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Associations of residential greenspace exposure and fetal growth across four areas in Spain

Maria Torres Toda[a,b], Marisa Estarlich[c,d,e,*], Ferran Ballester[c,d,e], Montserrat De Castro[a,b,e], Ana Fernández-Somoano[e,f,g], Jesús Ibarluzea[e,h,i,j], Carmen Iñiguez[d,e,k], Aitana Lertxundi[e,h,l], Mikel Subiza-Perez[h,m,n], Jordi Sunyer[a,b,e], Adonina Tardón[e,f,g], Maria Foraster[a,b,e,1], Payam Dadvand[a,b,e,1]

[a] Barcelona Institute for Global Health (ISGlobal), Dr. Aiguader 88, 08003, Barcelona, Spain
[b] Pompeu Fabra University, Plaça de La Mercè 10-12, 08002, Barcelona, Spain
[c] Faculty of Nursing and Chiropody, Universitat de València, C/Menendez Pelayo S/n, 46010, València, Spain
[d] Epidemiology and Environmental Health Joint Research Unit, Foundation for the Promotion of Health and Biomedical Research in the Valèncian Region, FISABIO-Public Health, FISABIO-Universitat Jaume I-Universitat de València, Av. Catalunya 21, 46020, València, Spain
[e] Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Av. Monforte de Lemos, 3-5. Pabellón 11, 28029, Madrid, Spain
[f] Unidad de Epidemiología Molecular Del Cáncer, Instituto Universitario de Oncología Del Principado de Asturias (IUOPA) - Departamento de Medicina, Universidad de Oviedo, Julian Clavería Street S/n, 33006, Oviedo, Asturias, Spain
[g] Instituto de Investigación Sanitaria Del Principado de Asturias (ISPA), Roma Avenue S/n, 33001, Oviedo, Spain
[h] Biodonostia Health Research Institute, Environmental Epidemiology and Child Development Group, 20014, San Sebastian, Spain
[i] Ministry of Health of the Basque Government, Sub-Directorate for Public Health and Addictions of Gipuzkoa, 20013, San Sebastian, Spain
[j] Faculty of Psychology of the University of the Basque Country, 20018, San Sebastian, Spain
[k] Department of Statistics and Operational Research, Universitat de València, Dr. Moliner, 50 46100, València, Spain
[l] Department of Preventive Medicine and Public Health of the University of the Basque Country, UPV/EHU, Leioa, Spain
[m] Department of Clinical and Health Psychology and Research Methods, University of the Basque Country UPV/EHU, Avenida Tolosa 70, 20018, Donostia-San Sebastián, Spain
[n] Bradford Institute for Health Research, Temple Bank House, Bradford Royal Infirmary, Duckworth Lane, BD9 6RJ Bradford, United Kingdom, BD9 6RJ, Bradford, United Kingdom

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ABSTRACT

An accumulating body of evidence has associated exposure to greenspace with improved birth outcomes, including higher birth weight and lower risk of low birth weight; however, evidence on such association with in-utero fetal growth is scarce. We explored the influence of maternal exposure to residential greenspace and fetal growth in four INMA (Infancia y Medio Ambiente) Spanish birth cohorts (2003–2008), with 2,465 participants. Residential greenspace was characterised by the Normalised Difference Vegetation Index (NDVI) average across 100 m, 300 m, and 500 m buffers around the residence. Repeated ultrasound measurements of the abdominal circumference (AC), biparietal diameter (BPD), femur length (FL), and estimated fetal weight (EFW) were used. We created customised-generalised least squares models to evaluate associations of residential greenspace exposure on each fetal growth parameter, controlled for the relevant confounders. There were associations between the 500 m buffer and BPD, FL, and AC. We also found associations in the 300 m buffer and FL and AC. The associations in the 100 m buffer were null. Estimates were higher among participants with lower socioeconomic status. Mediation analyses found that air pollution might explain 15–37% of our associations. Mediation by physical activity was not observed. Greenspace exposure may be beneficial for fetal growth.

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* Corresponding author. Universitat de València, Unitat mixta FISABIO-Universitat Jaume I-Universitat de València, Menendez Pelayo, 46010, València, Spain.
E-mail addresses: maria.torres@isglobal.org (M. Torres Toda), m.luisa.estarlich@uv.es (M. Estarlich), ferran.ballester@uv.es (F. Ballester), montserrat.decastro@isglobal.org (M. De Castro), montserrat.decastro@isglobal.org (A. Fernández-Somoano), mambien3-san@euskadi.eus (J. Ibarluzea), Carmen.Iniguez@uv.es (C. Iñiguez), aitana.lertxundi@ehu.eus (A. Lertxundi), mikel.subiza@ehu.eus (M. Subiza-Perez), jordi.sunyer@isglobal.org (J. Sunyer), atardon@uniovi.es (A. Tardón), maria.foraster@isglobal.org (M. Foraster), payam.dadvand@isglobal.org (P. Dadvand).

[1] These authors contributed equally.

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1. Introduction

An unprecedented displacement from rural to urban areas has occurred worldwide (United Nations, 2018). This displacement is expected to continue rapidly, and by 2050, 68% of the global population will be urban (United Nations, 2018). A well-planned city is a place for economic, political, and cultural opportunities and provides better infrastructures, health care and basic services than rural areas (UN-Habitat, 2020). However, poor urban planning may lead to consequences for the health of city dwellers, for example, more exposure to negative environmental factors, including air pollution, noise, high temperatures, chemicals, poor nutrition and housing, and lack of green spaces (UN-Habitat, 2020; WHO, 2016). In recent years, a growing body of studies has associated exposure to greenspace with positive health outcomes (Hu et al., 2021; Nguyen et al., 2021; Rojas-Rueda et al., 2019; Twohig-Bennett and Jones, 2018). Other studies have investigated the potential underlying pathways to explain these beneficial associations. For example, exposure to greenspace may promote physical activity, enhance social cohesion, restore stress and attention, and mitigate exposure to negative environmental factors (i.e., air pollutants, noise, and heat) (Markevych et al., 2017).

It is known that humans in the prenatal period are very vulnerable to the effects of exposure to environmental factors (Barouki et al., 2012; Nieuwenhuijsen et al., 2013). These environmental factors may arrive from the mother to the fetus and may induce changes in growth, gene expression, metabolism, hormones, and organ structure (Gluckman et al., 2004). The changes can persist and may be determinants for developing adverse health outcomes across life. One of the most studied changes is fetal growth (Damhuis et al., 2021). Restriction in fetal growth is associated with many risks for newborns as neonatal morbidity and neonatal death (American College of Obstetricians and Gynecologists, 2019). Moreover, fetal growth restriction is associated with cognitive delay (Sacchi et al., 2020) and asthma (Sonnenschein-Van Der Voort et al., 2016) in childhood, and increased risks of type 2 diabetes (Kensara et al., 2005), osteoporosis (Cooper et al., 1997), metabolic syndrome (Rinaudo et al., 2012), and cardiovascular diseases (Barker and Osmond, 1986; Kensara et al., 2005) in adulthood.

Previous studies found evidence for favourable associations between greenspace exposure and birth outcomes such as birth weight (Agay-Shay et al., 2019; Akaraci et al., 2021; Yin, 2019), small for gestational age (SGA, birth weight below the 10th percentile for gestational age and sex) (Agay-Shay et al., 2019; Lee et al., 2021; Villeneuve et al., 2022) and preterm birth (gestational age <37 weeks) (Akaraci et al., 2021; Lee et al., 2021; Villeneuve et al., 2022). However, evidence capturing an improvement in the fetal growth in utero is still very scarce. In pregnancy, greenspace may influence fetal health by promoting moderate maternal exercise (Mceachan et al., 2016), enhancing social interactions (Astell-Burt et al., 2022), reducing maternal stress (Verheyen et al., 2021) and depression (Mceachan et al., 2016), and decreasing ambient air pollutants (Dadvand et al., 2012a), noise (Ristovska et al., 2014), and heatwaves (Sun et al., 2020).

Capturing the fetal growth in utero may be relevant because birth outcomes sometimes may not sufficiently reflect the dynamics of fetal growth during pregnancy. Impairment in the fetal growth has been associated with adverse health outcomes even in adulthood and regardless of birth outcomes (Roseboom et al., 2001). Generally, birth outcomes are used as a proxy of what occurred in utero with the prenatal growth. However, classifying newborns as fetal growth-restricted using birth outcomes may lead to biased estimates (Damhuis et al., 2021). In addition, the traditional evaluation of fetal growth restriction in utero was addressed by comparing estimated fetal weight obtained by ultrasound measurements with specific population-based charts. Population-based fetal growth charts could induce misclassifications to identify pathological smallness instead of constitutionally small fetuses and identify fetuses within the normal population limits but with undetected fetal growth restriction (Gaillard et al., 2014). This problem may be addressed using customised models that could provide individual rather than population-based fetal growth charts and are expected to reduce the misclassifications mentioned above (Mamelle et al., 2001).

We are aware of one study that evaluated maternal exposure to residential greenspace and fetal growth using ultrasound measurements in Tongzhou District (Beijing, China) (Lin et al., 2020). The study found an increased z-score of estimated fetal weight, abdominal circumference, and head circumference associated with the participants being more exposed to residential greenspace.

The present study aims to investigate associations of exposure to maternal residential greenspace on different parameters of fetal growth during pregnancy across four areas in Spain, applying customised growth models. Another aim is to evaluate a potential effect modification of these associations by sex of the child and socioeconomic status (SES). Moreover, given the potential capability of greenspace to reduce exposure to air pollution (Dadvand et al., 2012a) and increase physical activity levels (Mceachan et al., 2016), we aimed to evaluate the role of air pollution and physical activity in the associations from this study, if any.

2. Materials and methods

2.1. Study area and population

This study was conducted as part of the INMA project (INfancia y Medio Ambiente; Environment and Childhood), a network of Spanish birth cohorts with standardised methodologies (Guxens et al., 2012). The pregnant women were included in each cohort during their first-trimester ultrasound visit at the hospital of reference and after signing a consent form approved by respective ethics committees. Criteria for inclusion were: (i) to be resident in one of the study areas, (ii) to be 16 years old minimum, (iii) to have a singleton-pregnancy, (iv) not to have impediments to communication, and (v) to deliver in the corresponding reference hospital. For our study, we included fetuses from pregnant women recruited from four areas across Spain: Asturias (2004–2006), Gipuzkoa (2006–2008), Sabadell (2004–2006), and València (2003–2005). Asturias and Gipuzkoa are part of the Eurosiberian biogeographic region in northern Spain, whereas València and Sabadell, located in eastern and north-eastern Spain, are part of the Mediterranean region (Alcaraz-Segura et al., 2009). The Eurosiberian region is characterised by a humid climate, with more annual precipitations and cold winters. The Mediterranean region is characterised by a dry climate, with mild winters and hot summers (Alcaraz-Segura et al., 2009).

2.2. Characterisation of residential greenspace

We used the Normalised Difference Vegetation Index (NDVI) to estimate residential greenspace in each area (Fig. 1). NDVI is a well-known indicator of vegetation derived from satellite imagery. For this study, we employed images from Landsat 4–5 Thematic Mapper and Landsat 7 Enhanced Thematic Mapper Plus data at 30 m × 30 m resolution. The images were selected on cloud-free days and the following dates: May 25, 2006 (Asturias), June 14, 2001 (Gipuzkoa), May 18, 2007 (Sabadell), and May 29, 2003 (València). To achieve maximum exposure contrast, we used the images corresponding to the greenest month for each study area. Values of NDVI vary from -1 to $+1$, where higher values represent denser and more photosynthetically active vegetation (U.S. Geological Survey, 2022). For each participant, we calculated an average of NDVI values within 100 m, 300 m, and 500 m circular buffers around the residential address when the mother was in the first trimester of pregnancy to avoid overlapping with ultrasound measurements (Dadvand et al., 2012b).

2.3. Fetal growth parameters

Ultrasound scans (Voluson 730 Pro and 730 Expert; Siemens Sienna) were scheduled at 12, 20, and 34 weeks of gestation and performed by obstetricians specialized in conducting this type of examinations at the respective reference hospitals in each cohort (Iñiguez et al., 2016). We had access to records of any other ultrasounds performed on women during pregnancy, which allows us to perform two to eight valid ultrasounds per woman between 7 and 42 weeks of gestation. The measurement of fetal growth included the following ultrasound parameters: abdominal circumference, biparietal diameter, femur length, and estimated fetal weight calculated using the Hadlock algorithm (Hadlock et al., 1984). Gestational age was established by crown-rump length measurement when the date of the last menstrual period reported by the pregnant women was $\geq$7 days. To reduce potential bias, 18 pregnant women were excluded because the difference between crown-rump length and self-reported last menstrual period was more than three weeks. Moreover, ultrasound parameters with ±4 SD outside the mean were eliminated to avoid extreme outliers ($n = 5$ for abdominal circumference, $n = 8$ for femur length, and $n = 8$ for biparietal diameter).

2.4. Main analyses

In our main analysis, fetal ultrasound parameters were longitudinally analysed through generalised least squares models (gls) (Pinheiro et al., 2009) because the variances of the observations were unequal, that is, when there is heteroscedasticity or a certain degree of correlation between the observations. The subject was used as the random effect and adjusted by constitutional determinants, in accordance with the method described in Iñiguez et al. (2016) (Iñiguez et al., 2016). Association estimates were expressed for a 1-interquartile range (IQR) increase in each NDVI buffer of residential greenspace. For each ultrasound parameter of the fetal growth, the association with residential greenspace was assessed by adding the variable greenspace in the respective model. A step-forward algorithm tested several covariates (likelihood ratio test, p-value$<$0.05) as potential constitutional determinants. In the final models, we included: maternal height (continuous, cm), maternal age (continuous, years), parity (binary, yes/no), sex of the child (binary, girl/boy), maternal country of origin (binary, Spain/outside Spain), maternal social class (categorical, high/medium/low), maternal educational level (categorical, primary/high school/university), maternal smoking during pregnancy (binary, yes/no), working status during pregnancy (binary, employed/unemployed), and cohort (categorical, Asturias/Gipuzkoa/Sabadell/València). These covariates were obtained from questionnaires in the first and third trimesters and anthropometric measurements by specialized nurses. Social class was obtained from the current or latest occupation of the mother and applying the Spanish classification system (Domingo-Salvany et al., 2000). Mothers were categorised as smokers during pregnancy if they reported still smoking in the third-trimester questionnaire. Additional modelling details could be found in the Supplementary Materials, S1. Statistical analyses were conducted in R software, version R-4.0.5 (Foundation for Statistical Computing, Vienna, Austria). Level of statistical significance was set at p-value $<$0.05.

As a sensitivity analysis and to evaluate the robustness of our main findings, we further adjusted the main models for alcohol consumption during pregnancy (binary, yes/no), paternal educational level (categorical, primary/high school/university), season of last menstrual period (categorical, summer/spring/autumn/winter), and ran the models without remove the data considered extreme outlier. We also evaluated the change in the effect over pregnancy by including an interaction term between greenspace and gestational age at ultrasound measurement in the gls models. We created a baseline model to represent the cross-sectional association between greenspace and fetal growth at the first visit (12 weeks of pregnancy), and then, we evaluated the effect modification by gestational age by adding the interaction term.

2.5. Further analyses

2.5.1. Effect modification by sex, SES, and region

To be able to detect an effect modification related to the sex of the child and social class (an indicator of SES), we expanded our main models with an interaction term between residential greenspace and sex or social class. Then, we compared our main models with and without the interaction term (one at a time) by applying Wald tests. We investigated the associations between the regions (Eurosiberian region: Asturias and Gipuzkoa, Mediterranean region; València and Sabadell) by stratifying our main models according to the region. Associations were reported by a 1-IQR increase in residential greenspace as in the

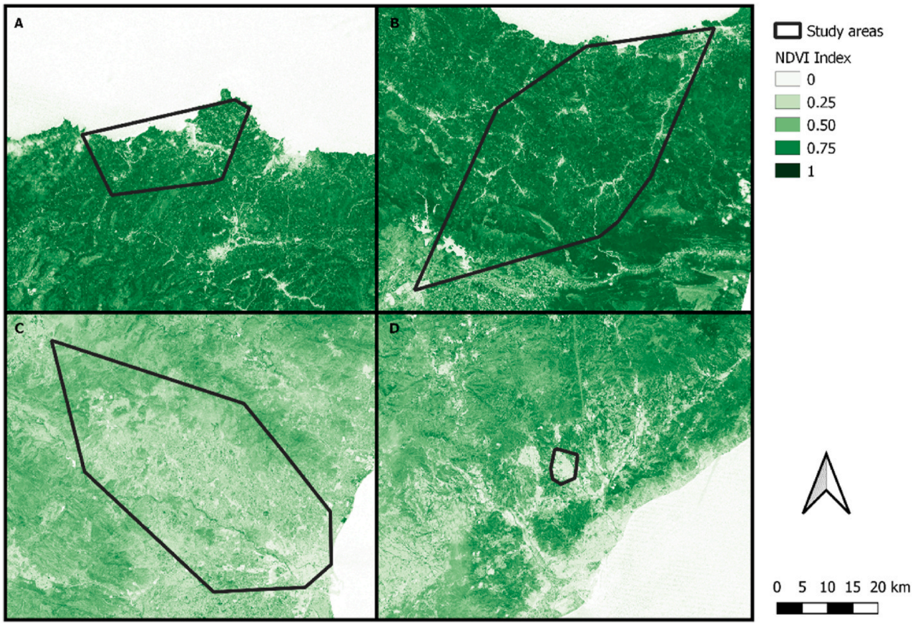


Fig. 1. Landsat NDVI imagery and study areas. A = Asturias, B = Gipuzkoa, C = València, D = Sabadell.

main analyses.

2.5.2. Influence of air pollution and physical activity

To explore the role of air pollution, we (i) further adjusted our main models for air pollution and (ii) conducted a mediation analysis calculating the percentage of the associations explained by air pollution (Preacher et al., 2011). Air pollutants, measured as NO_2 levels at the residence address for each participant in each pregnancy trimester, were estimated by land-use regression (LUR) models. Further details on these LUR models have been published previously (Estarlich et al., 2011). We used the following formula for the mediation percentage: (EI/ET) x 100, where ET was the coefficient estimate of the total effect (i.e., our main model), and EI was the coefficient estimate of the indirect effect. EI was calculated as $EI = ET\text{-}ED$, where ED was the direct effect coefficient estimate (i.e., our main model further adjusted for NO_2). A Jackknife approximation was used to calculate the confidence interval for the indirect effect (Preacher et al., 2011). To explore the role of physical activity we conducted a mediation analysis calculating the percentage of the associations explained by physical activity. Physical activity in the first trimester was calculated based on the total physical activity measured in metabolic equivalent of tasks (METs) hour/day in the previous year of pregnancy and obtained through questionnaires. METs is a widely used estimation of energetic cost performed in an activity-time, more technically is defined as the amount of oxygen inhaled in a sitting position (1 MET = 3.5 ml de O_2/kg/min) (Norman et al., 2001). We used the same methodology described above to calculate the mediation percentage.

3. Results

3.1. Study population and greenspace

In the study, we included 2465 participants. A detailed description of our study population characteristics can be found in Table 1. Most of the mothers were nulliparas (56.2%), were 30–34 years old (42.3%), had high school educational level (41.3%), were from low social class (43.6%), were born in Spain (91.8%), worked during pregnancy (83.5%), and non-smoked during pregnancy (68.4%). The NDVI values ranged from 0.14 to 0.22 in the Mediterranean region (Sabadell and València) and from 0.30 to 0.47 in the Eurosiberian region (Asturias and Gipuzkoa) (Supplementary Materials, Table S1). Spearman correlation coefficients between NDVI buffers and NO_2 are presented in Fig. S1. We observed positive correlations between NDVI buffers (0.81–0.96) and negative correlations between NDVI buffers and NO_2 from −0.62 to −0.72. Over the pregnancy, we obtained 1910 completed ultrasounds in the first, 2347 in the second, and 2453 in the third trimesters of pregnancy (Supplementary Materials, Table S2).

3.2. Main analyses

Table 2 presents the adjusted coefficient estimates of the associations between exposure to residential greenspace and each parameter of fetal growth. We found associations between a 1-IQR increase of NDVI in 300 m buffer and femur length and abdominal circumference, with coefficient estimates of 0.15 mm (95% CI (Confidence Interval): 0.02, 0.27) and 0.59 mm (95% CI: 0.06, 1.12), respectively. Moreover, a 1-IQR increase of NDVI in 500 m buffer was associated with an increased size in the biparietal diameter [0.17 mm (95% CI: 0.01, 0.35)], femur length [0.15 mm (95%CI: 0.01, 0.31)], and abdominal circumference [0.83 mm (95% CI: 0.19, 1.47)]. We did not find any statistically significant association between residential greenspace and the estimated fetal weight. Further adjustment of the main models for alcohol consumption, paternal education, and season of last menstrual period did not change the coefficient estimates (Supplementary Materials, Table S3). The use of the whole sample without exclusion of outliers also did not change the coefficient estimates (Supplementary Materials, Table S3). The interaction between green space and gestational age was not statistically significant (Supplementary Materials, Table S4).

Table 1
Table of the study population characteristics.

Variable	Asturias	Gipuzkoa	Sabadell	València	All cohorts
Number of participants	478 (19.3%)	600 (24.3%)	611 (24.7%)	776 (31.4%)	2465 (100.0%)
Gestational age at birth (median weeks, IQR)	39.5(2)	40(1.7)	39.8 (1.8)	39.8 (1.7)	39.8(1.8)
Sex of the child (n, %)					
Girl	227 (47.5%)	296 (49.4%)	305 (50.0%)	368 (47.4%)	1196 (48.5%)
Boy	251 (52.5%)	303 (50.6%)	306 (50.0%)	408 (52.6%)	1268 (51.5%)
Previous pregnancies (n, %)					
No	292 (61.1%)	324 (54.0%)	343 (56.3%)	426 (54.9%)	1385 (56.2%)
Yes	186 (38.9%)	276 (46.0%)	266 (43.7%)	350 (45.1%)	1078 (43.8%)
Maternal age (n, %)					
	24 (5.0%)	13 (2.2%)	54 (8.8%)	88 (11.3%)	179 (7.3%)
25–29 years old	130 (27.2%)	182 (30.3%)	204 (33.4%)	276 (35.6%)	792 (32.1%)
30–34 years old	202 (42.3%)	293 (48.8%)	247 (40.5%)	298 (38.4%)	1040 (42.2%)
	122 (25.5%)	112 (18.7%)	105 (17.2%)	114 (14.7%)	453 (18.4%)
Maternal educational level (n, %)					
Primary	88 (18.4%)	79 (13.2%)	171 (28.1%)	264 (34%)	602 (24.5%)
High School	213 (44.6%)	212 (35.6%)	261 (42.9%)	330 (42.5%)	1016 (41.3%)
University	177 (37%)	307 (51.3%)	176 (29%)	182 (23.5%)	842 (34.2%)
Social class (n, %)					
High	152 (31.9%)	265 (44.2%)	187 (30.6%)	169 (21.8%)	773 (31.4%)
Medium	105 (22.0%)	129 (21.5%)	172 (28.2%)	210 (27.0%)	616 (25.0%)
Low	220 (46.1%)	206 (34.3%)	252 (41.2%)	397 (51.2%)	1075 (43.6%)
Country of origin					
Spain	461 (96.4%)	576 (96.0%)	536 (88.9%)	683 (88.0%)	2256 (91.8%)
Outside Spain	17 (3.5%)	24 (4.0%)	67 (11.1%)	93 (12.0%)	201 (8.2%)
Working during pregnancy (n, %)					
No	130 (27.2%)	72 (12.0%)	70 (11.5%)	135 (17.4%)	407 (16.5%)
Yes	348 (72.8%)	528 (88.0%)	541 (88.5%)	641 (82.6%)	2058 (83.5%)
Maternal smoking (n, %)					
No	321 (71.5%)	445 (76.5%)	418 (69.8%)	456 (59.3%)	1640 (68.4%)
Yes	128 (28.5%)	137 (23.5%)	181 (30.2%)	313 (40.7%)	759 (31.6%)

3.3. Further analyses

Table S5 (Supplementary Materials) shows the comparison between our main models and models with the interaction term by sex of the child and SES. There were no statistically significant differences in the models with the interaction term by sex of the child. However, we found a statistically significant interaction by SES in the association between residential greenspace across 100 m buffer and femur length. Therefore, we conducted stratified analyses of our main models by SES (Table 3), and we found suggestions of stronger estimates in magnitude for those participants pertaining to lower SES. In particular, we found associations between higher residential greenspace and the more increased size

Table 2

Generalised least squares models for 1-IQR increase for each buffer of residential surrounding greenspace and difference in the average of fetal growth (mm) measurements and corresponding 95% confidence intervals (CI).

	Main effect[a]		Adjusted for air pollution[b]	
	Beta coefficient (95% CI)	**P value**	**Beta coefficient (95% CI)**	**P value**
Biparietal diameter				
NDVI 100 m buffer	−0.01 (−0.12, 0.11)	0.89	−0.05 (−0.17, 0.07)	0.41
NDVI 300 m buffer	0.13 (−0.02, 0.27)	0.08	0.08 (−0.08, 0.24)	0.32
NDVI 500 m buffer	**0.17 (0.01, 0.35)**	**0.05***	0.11 (−0.09, 0.31)	0.27
Femur length				
NDVI 100 m buffer	0.05 (−0.04, 0.15)	0.29	0.03 (−0.07, 0.14)	0.51
NDVI 300 m buffer	**0.15 (0.02, 0.27)**	**0.02***	0.12 (−0.01, 0.26)	0.07
NDVI 500 m buffer	**0.15 (0.01, 0.31)**	**0.04***	0.12 (−0.05, 0.29)	0.17
Abdominal Circumference				
NDVI 100 m buffer	0.19 (−0.22, 0.59)	0.36	0.07 (−0.37, 0.51)	0.75
NDVI 300 m buffer	**0.59 (0.06, 1.12)**	**0.02***	0.44 (−0.15, 1.02)	0.14
NDVI 500 m buffer	**0.83 (0.19, 1.47)**	**0.01***	0.64 (−0.07, 1.36)	0.07
Estimated Fetal Weight				
NDVI 100 m buffer	0.09 (−0.39, 0.56)	0.72	0.02 (−0.49, 0.53)	0.94
NDVI 300 m buffer	0.26 (−0.35, 0.87)	0.40	0.15 (−0.53, 0.82)	0.66
NDVI 500 m buffer	0.23 (−0.50, 0.97)	0.53	0.05 (−0.77, 0.88)	0.90

*$p < 0.05$.

[a] The main models were adjusted for: maternal height, maternal age, parity, country of origin, social class, maternal smoking, maternal education, sex of the child, working during pregnancy, and cohort.

[b] The models were further adjusted for [a] and NO_2.

of biparietal diameter, femur length, and abdominal circumference among fetuses of mothers with lower SES.

The results of stratified analyses by region can be found in Supplementary Materials, Table S6. The direction of the associations was similar to those of the main analyses. We did not observe a consistent pattern of stronger estimates in magnitude for either of the regions and heterogeneity was not detected (I^2). The only remarkable difference is that the associations between residential greenspace in 300 m and 500 m buffer and estimated fetal weight were stronger in Asturias (Eurosiberian region). Nevertheless, the associations between residential greenspace in the larger buffers and biparietal diameter were stronger in València (Mediterranean region).

We observed smaller association estimates between the greenspace exposure and fetal growth parameters when we further adjusted our main models for NO_2 levels (Table 2). The estimates were marginally significant (p-values between 0.05 and 0.1) for femur length in the 300 m NDVI buffer and abdominal circumference in the 500 m buffer. For the rest of the models, the associations were non-significant. The results of the mediation analysis are represented in Figs. 2 and 3. We conducted the mediation analysis for those associations where the total effect was statistically significant. The percentage of the association between residential greenspace in 500 m buffer and fetal growth explained by air pollution was 37% for biparietal diameter, 24% for femur length, and 23% for abdominal circumference. Further, the percentage mediated by air pollution of residential greenspace in 300 m buffer on fetal growth was 15% for femur length and 26% for abdominal circumference. Regarding physical activity, we did not observe a mediation.

Table 3

Generalised least squares models[(a)] for 1-IQR increase for each buffer of residential surrounding greenspace and difference in the average of fetal growth (mm) measurements and corresponding 95% CI, stratified by SES (social class).

	High	Medium	Low
Biparietal diameter			
NDVI 100 m buffer	−0.09 (−0.29, 0.11)	0.10 (−0.12, 0.32)	−0.02 (−0.19, 0.16)
NDVI 300 m buffer	0.02 (−0.24, 0.28)	0.22 (−0.06, 0.51)	0.15 (−0.08, 0.38)
NDVI 500 m buffer	0.03 (−0.28, 0.34)	0.21 (−0.13, 0.55)	**0.25 (-0.03, 0.54)**
Femur length			
NDVI 100 m buffer	−0.06 (−0.23, 0.11)	0.09 (−0.10, 0.28)	**0.13 (-0.02, 0.28)**
NDVI 300 m buffer	0.12 (−0.11, 0.34)	0.14 (−0.10, 0.38)	**0.18 (-0.02, 0.37)**
NDVI 500 m buffer	0.15 (−0.13, 0.42)	0.14 (−0.15, 0.43)	0.17 (−0.07, 0.42)
Abdominal Circumference			
NDVI 100 m buffer	−0.03 (−0.72, 0.67)	0.21 (−0.62, 1.05)	0.37 (−0.27, 1.01)
NDVI 300 m buffer	0.49 (−0.43, 1.41)	0.65 (−0.42, 1.72)	0.65 (−0.18, 1.48)
NDVI 500 m buffer	0.79 (−0.33, 1.92)	0.65 (−0.63, 1.93)	**0.99 (0.03, 2.00)**
Estimated Fetal Weight			
NDVI 100 m buffer	0.09 (−0.71, 0.89)	0.23 (−0.75, 1.20)	0.07 (−0.69, 0.83)
NDVI 300 m buffer	0.53 (−0.54, 1.60)	0.02 (−1.20, 1.24)	0.18 (−0.78, 1.14)
NDVI 500 m buffer	0.74 (−0.56, 2.04)	−0.32 (−1.76, 1.12)	0.02 (−1.15, 1.19)

*$p < 0.05$.

(a)The models were adjusted for: maternal height, maternal age, parity, country of origin, maternal smoking, maternal education, sex of the child, working during pregnancy, and cohort.

4. Discussion

This longitudinal study explored the associations between maternal residential greenspace exposure and fetal growth parameters. For each participant, satellite-imagery data was used to characterise residential greenspace exposure. We analysed repeated data on ultrasound parameters from four Spanish birth cohorts with remarkably different climates among the Eurosiberian and Mediterranean regions. We constructed customised fetal growth models for biparietal diameter, femur length, abdominal circumference, and estimated fetal weight. We found that more residential greenspace exposure during pregnancy in the 500 m NDVI buffer was associated with increased size in the biparietal diameter, femur length, and abdominal circumference. In addition, more exposure to residential greenspace in the 300 m buffer was associated with enhanced measures of femur length and abdominal circumference. We did not find associations for residential greenspace in 100 m buffer with any ultrasound parameters of fetal growth and any buffers with the estimated fetal weight. We did not find an effect modification by sex. However, we find an effect modification by SES in the association between greenspace exposure in 100 m buffer and femur length. Stratification by SES showed stronger estimates in magnitude for those participants from lower SES. After stratification of our main analyses by region, the associations did not show a consistent pattern. Once we further adjusted our main models for air pollution, we observed a weakening of the association estimates, and those statistically significant associations mentioned above disappeared or remained marginal. Our mediation analyses were suggestive of a potential mediatory role of air pollution in the association between greenspace exposure and fetal growth. Mediation by physical activity was not observed.

Our results were in line with those from previous studies. A recent study in Beijing (China) found that fetuses from participants with more residential greenspace exposure (i.e., 500 m NDVI buffer above the

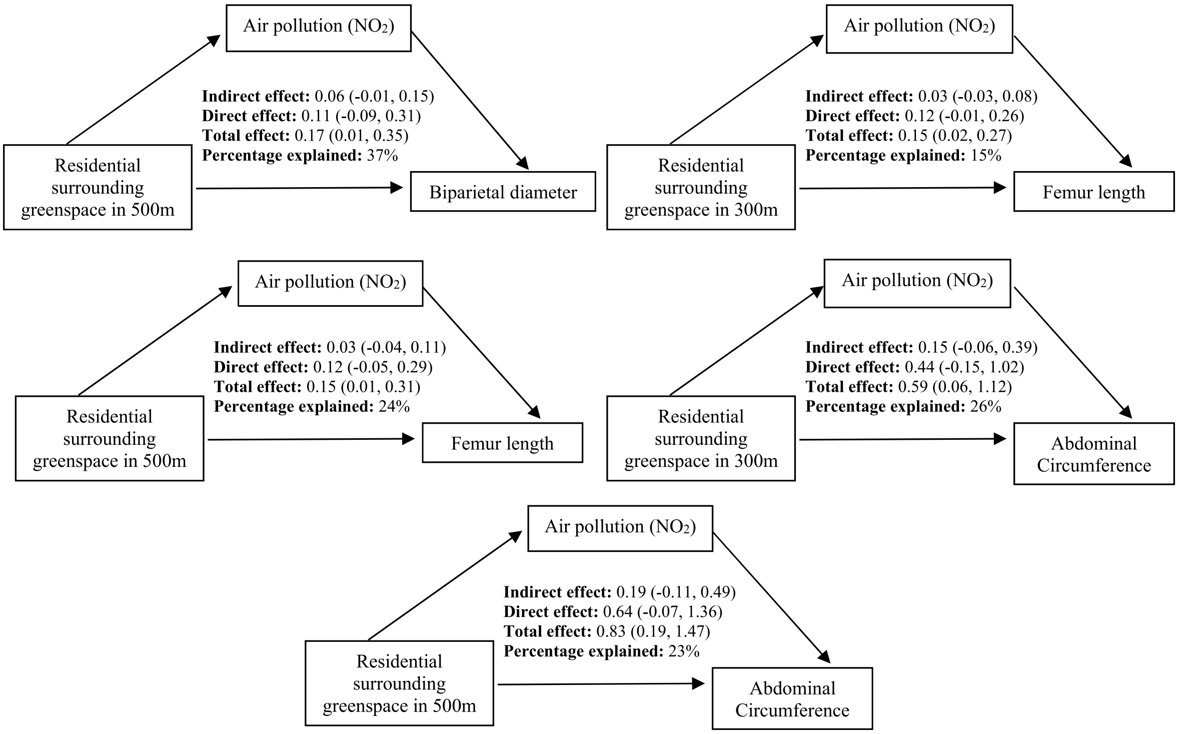
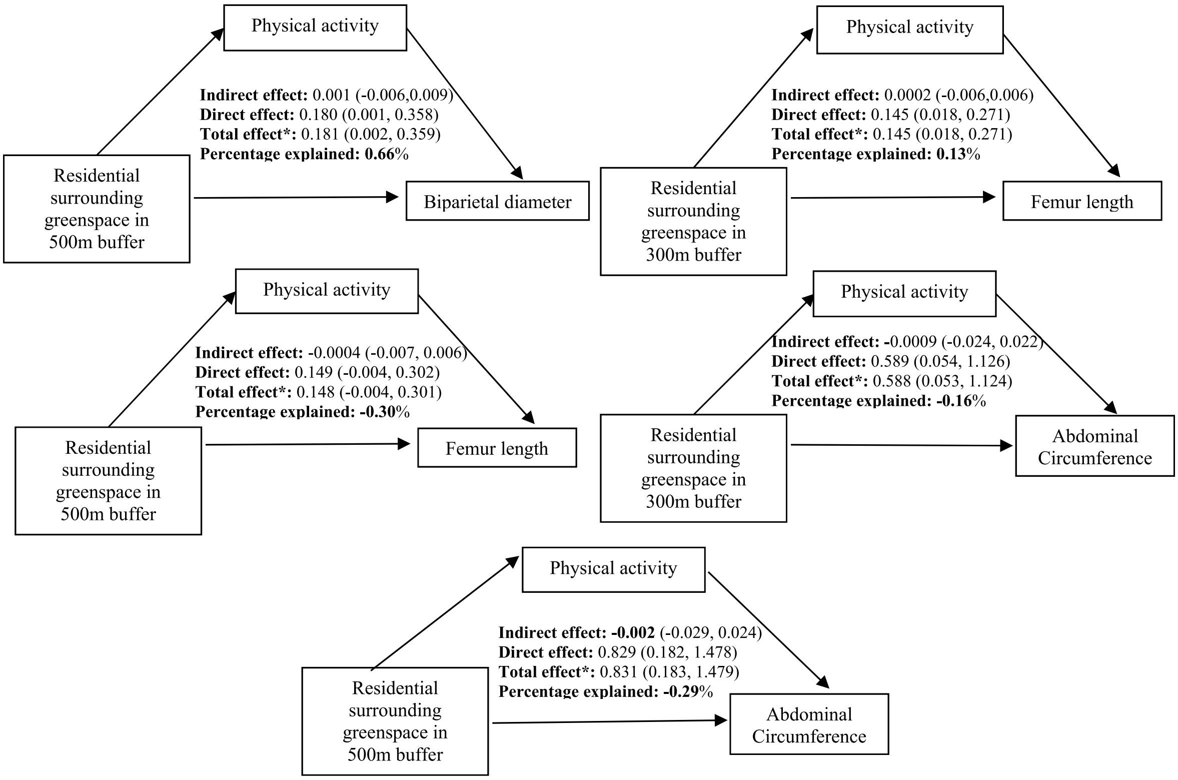


Fig. 2. Percentage explained of mediation of the association between residential surrounding greenspace and fetal growth by air pollution (NO_2).



*Total effect was calculated excluding cases with missing physical activity information.

Fig. 3. Percentage explained of mediation of the association between residential surrounding greenspace and fetal growth by physical activity.

median) had increased z-scores in estimated fetal weight of 0.05 (95% CI: 0.02, 0.08), in the abdominal circumference of 0.04 (95% CI: 0.01, 0.08), and the head circumference of 0.05 (95% CI: 0.02, 0.09) (Lin et al., 2020). In our study, we did not find a statistically significant association for any of the buffers of residential greenspace on estimated fetal weight, but the directions of the estimates were positive. Our abdominal circumference results were comparable to theirs, and we also found associations in the larger buffer sizes.

The previous study on greenspace exposure and fetal growth (Lin et al., 2020) did not observe interactions by sex of the child or SES in their models. Similarly, our study did not find an interaction by sex of the child. These findings may indicate that associations with residential greenspace may not depend on child sex. However, we found an interaction by SES in the association between residential greenspace (100 m NDVI buffer) and femur length. After stratification of the main models by SES, we observed some suggestions of more increased size of biparietal diameter, femur length and abdominal circumference associated with higher residential greenspace among fetuses of mothers with lower SES. Other studies on greenspace exposure and birth outcomes found a pattern of more benefits for those babies with mothers/fathers with the lowest maternal education, another indicator of SES (Dadvand et al., 2012c; Laurent et al., 2019). These findings are important because people from lower SES have an increased risk of poor fetal growth and worse health (Ball et al., 2013; Vos et al., 2014) compared to those from higher SES. Exposure to greenspace may have the capability to reduce this gap in health among people with different socioeconomic levels. Thereby, promoting greenspace in our cities can be a target for urban planners and policymakers to reduce health inequalities and increase environmental justice, especially in deprived areas. The present study was conducted across four areas in Spain within two different biogeographic regions. The associations across the specific areas were comparable, suggesting that these associations are not region-specific.

We are not aware of any other study besides the one by Lin et al. (2020), that evaluated greenspace exposure and fetal growth parameters. However, although birth outcomes may not correctly reflect the dynamics of fetal growth in utero, studies on maternal exposure to greenspace and positive birth outcomes are one of the most consistent associations found in studies about the health benefits of greenspace (Yang et al., 2021). Our research group previously investigated the association between residential greenspace and birth weight, birth head circumference, and gestational age at birth (Dadvand et al., 2012b). A 1-IQR increase in residential greenspace was associated with increases in birth weight [44.2 g (95% CI: 20.2, 68.2)] and head circumference [1.7 mm (95% CI: 0.5, 2.9)] but not with gestational age. A systematic review by Dzhambov et al. (2014) found that larger buffer sizes of NDVI had a more noticeable improvement in birth weight, while smaller buffer sizes tended to have more inconsistent results. Although in our study we analysed fetal growth parameters, birth weight is widely used as an indicator of impaired fetal growth, and those findings were similar compared to ours. A potential explanation for this could be that the social and physical activity function of residential greenspace reflected in larger buffers rather than stress reduction by visualisation in shorter buffers might be more relevant mechanisms underlying these associations. Although in our analyses no significant mediation by physical activity was found.

The mechanisms underlying the health benefits of greenspace exposure are yet to be established, but an emerging body of evidence has shed light on a number of them. For example, the ability of greenspace to reduce stress and depression (Verheyen et al., 2021), increase physical activity (Mceachan et al., 2016), and mitigate exposure to air pollution (Dadvand et al., 2012a) could underlie our observed associations between greenspace exposure and fetal growth. In our study, the statistically significant associations disappeared after further inclusion of NO_2 in our main models suggesting a potential mediatory role of NO_2. We then conducted a mediation analysis of NO_2, and we found that this air pollutant could explain 15–37% of our observed associations. We could not compare these findings to those of the previous studies with ultrasound measurements given the unavailability of such a mediation analysis. However, these findings are in line with various previous studies evaluating greenspace exposure and birth outcomes (e.g., birth weight, SGA, and low birth weight) (Dadvand et al., 2012b; Laurent et al., 2019; Lee et al., 2021). A previous study showed that particulate matter (PM) mediated approximately 5–19% of the association between first and third trimester greenspace and preterm birth and mediated approximately 15–37% of the association between greenspace and SGA (Lee et al., 2021). We did not observe a mediation by physical activity. We are aware of another study on greenspace and fetal growth that found an increase in the distance from outdoor fitness equipment explained 14% of the associations, used as a proxy of physical activity (Agay-Shay et al., 2019). For our mediation analyses, we used another variable of physical activity that probably could explain these differences on the results if we compare the two studies. Moreover, our physical activity variable was calculated based on the previous year of pregnancy and this inaccuracy might be explaining our null results.

Moreover, the application of customised models is a growing area of research. These models might improve the distinction between small fetuses that have achieved their growth potential and small fetuses because of a real pathological growth restriction (Gaillard et al., 2014). Fetuses identified as growth-restricted by population-based reference charts may include fetuses with intrauterine growth restriction with a higher risk of suffering adverse health outcomes and also constitutionally small but normal-growth fetuses (Gaillard et al., 2014).

Some limitations of our study should be considered. To begin with, we did not have data on other important aspects of the greenspace exposure, such as the time spent in green spaces, visual access to greenspace, or quality characteristics of the greenspace. A previous study by our research group found that visual access and time spent in green spaces were associated with higher birth weight (Torres Toda et al., 2020a). Quality characteristics of greenspace are also important to consider, given that an unattractive and unsafe greenspace may be discouraging for pregnant women to visit. To calculate our NDVI values, we relied on images from Landsat, a satellite that has better spatial resolution compared to others (i.e., MODIS) but with the price of losing some temporal resolution. However, some studies showed that NDVI values in short periods do not vary significantly (Dadvand et al., 2012b; Torres Toda et al., 2020b), and therefore we believed that for our study period having more spatial resolution would be better. Although it is a common practice in greenspace and health studies, another limitation was to rely on a single satellite image per study area which always is prone to some misclassification. We suggest to the future studies to try to overcome this limitation. Although we did not have information about previous residential mobility and preconceptional exposure to greenspace, we expect a minimal effect on results given that only 1–6% of INMA participants moved during pregnancy (Estarlich et al., 2011). Moreover, our sample size was limited, and our stratified analyses were possibly underpowered. Finally, a study comparing SGA classification from population-based models and customised models in 8162 pregnant women (Gaillard et al., 2011) found 16–25% differences between the two models. However, maternal and fetal characteristics used for customisation may not strongly predict fetal growth individually. More studies are needed to characterise these customised models for epidemiological and clinical utilisation. We recommend using larger sample sizes for future studies while accounting for data on the quality and type of greenspace. For future studies, we also recommend the evaluation of other potential mechanisms under the association between greenspace and fetal growth, such as stress levels.

To conclude, our results support the hypothesis that residential greenspace may positively influence fetal growth in utero and shed light on a potential mediatory role of air pollution on this association. Improving and implementing greenspace in urban areas could help to promote health in early life and reduce health inequalities among different SES.

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Declarations of competing interest

None.

Data availability

The data that has been used is confidential.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.healthplace.2022.102912.

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