# Residential Proximity to Major Roads and Term Low Birth Weight

## *The Roles of Air Pollution, Heat, Noise, and Road-Adjacent Trees*

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**Background:** Maternal residential proximity to roads has been associated with adverse pregnancy outcomes. However, there is no study investigating mediators or buffering effects of road-adjacent trees on this association. We investigated the association between mothers' residential proximity to major roads and term low birth weight (LBW), while exploring possible mediating roles of air pollution ($PM_{2.5}$, $PM_{2.5–10}$, $PM_{10}$, $PM_{2.5}$ absorbance, nitrogen dioxide, and nitrogen oxides), heat, and noise and buffering effect of road-adjacent trees on this association.

**Methods:** This cohort study was based on 6438 singleton term births in Barcelona, Spain (2001–2005). Road proximity was measured as both continuous distance to and living within 200 m from a major road. We assessed individual exposures to air pollution, noise, and heat using, respectively, temporally adjusted land-use regression models, annual averages of 24-hour noise levels across 50 m and 250 m, and average of satellite-derived land-surface temperature in a 50-m buffer around each residential address. We used vegetation continuous fields to abstract tree coverage in a 200-m buffer around major roads.

**Results:** Living within 200 m of major roads was associated with a 46% increase in term LBW risk; an interquartile range increase in heat exposure with an 18% increase; and third-trimester exposure to $PM_{2.5}$, $PM_{2.5–10}$, and $PM_{10}$ with 24%, 25%, and 26% increases, respectively. Air pollution and heat exposures together explained about one-third of the association between residential proximity to major roads and term LBW. Our observations on the buffering of this association by road-adjacent trees were not consistent between our 2 measures of proximity to major roads.

**Conclusion:** An increased risk of term LBW associated with proximity to major roads was partly mediated by air pollution and heat exposures.

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The developing fetus is known to be susceptible to environmental insults.[1] A growing body of evidence has associated maternal residential proximity to major roads with a number of adverse pregnancy outcomes, including low birth weight (LBW, birth weight <2,500 g), assuming that proximity to major roads is a surrogate for exposure to traffic-related air pollution.[2–7] However, there is no available study quantifying the contribution of air pollution to such an association. Furthermore, residential proximity to major roads can be accompanied by higher exposure to environmental factors other than air pollution. For example, traffic is a main source of noise,[8] and the road network is a major contributor to heat island effects in urban environments.[9] Although noise and heat may be relevant to pregnancy outcomes, there is no report on their contribution to the association between residential proximity to major roads and adverse pregnancy outcomes. This apportionment of the health effects of road proximity to more specific exposures, such as air pollution, noise, and heat, is of importance because

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an effect of road proximity itself cannot be explained biologically. A recent review of the literature on the health effects of residential proximity to major roads has highlighted the lack of evidence on underlying mechanisms for such effects.[10]

Road-adjacent trees are reported to reduce traffic-related air pollution, noise, and heat island effect.[11–13] Although road-adjacent trees might buffer the adverse impact of residential proximity to major roads on pregnancy outcomes, there is no published evidence of such a buffering effect.

This study aimed to explore the association of maternal residential proximity to major roads and term LBW, possible mediation of this association by air pollution, noise, and heat, and possible buffering by road-adjacent trees.

## METHODS

### Study Population

This study was based on a cohort of singleton term births (ie, gestational age at delivery ≥37 weeks) occurring at the obstetrics department of the Hospital Clinic de Barcelona between January 2001 and June 2005 to mothers residing in the city of Barcelona. Hospital Clinic de Barcelona is a major university hospital covering Barcelona city, with a catchment area of about one million inhabitants.[14] The hospital records detailed a wide range of prospectively collected data on maternal and fetal characteristics, together with clinical data on pregnancy and delivery, including ultrasound measures of gestational age for all pregnancies.[14]

Ethics approval (No. 2008/3115/I) was obtained from the Clinical Research Ethical Committee of the Parc de Salut MAR, Barcelona, Spain, to carry out this study.

### Residential Proximity to Major Roads

Street network geocoding was used to geocode the residence address of each study participant at the time of her delivery, based on postal code, street name, and house number. Major roads were determined according to the European Study of Cohorts for Air Pollution Effects guidelines.[15] We used 2 measures of proximity to major roads: (1) residential distance to a major road (hereafter referred to as "continuous distance") and (2) living within 200 m of a major road (hereafter referred to as "binary distance"). The selection of a 200-m distance was consistent with previous studies[2,3,16–18] and was informed by the Special Report 17 of the Health Effects Institute,[19] which suggested that after 200 m the levels of some air pollutants (eg, nitrogen dioxide) reduce to background levels—as it did in our study setting (eTable 1, http://links.lww.com/EDE/A790). We used EuroStreets map (version 3.1), which is a 1:10,000 digital road network based on the TeleAtlas MultiNet ('s-Hertogenbosch, Netherlands).[15]

### Exposure to Air Pollution, Noise, and Heat and Road-Adjacent Tree Coverage

The description of our applied methodologies to assess exposure to air pollution, noise, and heat and estimating road-adjacent tree coverage has been detailed in supplementary materials (eAppendix I, eTable 2, eFigures 1–4, http://links.lww.com/EDE/A790). In brief, we estimated the ambient levels of nitrogen dioxides ($NO_2$), nitrogen oxides ($NO_x$), particulate matter with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$), 2.5–10 μm ($PM_{2.5–10}$), and ≤10 μm ($PM_{10}$), and $PM_{2.5}$ light absorption (hereafter referred to as $PM_{2.5}$ absorbance) at the home address of each participant for each week of her pregnancy, using temporally adjusted land-use regression models.[15,20–22] We then averaged these exposure levels over the entire pregnancy, as well as each trimester of pregnancy. Exposure to noise was defined as the average of the long-term mean noise-level indicator for the 24-hour period ($L_{den}$, in dB(A)) within 50 m[23] and 250 m[24] of each home address, based on Barcelona's strategic noise map.[25] We assessed exposure to heat as the average of land-surface temperature within 50 m around each home address, based on 3 land-surface temperature maps derived from the Landsat 5 Thematic Mapper data. We abstracted the road-adjacent tree coverage as the average of percent tree coverage within 200 m on each side of that road, based on vegetation continuous field maps derived from data collected by the Moderate Resolution Imaging Spectroradiometer aboard the Terra satellite.[26]

### Statistical Analyses

#### Risk Estimates

We first used generalized additive models to explore the linearity of the associations (in the logit scale) between term LBW and continuous distance and mediators (air pollution, noise, and heat) that did not show any notable nonlinearity of associations (eFigure 5, http://links.lww.com/EDE/A790). We then developed logistic regression models with term LBW (yes/no) as the outcome and indicators of proximity to major roads and exposures to air pollution, heat, and noise exposure (one at a time) as predictors. To facilitate comparisons among these exposures, we reported the results for 1 interquartile range (IQR) increase in each exposure level. The analyses were adjusted for neighborhood socioeconomic status (MEDEA index),[27] ethnicity (white/non-white/mixed), education level (none or primary/secondary/university), marital status (single mother: yes/no), age, smoking during pregnancy (yes/no), alcohol consumption during pregnancy (yes/no), body mass index (BMI) less than 20 kg/m$^2$ (yes/no) at the time of admission, diabetes (gestational or pregestational: yes/no), infection (Rubella, Group B streptococci, *Toxoplasma gondii*, sexually transmitted diseases, or bacteriuria; yes/no), parity (0/1/2+), sex of baby (female/male), season of conception (summer/winter), and year of conception.

Of 6438 registered participants, 1,093 had one or more missing values for the covariates (mostly maternal education and BMI) for which the analyses were adjusted (Table 1). We conducted multiple imputation for missing data as described in eTable 3 (http://links.lww.com/EDE/A790) and analyzed

**TABLE 1.** Descriptive Statistics[a] of the Study Participants (n = 6,438), Barcelona, 2001–2005

| Variable | |
|---|---|
| Age (years); median (IQR) | 30 (8) |
| Ethnicity | |
| White | 3,913 (61) |
| Non-white | 883 (14) |
| Mixed | 1,588 (25) |
| Missing | 54 |
| Marital status | |
| Single | 868 (13) |
| Not single | 5,570 (87) |
| Education level | |
| None or primary school | 1,671 (26) |
| Secondary school | 2,605 (41) |
| University | 1,499 (23) |
| Missing | 663 |
| Smoking during pregnancy | |
| No | 5,289 (82) |
| Yes | 1,149 (18) |
| Alcohol consumption during pregnancy | |
| No | 6,171 (96) |
| Yes | 266 (4) |
| Missing | 1 |
| Diabetes | |
| No | 6,038 (94) |
| Yes | 400 (6) |
| Parity | |
| 0 | 3,752 (58) |
| 1 | 2,004 (31) |
| 2+ | 682 (11) |
| Infection during pregnancy[b] | |
| No | 5,210 (81) |
| Yes | 1,228 (19) |
| Body mass index <20 kg/m$^2$ | |
| No | 4,570 (80) |
| Yes | 1,170 (20) |
| Missing | 698 |
| Infant sex | |
| Girl | 3,143 (49) |
| Boy | 3,295 (51) |
| Season of conception | |
| Spring/summer | 3,443 (53) |
| Autumn/winter | 2,995 (47) |

[a]Data are presented as no. (%), except as noted.
[b]Rubella, Group B streptococci, *Toxoplasma gondii*, sexually transmitted diseases, or bacteriuria.

the resulting 100 data sets following the standard combination rules for multiple imputations.[28]

## Mediating Role of Air Pollution, Heat, and Noise

We calculated the percentage of the association between proximity to major roads and term LBW explained by each of the mediators as $(1 - [\beta_{pm}/\beta_p]) \times 100\%$, where $\beta_{pm}$ was the regression coefficient for proximity to major roads in the fully adjusted model including mediator (joint model) and $\beta_p$ was the regression coefficient for the proximity to major roads in the fully adjusted model without including any mediator.[29] This measure can lead to values greater than 100% if the regression coefficient for proximity after including the mediator is negative, and it can lead to negative values if the regression coefficient for proximity after including the mediator is greater than the coefficient obtained when the mediator is not included. We used bootstrap to obtain percentile-based 95% confidence intervals for this measure of mediation.

## Buffering Effect of Road-Adjacent Tree Coverage

We stratified the analysis of the association between residential proximity to major roads and term LBW according to the terciles of road-adjacent tree coverage to compare the associations across levels of road-adjacent tree coverage. We also checked the significance of the multiplicative interaction term of proximity to major roads with terciles of road-adjacent tree coverage by comparing models with and without interaction terms, using the likelihood ratio test.

## Further Analysis

We defined small for gestational age (SGA) as birth weight below the 10th percentile for the gestational age and sex according to national growth curves.[30] We repeated the aforementioned analyses using SGA as outcome (instead of term LBW) and removing sex as the covariate.

# RESULTS

## Study Population

During the course of the study, 6,438 singleton term births with mothers residing in the city of Barcelona were enrolled in the cohort. Of these, 190 (3%) were term LBW. Descriptive statistics of the characteristics of the study participants are presented in Table 1.

## Exposure Assessment

The median residential distance to major roads was 145 m (IQR = 216 m). About two-thirds of participants (n = 3,980) lived within 200 m of a major road. Participants living ≤200 m from a major road and those living farther away were similar with regard to all covariates except ethnicity and MEDEA index of neighborhood deprivation, with those living closer to a major road tending to be less deprived.

Summary statistics of estimates for exposure to air pollutants during each window period are shown in eTable 4 (http://links.lww.com/EDE/A790). As presented in eTable 5 (http://links.lww.com/EDE/A790), the trimester-specific exposures were weakly to moderately correlated. The correlation between exposures to air pollutants, noise, and heat and road-adjacent tree coverage is reported in eTable 6 (http://links.lww.com/EDE/A790). As presented in eTable

7 (http://links.lww.com/EDE/A790), those participants living within 200 m of a major road had higher median levels of exposure to air pollution, heat, and noise compared with those living farther away. Proximity to major roads could explain no more than 40% of the variation in fine particulate pollutants measured by the monitoring stations; for the other pollutants explained, the variation by major road proximity was less than 20% (eTable 8, http://links.lww.com/EDE/A790). The land-use regression models previously developed for these pollutants used more refined geographic information system variables and explained much larger percentages of variance.[21,31] The median percentage of road-adjacent tree coverage in a buffer of 200 m around the major road was 3% (IQR = 1%).

**TABLE 2.** Association[a] of Term LBW with Proximity to Major Roads and an IQR Increase Exposure to Heat and Noise in Single-Exposure Models and Exposures to Heat, $PM_{2.5}$ (During Trimester 3), and Noise (50 m Buffer) in the Joint Exposure Model, Barcelona, 2001–2005 (n = 6,438)

| | IQR | OR (95% CI) |
|---|---|---|
| **Single-exposure model** | | |
| Proximity | | |
| Continuous distance (m) | 216.4 | 0.84 (0.69 to 1.01) |
| Binary distance | — | 1.46 (1.05 to 2.04) |
| Noise (dB(A)) | | |
| 50 m buffer | 6.7 | 1.03 (0.84 to 1.27) |
| 250 m buffer | 3.7 | 1.04 (0.81 to 1.19) |
| Heat (°C) | 2.4 | 1.18 (0.95 to 1.45) |
| **Joint exposure model** | | |
| Heat (°C) | 2.4 | 1.21 (0.98 to 1.49) |
| $PM_{2.5}$ (μg/m$^3$) | 3.6 | 1.31 (1.07 to 1.61) |
| Noise (50m buffer) (dB(A)) | 6.7 | 0.89 (0.71 to 1.12) |

[a]Adjusted for neighborhood SES, ethnicity, education level, marital status, age, smoking during pregnancy, alcohol consumption during pregnancy, admission BMI < 20 kg/m$^2$, diabetes, infection during pregnancy, parity, infant sex, and season and year of conception.

## Term Low Birth Weight

### Risk Estimates

Living within 200 m of a major road was associated with a 46% increase in the risk of term LBW (Table 2). Consistently, longer distance to a major road was associated with a reduction in term LBW risk (Table 2). Although exposure to heat was associated with increased risk of term LBW, our findings for the noise exposure were not conclusive (Table 2). We also observed increased risk of term LBW associated with the third-trimester exposure to particulate air pollutants, except $PM_{2.5}$ absorbance (Table 3). After including exposures to $PM_{2.5}$ (third-trimester), heat, and noise (50 m buffer) in a fully adjusted model without any indicator of residential proximity to a major road, exposures to $PM_{2.5}$ and heat were associated with increased risk of term LBW (Table 2). These risk estimates were robust to the exclusion of subjects with missing data (complete case analysis).

### Mediating Role of Air Pollution, Heat, and Noise

For air pollutants, we checked the mediating role of those exposure windows for which we found the strongest association with term LBW (ie, first trimester for $NO_2$, $NO_x$, and $PM_{2.5}$ absorbance and third trimester for $PM_{2.5}$, $PM_{2.5–10}$, and $PM_{10}$). The risk estimates for mediators and proximity to major roads in the joint models are presented in Table 4. As shown in Table 5, the percentages of the association between the major road proximity-term LBW that could be explained by the mediators were generally higher when continuous distance was used. The largest percentage of the association between major road proximity and term LBW explained by air pollutants was due to exposure to $PM_{2.5}$ (Table 5). Exposure to heat could also explain about 8% of this association, whereas exposure to noise explained none. Exposure to heat and $PM_{2.5}$ could jointly explain one-fourth of this association when the binary distance was used and more than one-third when continuous distance was used (Table 5).

**TABLE 3.** Association[a] of Term LBW with 1 IQR Increase in Exposure to Each Pollutant Separately for Each Exposure Window Period, Barcelona, 2001–2005 (n = 6,438)

| | Entire Pregnancy | | Trimester 1 | | Trimester 2 | | Trimester 3 | |
|---|---|---|---|---|---|---|---|---|
| Pollutant | IQR | OR (95% CI) | IQR | OR (95% CI) | IQR | OR (95% CI) | IQR | OR (95% CI) |
| $NO_2$ (μg/m$^3$) | 16.8 | 1.05 (0.94 to 1.17) | 20.5 | 1.06 (0.94 to 1.20) | 19.9 | 1.04 (0.91 to 1.18) | 18.7 | 1.03 (0.90 to 1.18) |
| $NO_x$ (μg/m$^3$) | 41.3 | 1.05 (0.96 to 1.14) | 59.0 | 1.06 (0.96 to 1.18) | 57.6 | 1.06 (0.96 to 1.17) | 56.8 | 1.02 (0.89 to 1.17) |
| $PM_{2.5}$ (μg/m$^3$) | 3.1 | 1.17 (0.98 to 1.39) | 3.7 | 1.07 (0.88 to 1.29) | 3.7 | 1.19 (0.97 to 1.45) | 3.6 | 1.24 (1.03 to 1.49) |
| $PM_{2.5–10}$ (μg/m$^3$) | 2.3 | 1.11 (0.91 to 1.35) | 3.4 | 0.95 (0.77 to 1.18) | 3.4 | 1.12 (0.87 to 1.43) | 3.1 | 1.25 (1.01 to 1.54) |
| $PM_{10}$ (μg/m$^3$) | 3.9 | 1.16 (0.98 to 1.37) | 5.7 | 1.00 (0.82 to 1.22) | 5.6 | 1.20 (0.96 to 1.48) | 5.2 | 1.26 (1.06 to 1.51) |
| $PM_{2.5}$ absorbance ($10^{-5}$ m$^{-1}$) | 1.1 | 1.16 (0.97 to 1.39) | 1.6 | 1.17 (0.98 to 1.38) | 1.6 | 1.14 (0.95 to 1.38) | 1.5 | 1.07 (0.85 to 1.36) |

[a]Adjusted for neighborhood SES, ethnicity, education level, marital status, age, smoking during pregnancy, alcohol consumption during pregnancy, admission BMI <20 kg/m$^2$, diabetes, infection during pregnancy, parity, infant sex, and season and year of conception.

**TABLE 4.** Association[a] of Term LBW with Residential Proximity to Major Roads (an IQR Increase in Distance to and Being Within 200 m from a Major Road) and 1 Interquartile Range Increase in Exposure to Each Pollutant During the Third Trimester, Heat, and Noise (250 m Buffer) in the Joint Models, Barcelona, 2001–2005 (n = 6,438)

| Models | Continuous Distance | Binary Distance |
|---|---|---|
| Model 1[b] | | |
| Proximity to major roads | 0.84 (0.69 to 1.01) | 1.46 (1.05 to 2.04) |
| Model 2[c] | | |
| $NO_2$ | 1.04 (0.92 to 1.19) | 1.05 (0.92 to 1.19) |
| Proximity to major roads | 0.84 (0.69 to 1.02) | 1.44 (1.03 to 2.01) |
| Model 3[d] | | |
| $NO_x$ | 1.04 (0.93 to 1.17) | 1.05 (0.94 to 1.17) |
| Proximity to major roads | 0.85 (0.70 to 1.03) | 1.43 (1.03 to 2.01) |
| Model 2[e] | | |
| $PM_{2.5}$ | 1.20 (1.00 to 1.46) | 1.20 (0.99 to 1.45) |
| Proximity to major roads | 0.87 (0.72 to 1.06) | 1.37 (0.97 to 1.92) |
| Model 3[f] | | |
| $PM_{2.5–10}$ | 1.21 (0.98 to 1.50) | 1.21 (0.98 to 1.49) |
| Proximity to major roads | 0.86 (0.71 to 1.05) | 1.39 (1.00 to 1.95) |
| Model 4[g] | | |
| $PM_{10}$ | 1.24 (1.03 to 1.48) | 1.24 (1.03 to 1.49) |
| Proximity to major roads | 0.86 (0.71 to 1.05) | 1.41 (1.01 to 1.97) |
| Model 7[h] | | |
| $PM_{2.5}$ absorbance | 1.18 (0.94 to 1.49) | 1.18 (0.94 to 1.49) |
| Proximity to major roads | 0.85 (0.70 to 1.04) | 1.42 (1.01 to 1.98) |
| Model 8[i] | | |
| Heat | 1.15 (0.93 to 1.43) | 1.15 (0.93 to 1.43) |
| Proximity to major roads | 0.85 (0.70 to 1.03) | 1.43 (1.02 to 1.99) |
| Model 8[j] | | |
| Noise | 0.99 (0.81 to 1.22) | 0.99 (0.81 to 1.22) |
| Proximity to major roads | 0.83 (0.68 to 1.02) | 1.46 (1.04 to 2.05) |
| Model 10[k] | | |
| Heat | 1.17 (0.94 to 1.46) | 1.17 (0.94 to 1.45) |
| $PM_{2.5}$ | 1.22 (1.00 to 1.47) | 1.21 (1.00 to 1.46) |
| Proximity to major roads | 0.89 (0.73 to 1.08) | 1.33 (0.95 to 1.87) |

[a]Adjusted for neighborhood SES, ethnicity, education level, marital status, age, smoking during pregnancy, alcohol consumption during pregnancy, admission BMI <20 kg/m², diabetes, infection during pregnancy, parity, infant sex, and season and year of conception.
[b]Adjusted model including only residential proximity to major roads.
[c]Adjusted model including both residential proximity to major roads and $NO_2$ exposure during the first trimester.
[d]Adjusted model including both residential proximity to major roads and $NO_x$ exposure during the first trimester.
[e]Adjusted model including both residential proximity to major roads and $PM_{2.5}$ exposure during the third trimester.
[f] Adjusted model including both residential proximity to major roads and $PM_{2.5–10}$ exposure during the third trimester.
[g]Adjusted model including both residential proximity to major roads and $PM_{10}$ exposure during the third trimester.
[h]Adjusted model including both residential proximity to major roads and $PM_{2.5}$ absorbance exposure during the first trimester.
[i]Adjusted model including both residential proximity to major roads and heat exposure.
[j]Adjusted model including both residential proximity to major roads and noise (50 m buffer) exposure.
[k]Adjusted model including residential proximity to major roads, heat and $PM_{2.5}$ exposure during the third trimester.

**TABLE 5.** Percentage of the Association[a] Between Residential Proximity to a Major Road and Term LBW (Fully Adjusted Model) That Was Explained by Each of the Mediators

| Mediators | Continuous Distance | Binary Distance |
|---|---|---|
| | % Explained (95% CI) | % Explained (95% CI) |
| $NO_2$[b] | 5% (−16 to 33) | 3% (−9 to 19) |
| $NO_x$[b] | 7% (−16 to 39) | 4% (−8 to 22) |
| $PM_{2.5}$[c] | 25% (−8 to 135) | 17% (−3 to 80) |
| $PM_{2.5–10}$[c] | 19% (−12 to 100) | 12% (−4 to 57) |
| $PM_{10}$[c] | 18% (−1 to 102) | 10% (1 to 45) |
| $PM_{2.5}$ absorbance[b] | 12% (−16 to 79) | 7% (−4 to 41) |
| Heat | 8% (−11 to 50) | 5% (−5 to 25) |
| Noise | −1% (−51 to 39) | −1% (−30 to 24) |
| Heat and $PM_{2.5}$[c] | 36% (−12 to 216) | 24% (−1 to 111) |

[a]Adjusted for neighborhood SES, ethnicity, education level, marital status, age, smoking during pregnancy, alcohol consumption during pregnancy, admission BMI <20 kg/m², diabetes, infection during pregnancy, parity, infant sex, and season and year of conception.
[b]Exposure during the first trimester.
[c]Exposure during the third trimester.

**TABLE 6.** Association[a] of Term LBW with Proximity to Major Roads, Stratified According to the Terciles of Road-Adjacent Tree Coverage, Barcelona, 2001–2005 (n = 6,438)

| Road-Adjacent Tree Coverage | Continuous Distance OR (95% CI) | Binary Distance OR (95% CI) |
|---|---|---|
| First tercile (least green) | 0.80 (0.53 to 1.20) | 1.88 (0.96 to 3.69) |
| Second tercile | 0.91 (0.64 to 1.31) | 1.41 (0.81 to 2.48) |
| Third tercile (greenest) | 0.82 (0.61 to 1.10) | 1.27 (0.73 to 2.21) |

[a]Adjusted for neighborhood SES, ethnicity, education level, marital status, age, smoking during pregnancy, alcohol consumption during pregnancy, admission BMI <20 kg/m², diabetes, infection during pregnancy, parity, infant sex, and season and year of conception.

## Buffering Effect of Road-Adjacent Tree Coverage

We observed the suggestion of a tree-related trend in odds ratios (ORs) for the association of term LBW with binary distance; the risk of term LBW associated with proximity to the greenest major roads was about one-third of that associated with proximity to the least green major roads (Table 6). There was no evidence for trend with continuous distance (Table 6). For the multiplicative interaction term of proximity to major roads with terciles of road-adjacent tree coverage, $P = 0.24$ for binary distance and $P = 0.35$ for continuous distance.

## Small Size for Gestational Age

There were 803 (12%) newborns identified as SGA in our data set. As presented in eTables 9 and 10 (http://links.lww.com/EDE/A790), the direction of associations between SGA and residential proximity to a major road—as well as exposure to air pollution, heat, and noise—was consistent with those of term LBW; however, the associations for SGA were generally weaker (except for noise). Exposure to air pollution, noise, and heat (separately) could explain 2–14% of the association between maternal residential proximity to major roads and SGA (eTable 11, http://links.lww.com/EDE/A790). Exposure to heat and noise and the third-trimester exposure to $PM_{2.5}$ could jointly explain about one-fourth of this association (eTable 11, http://links.lww.com/EDE/A790). The OR for SGA associated with proximity to major roads with the highest tree coverage was half of that associated with proximity to major roads with the lowest tree coverage; however, there was no clear trend for associations across the strata of tree coverage (eTable 12, http://links.lww.com/EDE/A790).

## DISCUSSION

This study provides a comprehensive view of the association between residential proximity to major roads and adverse pregnancy outcomes, quantifying the contributions of air pollution, heat, and noise exposures to such an association. It also investigated the buffering effect of road-adjacent tree coverage on this association. We found increased risk of term LBW in association with maternal residential proximity to major roads, as well as with heat exposure and third-trimester exposure to $PM_{2.5}$, $PM_{2.5-10}$, and $PM_{10}$. Up to one-third of the association between residential proximity to major roads and term LBW could be explained by exposure to air pollution and heat. There were also some indications that road-adjacent trees could buffer the impact of residential proximity to major roads on term LBW, although our findings were not consistent between our indicators of proximity to major roads. Our findings for SGA were less conclusive.

The increased risk of term LBW associated with residential proximity to major roads in our study was in-line with findings of other studies reporting increased placenta/birth weight ratio[3] (a marker of the placental transport dysfunction) and increased risk of LBW associated with residential proximity to major roads.[2,4,5] We also observed increased risk of term LBW associated with exposure to particulate air pollution (excluding $PM_{2.5}$ absorbance) consistent with other evidence.[32,33] Because of high correlation between the second- and third-trimester exposures to $PM_{2.5}$ (Spearman's $\rho = 0.77$), it was not possible to determine which trimester is the most relevant for this exposure. However, our observation for other particulate air pollutants showing the strongest associations with third-trimester exposures, without a high correlation between the second and trimester exposures, could give more confidence about the relevance of the third-trimester exposure for $PM_{2.5}$.

We found increased risk of term LBW associated with heat exposure. Given the expected larger temporal variability compared with spatial variability in temperature, our observed small difference in heat-term LBW associations in the unadjusted (ie, not adjusted for season) and adjusted models (ie, adjusted for season) might suggest that the land-surface temperature could have been a surrogate for some other spatially varying exposure. However, our observed increase in the risk of term LBW associated with heat exposure is in-line with those of studies reporting seasonality in birth weight and LBW and associating heat with reduction in birth weight.[34] Heat stress is a function of the interaction between internal heat production, ability for heat loss to the environment, and environmental heat load.[35] During pregnancy, the increase in fat deposition and decrease in the ratio of body surface area to body mass (due to weight gain) result in less capacity for heat loss to the environment,[35–37] making pregnant women more vulnerable to heat stress due to environmental heat load.[35] Heat stress leads to the release of heat shock proteins (HSP) including HSP-70 in humans.[38] Increased levels of HSP-70 have been linked to a range of adverse pregnancy outcomes, including reduction in birth weight.[39] This reduction in birth weight is consistent with the suggested role of heat stress in the natural selection of body size and shape, in that reduction in birth weight could be an adaptation response to environmental heat load.[35]

Our findings for noise exposure were not conclusive. The available evidence on the impact of noise exposure on birth weight is based primarily on exposure to occupational or aircraft noise.[40] Studies on the association between traffic-related noise exposure and term LBW are scarce and generally do not support such an association.[41,42]

Our observed associations for SGA were consistent with those of term LBW in terms of direction, but they were generally weaker for SGA. Although the use of SGA could result in a larger number of cases (ie, higher statistical power) compared with term LBW, applying SGA as an indicator of impaired fetal growth has been a source of concern.[43] By definition, SGA is dependent on the applied growth curve. We used the only available growth curve applicable to our study sample, which was relatively old and did not have an ethnic composition that was comparable to our study population. Considering the descriptive nature of the SGA definition, SGA cases may include those who are genetically small compared with the rest of population.[43] Furthermore, SGA relies on the weight distribution of infants born at a specific gestational age instead of the weight distribution of all fetuses at that gestational age.[43] In our study population, the median gestational age for cases of term LBW (273 days) was shorter than that of cases of term SGA (282 days).

We are unaware of any previous report on the combined contribution of air pollution, heat, and noise or the buffering effect of road-adjacent tree coverage on the health effects of residential proximity to major roads in general or on pregnancy outcomes in particular. It is therefore not possible to compare these findings with others. Our measures of noise exposure did not seem to mediate the association between residential proximity to major roads and term LBW. Exposure to heat explained up to 8% of this association, whereas exposure to selected air pollutants explained up to about one-fourth of this association. These exposures jointly explained about one-third of this association, indicating that there should be potential mediator(s) other than those included in our analysis. The contribution of other mediators remains an open question for future studies. These mediators may include other air pollutants that are routinely monitored (eg, carbon monoxide) or those that are not routinely monitored (eg, ultrafine particles, volatile organic compounds, or polycyclic aromatic hydrocarbons), physical activity levels, or diet patterns, for which we did not have data. In addition to other possible mediators, the unexplained part our observed association between residential proximity to major roads and term LBW could be from possible misclassification of exposure, as discussed below.

We found some indications for a buffering effect of road-adjacent trees on the association between proximity to major roads and term LBW when we used binary distance. Such a buffering effect was not apparent when we applied continuous distance. Therefore, our findings regarding this buffering effect should be interpreted with caution. Hypothetically, such a buffering effect could be explained, at least in part, by the ability of road-adjacent trees to mitigate the traffic-related air pollution and heat[11–13,44–46] (both of which we found to be associated with term LBW and to mediate our observed association between proximity to major roads and term LBW). However, the available evidence on the mitigating effect of road-adjacent trees on air pollution is not consistent, and there are some other reports that do not support such an effect.[47,48]

Our study faced some limitations, and our findings therefore require further confirmation by future studies. The number of cases of term LBW (n = 208) was relatively small. Our exposure assessments were based on ambient levels of air pollution, noise, and heat, which could overlook the potential variation between ambient and personal exposure levels. Our assessment of noise exposure, for example, was based on total ambient levels of noise, which overlooks the contribution of factors such as acoustic insulation of homes and the location of bedrooms. Furthermore, our assessment of exposure to air pollution, noise, and heat was based on the home address at the time of delivery, which did not account for possible maternal residential mobility during pregnancy. A study of 4 Spanish birth cohorts during 2003–2008 has reported a mobility rate between 1% and 6%.[49]

Using heat and noise maps and spatial estimates of air pollutant levels generated by land-use regression models, we effectively assumed that the city spatial surface and the spatial distribution of heat, noise, and air pollutants remained constant over the study period. There are some reports supporting the stability of the spatial contrasts for noise and air pollution in Europe and North America over a long period.[50–54] Furthermore, to our knowledge, there was no major change in land use, emissions profiles, or traffic flow (eg, construction of new major roads and implementing new traffic rules) between the year of land-use regression model construction and the years of our study.

To assess exposure to heat, we used 3 land-surface temperature maps based on a Landsat 5 Thematic Mapper images. The lack of temporal component in our assessment of exposure to heat could have resulted in exposure misclassification; however, the adjustment of analyses for the season of conception should have, at least in part, addressed the temporal variability in exposure to heat. Furthermore, to investigate the impact of potential change in the spatial contrast of the heat over the study period (2001–2005) on our findings, we generated another land-surface temperature map using a Landsat 7 Enhanced Thematic Mapper Plus images captured on 26 June 2001 and included it in our measure of heat exposure. We repeated the analysis of the association between heat exposure and term LBW using this alternative measure of heat exposure (based on 4 land-surface temperature maps) and observed an OR of 1.16 (95% confidence interval = 0.96–1.41) for term LBW associated with an IQR increase (1.7°C) in exposure to heat.

In addition, there could be a difference in the degree of misclassification of exposures to our studied mediators. This difference could affect our findings of the mediating role of these exposures, in that those mediators with better exposure classification might explain more of the association compared with mediators with greater misclassification. Moreover, all our land-use regression models included some traffic-related predictors, which could have interfered in our analyses of mediator effect of air pollutants.

Our study showed an increased risk of term LBW associated with maternal residential proximity to major roads; this increased risk was partly mediated by exposure to air pollution and heat but not noise. There were some indications of a buffering effect of road-adjacent trees on the association between residential proximity to major roads and term LBW when we used binary distance, which should be interpreted with caution as these findings were not replicated using continuous distance. The results suggest that future studies of the health effects of residential proximity to major road should take account of potential exposures other than air pollution (eg, heat) and the potential buffering effect of road-adjacent trees. Moreover, our findings for heat exposure are relevant for assessing the possible health effects of predicted changes in future climate. Further studies are required to confirm our findings in other settings and to investigate the possible contribution of other mediators.

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