW rate: With reference to LBW, the spatial distribution of term LBW can be similarly described, however concentrations for both the low (<2 cases) and high levels (5 – 21 cases) are less aggregately concentrated (figure 4).

Figure 3. Spatial distribution of LBW rate

Figure 4. Spatial distribution of term LBW rate

3.1.2 Spatial distribution of exposures

NO_2: All average concentration level tertiles are above the EU annual limit. The lowest tertile level of NO_2 air concentration (37.00 – 49.46μg/m^3) is located in the south-east, with the highest concentration level (56.07 – 85.28μg/m^3) located in the north-eastern part of the city, as well as around the perimeter. The medium level (49.47 – 56.06μg/m^3) of the pollutant's air concentration is also located in much of the north-eastern part of the city bordering the highest level aggregation (figure 5).

$PM_{2.5}$: All average concentration level tertiles are below the EU annual limit. However, similar to NO_2, the lowest level of exposure to $PM_{2.5}$ (17.22 – 19.17µg/m^3) is also located in the south-eastern part of the city, however less aggregated. Meanwhile the highest level (20.28 – 24.50µg/m^3) of $PM_{2.5}$ concentration is found mainly in the Northern region and throughout the perimeter. The medium level of exposure (19.18 – 20.27µg/m^3) is more dispersed throughout the city in comparison to NO_2, however less so in the south east (figure 6).

PM_{10}: All average concentration level tertiles are below the EU annual limit. The spatial distribution of exposure to PM_{10} can be similarly described as $PM_{2.5}$ (figure 7).

Social deprivation: The wealthiest census blocks (-1.85 – -1.06) are located in the western part of the city. Meanwhile the less wealthy (-0.51 – 1.84) are heavily located in the north-east and along the perimeter. The census blocks classified with a medium deprivation level can be geographically described as dividing the wealthiest and less wealthy census blocks (figure 8).

Figure 5. Spatial distribution of NO_2 level of air concentration

Figure 6. Spatial distribution of $PM_{2.5}$ level of air concentration

Figure 7. Spatial distribution of PM_{10} level of air concentration

Figure 8. Spatial Distribution of social deprivation

3.1.3 Individual level summary

The individual explanatory variables used in the multilevel analysis are summarized by category with the birthweight mean for the entire sample population, and with the frequency percentage between both term LBW and it's comparison group (all births: 24 – 44 weeks, 299 – 5550 grams) in table 1. Fetal growth predictor and socio-economic related variables are infant specific such as gender and maternal specific: education level, occupation, activity type, age, number of pregnancies and number of deliveries. Variables including maternal age, number or pregnancies and number of deliveries were categorized for the purpose of the descriptive analysis only.

On average, the birthweight for female infants is 137 grams lower than the mean birthweight for male infants. In addition, there are almost twice as many female infants (64.5%) within the term LBW case group than there are male infants (35.5%), while the infant gender ratio is approximately equal within the control group.

With regards to maternal education, the observed average birthweight increases in parallel with each increase in educational level achievement. However, the proportion of mothers with lower educational achievement is greater in the case group in comparison to the control group. Although the prevalence of primary level attainment is slightly higher in the control group by 0.57%, secondary level attainment is more than twice as great in the case group, with lower proportions of higher educational achievement including Baccalaureeate (7.77%) and higher level achievement (84.8%) compared to the control (8.29 and 87.01% respectively).

Infants with higher mean birth weights are observed from mothers with an intellectual profession (3319g) compared to the lowest mean birthweight from mothers who are farmers (3176g). The control group has a greater proportion of mothers from intellectual (61.23% compared 57.54%) and intermediary (10.21% compared to 8.12%) professions with lower proportions observed in the rest of the categories (farmer, craftsman/trader, employee, labor worker) compared to the case group.

As per maternal activity, the lowest average birthweight (3270g) is found among mothers who are inactive compared to the highest mean birthweight from mothers who are retired (3461g). The case group has a higher proportion of inactive mothers (2.55% in comparison to 1.59%) with lower proportions found among all other categories (active, retired, at home, parental leave, unemployment, and student) in comparison to the control group.

Younger mothers (≤25) have on average, newborns with lower birthweight (3255g) compared to older mothers (age groups 26-32 and 33-39, 3306g and 3303g, respectively). However, the observed risk of low birthweight also increases for mothers who are 40 years old and older. Among term LBW infants, the proportion of mothers who are 40 years old and older are almost a twice as great (9.16%) in comparison to the control group (5.89%).

Newborn birthweight increases in parallel with the maternal number of deliveries. However, mothers who have had 2 deliveries or less are slightly more prevalent among the control group (87.27%). Furthermore, the prevalence of mothers whom have had 3 deliveries or more is greater among infants with term LBW (3-5 and ≥6, 12.65% and 0.58%, respectively) than the control group (3-5 and ≥6, 12.46% and .27%, respectively).

Similar to the number of deliveries, mothers who have had 2 pregnancies or less, have on average infants with lower birthweights (3285g), although mothers who have in between 3 to 5 pregnancies as opposed to 6 or greater like the deliveries category, give birth to infants with the greatest birthweight (3350g). As such, there is smaller proportion of mothers who have had 3 to 5 deliveries in the case group (19.3%) compared to the control group (23.49%) while proportions among the other two categories are greater in the cases compared to the control.

Table 1. The descriptive analysis for individual characteristics

Categorical variables	**Mean birthweight (in grams)**	**(SD)**	**Term LBW N (%)**		**Control N (%)**	
Gender of infant						
Male	3369	506	306	35.5	17535	50.9
Female	3232	494	556	64.5	16917	49.1
Maternal education						
Primary level (≤5 years)	3194	542	12	1.39	283	1.96
Secondary level (>5 – 12 years)	3218	595	52	6.03	1338	2.53
Baccalaureate (13 – 14 years)	3272	545	67	7.77	2856	8.29
High level (≥15 years)	3308	495	731	84.8	29975	87.01
Maternal Occupation						
Farmer	3176	605	2	.23	56	0.16
Craftsman/trader/company manager	3302	510	38	4.41	1339	3.89
Intellectual profession	3319	588	496	57.54	21095	61.23
Intermediary profession	3286	521	70	8.12	3516	10.21
Employee	3265	533	248	28.89	8273	24.01
Labor worker	3237	519	7	.81	173	0.50
Maternal activity						
In activity	3298	505	761	88.28	30034	97.18
Retired	3461	267	0	0	17	.05
At home	3339	504	27	3.13	1159	3.36
Parental leave	3336	506	15	1.74	926	2.69
Unemployment	3316	491	32	3.71	1373	3.99
Student	3311	451	5	.58	394	1.14
Other inactivity	3270	565	22	2.55	549	1.59
Maternal age*						
≤25	3255	481	32	3.71	1524	4.42
26-32	3306	494	352	40.84	16058	46.61
33-39	3303	512	399	46.29	14840	43.07
≥40	3277	547	79	9.16	2030	5.89
Previous # of deliveries*						
≤2	3294	499	748	86.77	30066	87.27
3-5	3347	541	109	12.65	4292	12.46
≥6	3419	593	5	.58	94	0.27
Parity*						
≤2	3285	498	677	78.54	25845	75.02
3-5	3350	517	167	19.3	8092	23.49
≥6	3345	583	18	2.09	515	1.49

* Variables are categorized only for the purpose of the descriptive analysis

3.2 Spatial results

3.2.1 Identification of LBW clusters in Paris-City

Figure 9 illustrates the spatial distribution of unadjusted LBW clusters in Paris-city. The most likely cluster area located in the northeast has a LBW risk that is 1.22 times greater in comparison to the rest of the study area (p-value = 0.14, not significant). This cluster comprises of 50 census blocks and hosts a population of 6210 inhabitants. However, none of the clusters (most likely and secondary) were statistically significant in the crude analysis for LBW, thus we cannot reject the hypothesis that the risk of LBW is equally distributed in Paris at the census block level. For this reason, we didn't include the LBW adjusted analysis. Table 2 summarizes the results of the unadjusted LBW analysis.

Figure 9. Distribution of unadjusted LBW clusters in Paris

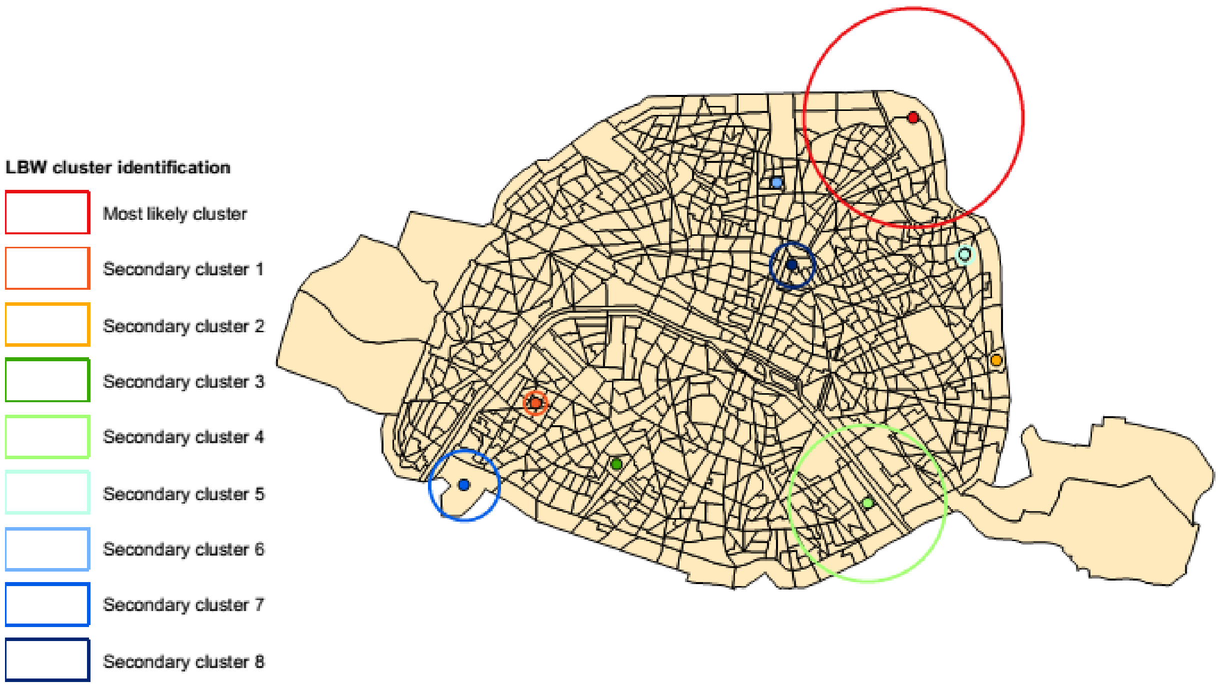

Table 2. The mostly likely and secondary clusters for LBW resulting from the unadjusted analysis

		Confounders	Radius (meter)	Census block included	Expected cases	Observed Cases	RR	LLr	P-value
Most likely Cluster		None	2106.29	50	427.52	511	1.22	8.36	0.14
Secondary Clusters	1	None	218.94	2	11.91	2.35	2.36	7.87	0.20
	2	None	0	1	7.44	2.69	2.70	7.24	0.31
	3	None	0	1	7.16	2.65	2.66	6.72	0.47
	4	None	1507.69	52	269.80	328	1.23	6.19	0.66
	5	None	170.68	2	9.02	21	2.33	5.78	0.78
	6	None	0	1	9.70	22	2.27	5.72	0.79
	7	None	672.96	3	12.67	26	2.05	5.38	0.89
	8	None	424.14	10	64.23	91	1.42	5.00	0.96

LLr: log likelihood ratio.
RR: Relative Risks.

3.2.1 Identification of term LBW clusters

3.2.1.1 Unadjusted analysis

Figure 10 illustrates the spatial distribution of unadjusted term LBW clusters in Paris-city. The most likely cluster area has a term LBW risk that is 1.23 times greater in comparison to the rest of the study area (p-value = 0.0001, statistically significant). This cluster is located in the north-eastern part of Paris-city and comprises of 250 census blocks and hosts a population of 28,099 inhabitants. Three secondary clusters are identified with no statistical significance. Table 3 summarizes the results of the unadjusted term LBW analysis.

Figure 10. Distribution of unadjusted term LBW clusters in Paris

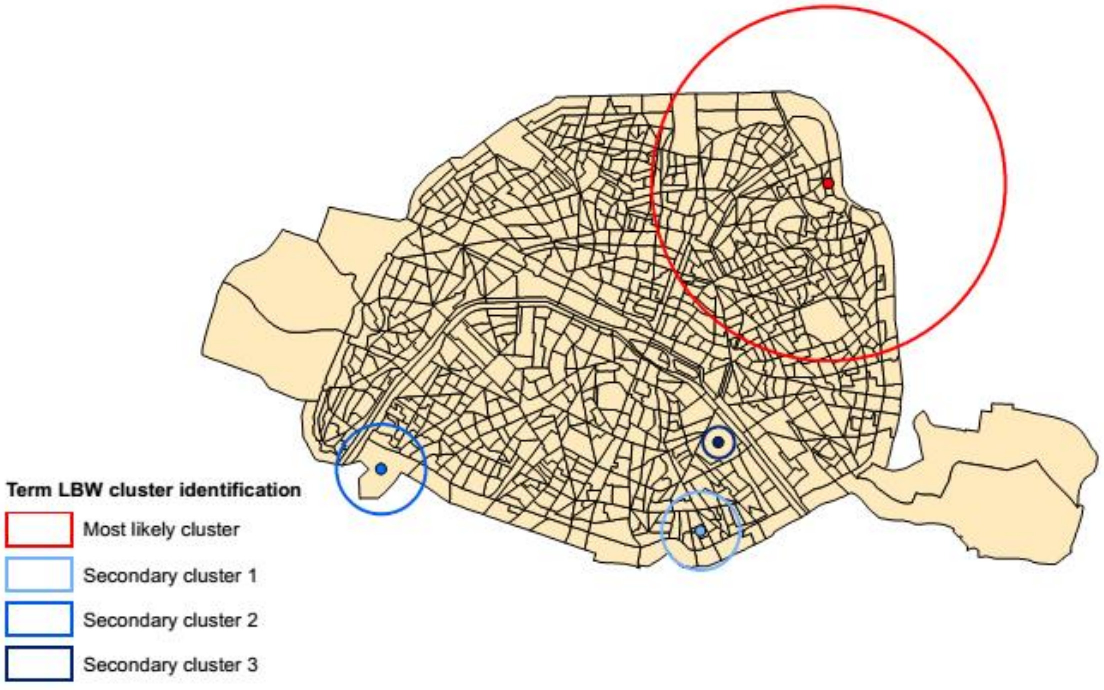

Table 3. The mostly likely and secondary clusters for term LBW resulting from the unadjusted analysis

		Confounders	**Radius (meter)**	**Census block included**	**Expected cases**	**Observed Cases**	**RR**	**LLr**	**P-value**
Most likely Cluster		None	3559.99	250	1174.95	1335	1.23	16.50	0.0001
Secondary Clusters	1	None	786.90	23	93.87	128	1.38	5.74	0.79
	2	None	900.21	7	15.89	31	1.96	5.64	0.80
	3	None	315.26	2	5.94	15	2.53	4.85	0.96

LLr: log likelihood ratio
RR: Relative Risks

3.2.1.2 Adjusted analysis

The series of adjusted analysis for term LBW includes assessing the effect of each exposure alone, followed by adjusting for the covariates together (each air pollutant with social deprivation), and lastly investigating if an interaction exists between the two covariates as summarized in table 4.

After adjusting for environmental air pollutants NO_2, $PM_{2.5}$ and PM_{10} individually, the most likely cluster identified is the same as in the unadjusted model (p-value = 0.0001, RR =1.23). NO_2 had two secondary clusters that were statistically significant comprising of three census blocks (P-value = 0.003, RR = 2.79) and the other of 205 census blocks (p-value = 0.004, RR = 1.20), although not illustrated. The LLR for the most likely cluster of each pollutant decreased in the adjusted model from the LLR obtained in the unadjusted model (16.50), suggesting that each air pollutant alone partially explain the excess risk.

The most likely cluster shifts location and decreases in size to one census block with no radius after adjusting for social deprivation index (p-value = 0.01, statistically significant). One secondary cluster with borderline significance was also detected (p-value = 0.08, RR = 1.64, LLR = 9.15), although not illustrated. The most likely cluster has an increased risk of 3.75, in addition to a decreased LLR of 11.16, indicating that social deprivation explains a great part of the excess risk.

With reference to the adjustment of social deprivation alone, the mostly likely clusters for the interaction between social deprivation and each air pollutant (NO_2, $PM_{2.5}$, PM_{10}) increases in size to three census blocks, but does not shift in location (figure 9.). The risk increases from the unadjusted model (RR = 1.23), but decreases from the effect of social deprivation alone (RR = 3.75) on term LBW to 2.43 for NO_2 and 2.41 for $PM_{2.5}$ and PM_{10}. In addition, the LLR further decreases after adjusting for the interacting covariates to 10.20 for NO_2 (p-value = 0.03, statistically significant) and 9.95 for both PM2.5 and PM10 (p-value = 0.03 and 0.04, respectively, both statistically significant) indicating that the covariates between social deprivation and environmental air pollutants in the adjusted model explains the greatest part of excess term LBW observed in the unadjusted model. Figure 9 illustrates the spatial distribution of the adjusted most likely cluster with the best fitted explanation of excess term LBW.

As such, we suspected an interaction, of which social deprivation may possibly be moderated by air pollution exposure. However, after assessing the effect of each interaction term between each air pollutant NO_2, $PM_{2.5}$ and $PM_{2.5}$ with social deprivation, no model yielded an improved LLR value (10.63, 10.78, and 10.93, respectively, with global p-value = 0.02).

After a final cluster analysis done, with all exposures classified into quantiles instead of tertiles, the cluster disappears in total. Social deprivation adjusted with each air pollutant NO_2, $PM_{2.5}$, and PM_{10} yields a risk of 3.19 (p-value = 0.09, LLR = 8.95), 2.24 (p-value = 0.13, LLR = 8.6) and 2.25 (p-value = 0.11, LLR = 8.6) respectively. Although all adjusted covariates are borderline significant, the LLR further reduces, producing the best fitted models in fully explaining term LBW excess risk.

Figure 11. Adjusted most likely cluster with best fitted explanation of excess term LBW

The figure illustrates the cluster with the best fitted explanation. The centroid is in the same location for the adjustment of the interaction between social deprivation and all three air pollutant types (categorized in tertiles), with a radius that includes three districts.

Table 4. The mostly likely clusters for term LBW resulting from the adjusted analysis

Confounders	**Radius (meter)**	**Census block included**	**Expected cases**	**Observed Cases**	**RR**	**LLr**	**P-value**
NO_2	3559.99	250	1175.80	1335	1.23	16.32	0.0001
$PM_{2.5}$	3559.99	250	1175.40	1335	1.23	16.41	0.0001
PM_{10}	3559.99	250	1175.34	1335	1.23	16.42	0.0001
Social deprivation	0	1	5.08	19	3.75	11.16	0.01
NO_2& social deprivation	388.90	3	14.02	34	2.43	10.20	0.03
$PM_{2.5}$& social deprivation	388.90	3	14.20	34	2.41	9.95	0.03
PM_{10}& social deprivation	388.90	3	14.19	34	2.41	9.95	0.04

LLr: log likelihood ratio
RR: Relative Risks

3.3 Multilevel results

We carried out three analytical steps to produce the final two level model with adjusted individual and census tract covariates explaining term LBW (table 7). For the first step, we produced a multivariate adjusted model with the estimated effects from individual specific variables on term LBW. Table 5 summarizes the univariate analysis that was performed to measure the estimated coefficient between each variable and the outcome, followed by the multivariate analysis where each significant variable (p-value: 0.05) was added one by one into the multivariate model (on the right) according to the strength of the effect while observing changes in the coefficient.

Based on the univariate estimates, the effect of infant gender, maternal parity, and maternal age were highly significant (p-value: 0.000) on the effect of term LBW. Female infants are 1.89 times as likely to be term LBW in comparison to male infants. In addition, per every unit increase in parity and maternal age, the odds of having a term LBW infant decreases by 9% and increases by 4%, respectively. The inverse association found between parity and term LBW can be due to a lack of sampling validity, as the cases are disproportionately comparable to the controls resulting in a lack of statistical power (descriptive table). When adjusting for other individual specific covariates based on a 0.20 p-value cutoff, the effect of infant gender did not significantly change, while the effect of parity further decreased by approximately 9% and maternal age slightly increased by 2%. Maternal education was borderline significant in the univariate analysis (Baccalaureate and high level, p-value: 0.06 and 0.07, respectively), but becomes significant (0.04 and 0.02, respectively) when adjusted with the covariates, suspecting of being modified with the presence of maternal age. The effect of having obtained a Baccalaureate degree and received more than 15 years of education in comparison to having only obtained a primary level of education decreases a mother’s odds of having a term LBW infant by 49% and 51%, respectively. Maternal activity category “other inactivity” was the only significant category (p-value: 0.03) with an effect that slightly decreased in the multivariate model where the chance of giving birth to a term LBW is multiplied by 1.54 per every unit increase in maternal inactivity (p-value: 0.05, 95%CI 0.99 – 2.38). Maternal occupation and previous number of deliveries were not significant in the univariate analysis, thus were not considered for the multivariate model.

Although, the model’s estimates (table 5) are analogous to the estimates one would find from a classical logistic regression, the random effect had been specified to the iris level, thus these models generalize the random effects at both the iris and the individuals within the iris level. The likelihood-ratio test (lrtest) comparing the specified model with one-level ordinary linear regression (model without uj), is provided and is highly significant for these data.

Table 5. Univariate analysis (left) with final multivariate model (right) of individual characteristics on the effect of term LBW

	Univariate Analysis				**Multivariate Model**			
Categorical variables	**OR**	**P-value**	**CI (95%)**	***Lrtest**	**OR**	**P-value**	**CI (95%)**	***Lrtest**
Gender of infant								
Male	Ref.				Ref.			
Female	1.89	0.000	1.64 – 2.18	*0.045	1.91	0.000	1.66 – 2.20	
Parity	0.91	0.002	0.85 - 0.97	*0.058	0.82	0.000	0.77 - 0.88	
Maternal Age	1.04	0.000	1.03 – 1.06	*0.047	1.06	0.000	1.05 – 1.08	
Maternal education								
Primary level (≤5 years)	Ref.				Ref.			
Secondary level (>5 – 12 years)	0.92	0.790	0.48 – 1.74		0.94	0.856	0.49 – 1.80	
Baccalaureate (13 – 14 years)	0.55	0.064	0.29 – 1.03		0.51	0.037	0.27 – 0.96	
High level (≥15 years)	0.58	0.065	0.32 – 1.04	*0.064	0.49	0.017	0.69 - 0.88	
Maternal activity								
Other inactivity	1.60	0.032	1.04 – 2.47		1.54	0.054	0.99 – 2.38	*0.049
In activity	1.00	0.975	0.77 – 1.31					
Retired	_							
At home	0.93	0.218	0.58 – 1.47					
Parental leave	0.64	0.126	0.36 – 1.13					
Unemployment	0.93	0.690	0.65 – 1.33					
Student	0.51	0.132	0.21 - 1.23	*0.056				
Maternal Occupation								
Farmer	Ref.							
Craftsman/trader/company manager	0.80	0.764	0.19 – 3.42					
Intellectual profession	0.66	0.572	0.16 – 2.74					
Intermediary profession	0.56	0.430	0.13 – 2.35					
Employee	0.85	0.820	0.21 – 3.51					
Labor worker	1.14	0.870	0.23 – 5.69	*0.068				
Previous # of deliveries	1.01	0.855	0.93 - 1.09	*0.057				

*lrtest: p-value with alpha risk 0.05 for likelihood ratio test specified for entire indicated model

In the second step, we conducted the same procedure as in the individual adjusted model, only with contextual specific variables (table 6). However, median income was the only contextual variable that was significant in a total of 18 variables including exposure to air pollutants NO_2, $PM_{2.5}$ and PM_{10}. In comparison to being a part of the lowest median income bracket (≥ 7,089 – 19,551), the odds of having a term LBW infants decreases by 16% for mothers belonging to the second (19,551 ≤ 25,950) and third median income bracket level (25,950 ≤ 54,110). It was suspected that median income would have a spatial structure due to the significance of the effect on the individual level. Although, the lrtest is not significant for this data (0.0801), when specifying median income as a random effect, hence treated as a contextual variable, the lrtest decreases to 0.0481. As such, the association of a spatial heterogeneity of the outcome due to the variation of median income between census blocks is strengthened. To further illustrate, when extending median income with a random slope, the model uses the covariance structure for both IRIS and the level of median income at census block level to generalize the spatial structure of median income across IRIS's and the individuals nested from each IRIS.

Table 6. Univariate model (left) and mixed effects model (right) with median income (extended as random effect) at census tract level on the effect of term LBW

	Univariate Analysis				Median income by census tract			
	OR	P-value	CI (95%)	*Lrtest	OR	P-value	CI (95%)	*Lrtest
Median income								
≥ 7,089 – 19,551	Ref.				Ref.			
19,551 ≤ 25,950	0.84	0.039	0.71 - 0.99		0.84	0.043	0.70 - 0.99	
25,950 ≤ 54,110	0.84	0.043	0.71 – 0.99	*0.0801	0.84	0.046	0.71 – 0.99	*0.0481

*lrtest: p-value with alpha risk 0.05 for likelihood ratio test specified for entire indicated model

Lastly, the individual multivariate model combined with median income as a random effect were combined to produce the final two level, mixed effects model (table 7). The effect of the covariates are considerably unaltered in comparison to the individual multivariate model. However, the lrtest p-value significantly decreased (0.0264) with the extension of the random slope to include median income, providing the best fitted model in our analysis in explaining a part of the variability to the distribution of term LBW.

Table 7. Final two level model for term LBW stratified by median income at census tract with adjusted individual level covariates as the contextual variable

	Median Income by census tract			
Model covariates	**OR**	**P-value**	**CI (95%)**	***Lrtest**
Gender of infant				
Male	Reference			
Female	1.91	0.000	1.67 – 2.20	
Parity				
	0.82	0.000	0.77 - 0.88	
Maternal age				
	1.06	0.000	1.05 – 1.08	
Maternal education				
Primary level (≤5 years)	Ref.			
Secondary level (>5 – 12 years)	0.94	0.854	0.49 – 1.80	
Baccalaureate (13 – 14 years)	0.51	0.037	0.27– 0.96	
High level (≥15 years)	0.49	0.017	0.69 - 0.88	
Maternal activity				
Other inactivity	1.54	0.053	0.99 – 2.38	*0.026

*lrtest: p-value with alpha risk 0.05 for likelihood ratio test specified for entire indicated model

4. Discussion

4.1 Multilevel results

To our knowledge, this is the first study using two different analytical methods including spatial and multilevel analysis to assess the hierarchical set of reduced birthweight risk factors in Paris. Although both methods used in our study yielded results that are inconsistent of each other, further explanation is highlighted.

The spatial analysis revealed that LBW is likely to be randomly distributed, while term LBW is not likely to be randomly distributed with a spatial aggregation located in the northeast of Paris-city. After controlling for social deprivation, the high risk cluster shifts location and increases in radius after adjusting for the combining effect with exposure to each of the three air pollutant types. Our findings suggest that social deprivation in combination with air pollution exposure at the census block level, can explain a great deal of the excess risk of term LBW.

The multilevel analysis, however, revealed a lack of association between term LBW and census tract variable's, social deprivation and air pollution concentration alone and in combination with each other. A possible explanation for the contradicting results may be due to the smaller sample size used in the multilevel analysis which had been reduced by more than half from the original dataset used in the spatial analysis due to missing information. A substantial proportion of the mothers to term LBW infants belonging in the Northeastern cluster may have been removed from the multilevel dataset which can be argued for, given that it is usually more difficult to reach and obtain information from lower socioeconomic groups.

4.2 Interpretation of results and associative findings

Nonetheless, the two level model did reveal a strong association with certain individual and contextual SES variables. With regards to socioeconomic-related factors, the individual risk of a mother giving birth to a term LBW infant decreases with greater educational attainment and increases with occupational inactivity, consistent with other findings.[20,65] Also similar to another European study, although having used different neighborhood level deprivation variables, our study found that with median income as a proxy measurement, term LBW varied among the different socioeconomically stratified neighborhoods with greater risks in poorer neighborhoods after adjustment for individual risk factors.[56]

A US study found a regional variation of low birth weight rates across the country after controlling for maternal and contextual risk factors, with 67 (27.0%) regions having significantly below and 98 (39.8%) regions having rates significantly higher than the national rate of 6.0 per 100 live births. The authors concluded that a significant part of the risk of low birth weight remains unexplained and is associated with maternal place of residence and perinatal and intra-partum care at the contextual level.[66]

However, as opposed to the US where there are greater health access inequalities due to limited health insurance coverage, a French population based study assessing the relationship between poor antenatal care and LBW, showed that very few women in France received little or no ante-natal care.[67] In addition, the study found that poor attenders of antenatal care, defined as women who had attended fewer than four visits (national recommendation is 7 visits) or if they had begun antenatal care during the last three months, was not statistically significantly associated with adverse birth outcomes for vulnerable subgroups including women under 20 and foreigners. However, there was a significant association with LBW for French women over 20 (OR: 2.6, 95% CI: 1.5 - 4.4). According to the survey, reasons for poor attendance for these women included unwanted pregnancy or serious worries such as unemployment, marital conflicts, and financial difficulties. The authors suggested that special attention should be given to women who are confronted with no major structural barrier to medical care to prevent adverse birth outcomes by helping them overcome their psychological distress.

Another French-based study having found green space associated with infant mortality after adjusting for neighborhood deprivation (p value = 0.12) in Lyon, suggested a pathway by stress reduction from exposure to green space towards a more favorable birth outcome.[58] Proposed biological mechanisms of stress reduction from contact with natural environments include psycho-neuroendocrine mechanisms, including the functioning of the hypothalamic pituitary adrenal axis which regulates cortisol secretion, processes associated with the nutrition and oxygenation fetal-maternal exchanges restricting fetal growth.[68] Future analysis can be done to focus on green space at contextual level adjusting for neighborhood socioeconomic deprivation to assess its potential contributing role in explaining a part of the reduced birth weight variation in Paris metropolitan area.

Apart from SES related indicators, other individual risk factors for a mother to give birth to a term LBW infant include maternal age, maternal parity and gender of infant after adjustment for SES variables. The risk of term LBW is positively associated with maternal age as a continuous variable, and in addition, the proportion of cases increases with each age group compared to the control with the greatest contrast found among the oldest age group (>40) according to the descriptive analysis. It has been suggested the increased risk among older mothers could be in part due to increased morbidity and obstetric problems during pregnancy and delivery, although the underlying mechanisms are substantially unknown.[69] Maternal parity which is a common fetal growth predictor, inconsistent with most studies,[1,20-22] has an inverse relationship most likely due to population sampling inadequacy as indicated in the results section. Results for infant sex has been poorly examined in existing studies as a factor influencing adverse birth outcomes. However, male infants generally have a consistently higher birthweight mean throughout gestation compared to females, thus a higher proportion of females tend to be LBW.[70]

4.3 Statistical weaknesses

A major weakness in our study is that we did not control for other measures that are also known to be strongly associated to reduced birth weight due to unavailable information. Such unaccounted confounders include maternal smoking, alcohol consumption and marital status as indicated in the literature review. Furthermore, a major hindrance in our study is that we did not adjust our sample population by the number of fetuses carried to term. Most studies we reviewed have only included singleton births in their study sample population, as multiple births (more than one fetus) is the most common reason for babies to be born with low birthweight. In addition, research indicates that the overall increase of low birthweight rates after 1980, is partly due to a parallel increase of multiple births, though the rate of low birthweight among singleton births have also increased.[71]

4.4 Alternative findings and future study recommendations

On a separate analysis including a greater sample size population of 65,535 observations and 953 IRIS groups, singleton term LBW cases were found to be randomly distributed (p-value: 0.27) in Paris. However, small for gestational age (SGA), another adverse birth outcome used as an indicator for intrauterine growth restriction, was not found to be randomly distributed across the census blocks (p-value: 0.03). SGA babies include the lowest 10th percentile of the total weight distribution for each gestational week. To better represent intrauterine growth retardation, we adjusted the SGA cases with only including infants born full term (>36 weeks). As most of the individual data was missing, brief analysis was done to assess the effect of environmental exposures (quantiles) and median income (tertiles) as the SES contextual variable on SGA, with adjusted available individual risk factors (table 8).

The only environmental pollutant that had a significant effect on SGA alone was $PM_{2.5}$ (Lrtest: 0.05) which is the air pollutant considered to be the most consistently associated with adverse birth outcomes as previously mentioned in the literature. After adjustment for individual risk factors with a p-value cutoff of 20 percent, the risk of having an SGA infant decreases by 7% (p-value = 0.09, 95% CI 0.85 – 1.01) and 9% (p-value = 0.03, 95%CI 0.84 – 0.99) for the second (19.70 – 20.33) and third (20.33 – 20.98) highest PM2.5 concentration levels in comparison to the lowest level of $PM_{2.5}$ concentration level (18.16 – 19.69) with insignificant effects for the last two highest exposure concentration levels. Such findings contradict with our original spatial analysis results on term LBW. The lack of adjustment for singleton births only of term LBW may have hindered our findings of true at risk mothers.

This inverse association between air pollutant exposure and SGA can possibly be explained by the socio-demographic distribution of Paris. Although PM was not measured, another study found that the census blocks with the highest SES in Paris experience higher levels of NO_2[72] which can be similarly observed within our own visual spatial maps (Figure 5). As consistently indicated in our study and with the comparison model (table 8), the increase in the level of median income at census block level decreases a mothers odds of giving birth to an

SGA infant. This could possibly indicate that the protection against SGA arising from a better SES is stronger than the effect of exposure to air pollution. Such a conclusion would be interesting, as higher exposure to air pollution found among richer populations has been very much exclusively found in European cities[44,73,74] despite the literature usually generalizing the opposite.

In addition, the odds of being SGA is 1.69 times as likely among female infants compared to male infants when adjusted for $PM_{2.5}$ exposure at census block level, which is reduced by 22% (OR 1.91, p-value: 0.00, 95% CI 1.67 – 2.20) in comparison to the final two level model with half the observations for term LBW adjusted by median income at the contextual level (table 7). Although not looking at SGA, the only systematic review assessing differential gender effects of air pollution on pregnancy outcomes, found that despite females being at greater risk of being LBW (OR: 1.44, CI1.34–1.55), males were found to be at greater risk of LBW in the presence of air pollution.[68] Although $PM_{2.5}$ results remained inconclusive in the review, stratified results by air pollutant and gender include OR's 1.01 (0.92–1.11) for females compared to 0.95 (0.87–1.04) for males specified for PM_{10} and 1.14 (1.04–1.25) for females and 1.08 (0.99–1.19) for males specified for NO_2.

To identify and conclude true at risk mothers and neighborhoods in Paris of reduced birthweight, further analysis would need to be done to build a more comprehensive model on SGA. Such models should continue to include singleton births only, adjusting for air pollution exposure and individual risk factors to identify protective and risk factors within income strata in Paris. Further analysis can also be conducted to assess risk by gender and air pollution on the effect of adverse birth outcomes in Paris.

Table 8. Additional analysis: two level model adjusted by $pm_{2.5}$ (left) and median income (right) at census tract level with fixed effect covariates on the effect on SGA

	$PM_{2.5}$ exposure by census tract		
Model covariates	**Coef.**	**P-value**	**CI (95%)**
Gender of infant			
Male	Reference		
Female	1.69	0.000	1.61 – 1.79
Parity			
	0.87	0.000	0.84 - 0.9
$PM_{2.5}$			
18.16 – 19.69	Reference		
19.70 – 20.33	0.93	0.091	0.85 – 1.01
20.33 – 20.98	0.91	0.033	0.84 – 0.99
20.98 – 21.82	1.01	0.888	0.93 – 1.09
21.82 – 25.98	0.97	0.492	0.89 – 1.06
		Lrtest: 0.008	

	Median Income by census tract		
Model covariates	**Coef.**	**P-value**	**CI (95%)**
Gender of infant			
Male	Reference		
Female	1.70	0.000	1.61 – 1.79
Parity			
	0.86	0.000	0.84 - 0.88
Median Income			
Level 2	0.92	0.013	0.86 - 0.98
Level 3	0.83	0.000	0.76 – 0.88
			Lrtest: 0.02

4.4 Exposure assessment limitations

With regards to our exposure level measurements for air pollution concentration, other limitations need to be considered. Although the dispersion model used in Paris such as the ESMERALDA give acceptable results, uncertainty may arise from data sources, estimation methods or measurement tools, thus the amount of input data required by the model is limited. However, the air pollutant modeling provides estimate pollutant concentrations over a fine spatial scale, showing high correlations between the model's predictions and the measured air pollutant values obtained from the monitoring stations.[72] Another weakness in our exposure assessment is that by using annual mean concentration values, we didn't account for time series or seasonality of exposure compromising temporal resolution and pregnancy duration sensitivity.

4.5 Exposure assessment strengths

Nonetheless, there are major strengths found regarding the exposure assessment. The fine spatial resolution yields a stronger associative relationship between SES and air pollution, capturing the intra-urban differences and identifying the geographical distribution of existing neighborhood inequalities. Several studies that had used SES characteristics measured at a macro-scale level (cities, counties, and states) did not find the effect of pollution to vary across different areas.[75] In contrast, studies that have measured SES indicators at a more micro scale (district, neighborhood or census block) did reveal a variation of the combining effects, as in our study.

5. Conclusion

In conclusion, there is a citywide variation in the incidence of reduced birthweight in the metropolitan area of Paris after adjustment for environmental exposures and socioeconomic risk factors at the French census block level. Intra-urban differences were identified with regards to the different levels of exposure to air pollution and social deprivation, of which, we speculate this variation can explain the remaining difference. However, greater study elaboration is needed in extending research towards the development of low birth weight interventions and environmental policy regulation in Paris-city. Furthermore, addressing the issue requires a multidisciplinary approach from both public health sociologists and environmentalists to protect at risk neighborhoods.

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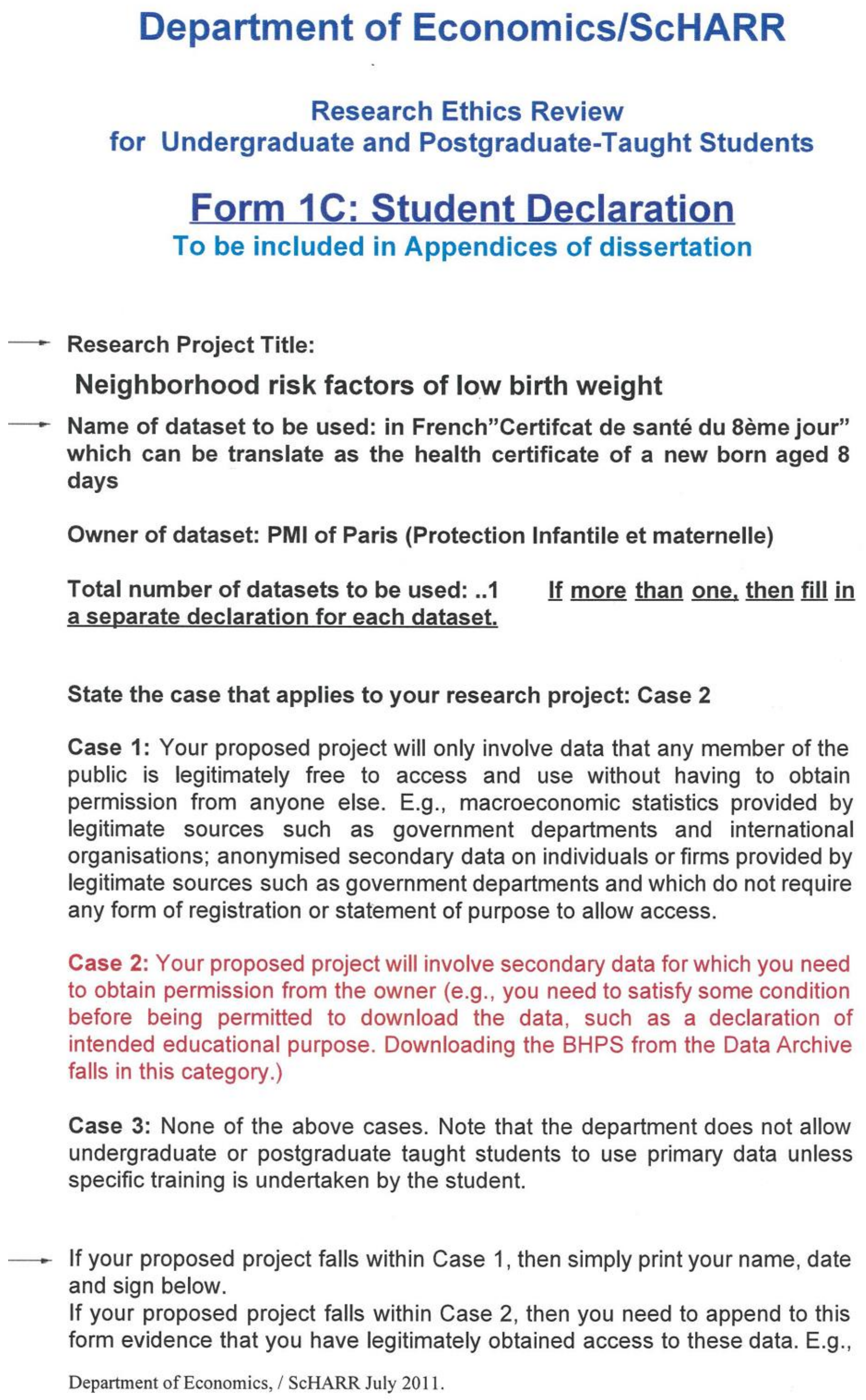
Annex 1. University of Sheffield ethical approval



Department of Economics/ScHARR

Research Ethics Review
for Undergraduate and Postgraduate-Taught Students

Form 1C: Student Declaration

To be included in Appendices of dissertation

→ **Research Project Title:**

Neighborhood risk factors of low birth weight

→ **Name of dataset to be used: in French"Certifcat de santé du 8ème jour" which can be translate as the health certificate of a new born aged 8 days**

Owner of dataset: PMI of Paris (Protection Infantile et maternelle)

Total number of datasets to be used: ..1 **If more than one, then fill in a separate declaration for each dataset.**

State the case that applies to your research project: Case 2

Case 1: Your proposed project will only involve data that any member of the public is legitimately free to access and use without having to obtain permission from anyone else. E.g., macroeconomic statistics provided by legitimate sources such as government departments and international organisations; anonymised secondary data on individuals or firms provided by legitimate sources such as government departments and which do not require any form of registration or statement of purpose to allow access.

Case 2: Your proposed project will involve secondary data for which you need to obtain permission from the owner (e.g., you need to satisfy some condition before being permitted to download the data, such as a declaration of intended educational purpose. Downloading the BHPS from the Data Archive falls in this category.)

Case 3: None of the above cases. Note that the department does not allow undergraduate or postgraduate taught students to use primary data unless specific training is undertaken by the student.

→ If your proposed project falls within Case 1, then simply print your name, date and sign below.
If your proposed project falls within Case 2, then you need to append to this form evidence that you have legitimately obtained access to these data. E.g.,

confirmation email, and statement of purpose if one was required. Then print your name, date and sign below.
If your proposed project falls within Case 3, then contact your supervisor or supervisory team as soon as possible. You may not be able to use the proposed data.

Name of student:
Nina Ahlers

Signature of student:

Date: 15/1/15

~~15/1/15~~

Name of supervisor:
Robert Akparibo

Signature of Supervisor:

Date: 15/05/15

Abstract

Introduction: As one of the single most important factors determining child survival with straining emotional and economic costs, low birth weight is a critical child and maternal health issue. Addressing this challenge requires greater epidemiological investigation to design more effective interventions. Studies need to conceptually expand on the observing set of exposures linked to LBW, such as the environmental context associated with social conditions to identify true at risk mothers.

Methods: Census block data including environmental exposures (NO_2, $PM_{2.5}$, and PM_{10}) and socioeconomic measures from the 2006 national French census are assessed simultaneously with individual characteristics extracted from 79,876 birth certificates on the effect of low birth weight and full term low birth weight in Paris metropolitan area. Two methodological objectives include: i) a spatial analysis to assess the correlation between the distributions of the contextual exposures to low birthweight (LBW) and full term low birthweight (term LBW) ii) a multilevel analysis to analyze the effect of social and environmental determinants on the risk of LBW at the individual and contextual level. As such, the aim of our study is to assess the role of environmental exposures and social characteristics on the risk of LBW at both the individual and neighborhood levels in Paris-city.

Results: Both methods used in our study yielded results that are inconsistent of each other with regards to air pollution exposures, most likely due to different population sample sizes. Nonetheless, adjusting for both socioeconomic related contextual (median income specific) and individual characteristics, the two-level model improves significantly in explaining a part of the variability to the distribution of term LBW (LLr p-value = 0.03). Where the logistic multilevel model did not find any significant association with air pollution exposure, the spatial analysis revealed that the covariates between social deprivation with each air pollutant exposure at census block level: NO_2 (RR 2.43, p-value = 0.03), $PM_{2.5}$ (RR 2.41, p-value = 0.03) and PM_{10} (RR 2.41, p-value = 0.04) provides the best fitted model in explaining the greatest part of excess term LBW risk in Paris-city.

Conclusion: There is a citywide variation in the incidence of reduced birthweight in the metropolitan area of Paris after adjustment for environmental exposures and socioeconomic risk factors at the French census block level. Intra-urban differences were identified with regards to the different levels of exposure to air pollution and social deprivation, of which, we speculate this variation can explain the remaining difference.

Abstrait

Introduction: Le poids de naissance faible est un sujet critique dans le domaine de la santé maternelle et des enfants, qui reste un des facteurs les plus importants qui déterminent la survie des enfants nés dans des circonstances de difficultés émotionnelles et économiques. Relever ce défi exige une plus grande enquête épidémiologique afin d'effectuer des interventions plus efficaces. Les études doivent élargir conceptuellement sur l'ensemble observant des expositions liées à l'IPN, tels que le contexte environnemental associé aux conditions sociales pour identifier des mères qui sont à vrai risque.

Méthodes: Les données de blocs de recensement, y compris les expositions environnementales (NO_2, $PM_{2.5}$ et PM_{10}) et les mesures socio-économiques du recensement de 2006 sont évalués en même temps que les caractéristiques individuelles extraites de 79,876 certificats de naissance sur l'effet de faible poids de naissance et de faible poids de naissance à terme en Paris région métropolitaine. Deux objectifs méthodologiques comprennent: i) une analyse spatiale pour évaluer la corrélation entre les distributions des expositions contextuels avec covariables rajusté en fonction de l'IPN et l'IPN terme ii) une analyse à plusieurs niveaux pour analyser l'effet des déterminants sociaux et environnementaux sur le risque de faible poids de naissance au niveau individuel et contextuel. En tant que tel, le but de notre étude est d'évaluer le rôle des expositions environnementales et les caractéristiques sociales sur le risque de faible poids de naissance à la fois au niveau individuel et de quartier à Paris intra-muraux.

Résultats: probablement lié aux différentes tailles d'échantillon de la population, les deux méthodes utilisées dans notre étude ont donné des résultats qui sont incompatibles les uns des autres en ce qui concerne l'exposition à la pollution atmosphérique. Néanmoins, l'ajustement sur les caractéristiques individuelles (revenus médians spécifiques) et contextuelle liées au statut socio-économique, le modèle à deux niveaux s'améliore significativement en expliquant une partie de la variabilité dans la distribution du poids de naissance faible (LLR p: 0,03). Lorsque le modèle à plusieurs niveaux logistique n'a pas trouvé d'association significative pour l'exposition à la pollution de l'air, l'analyse spatiale a révélé que les covariantes entre la précarité sociale avec chaque exposition à des polluants de l'air au niveau de l'îlot de recensement: NO_2 (RR 2,43, p: 0,03), $PM_{2.5}$ (RR 2,41, p: 0,03) et les PM_{10} (RR 2,41, p-valeur: 0,04) fournissent le modèle le mieux équipé pour expliquer la plus grande partie du risque IPN excès terme à Paris intra-muraux.

Conclusion: Il existe une variation dans toute la ville de l'incidence du poids de naissance réduit dans la zone métropolitaine de Paris après l'ajustement pour les expositions environnementales et les facteurs de risque socio-économiques au niveau de l'îlot de recensement français. Des différences intra-urbaines ont été identifiés en ce qui concerne les différents niveaux d'exposition à la pollution de l'air et de privation sociale, dont, nous spéculons cette variation peut expliquer la différence restante.