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Exposure to natural environments during pregnancy and birth outcomes in 11 European birth cohorts

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ABSTRACT

Research suggests that maternal exposure to natural environments (i.e., green and blue spaces) promotes healthy fetal growth. However, the available evidence is heterogeneous across regions, with very few studies on the effects of blue spaces. This study evaluated associations between maternal exposure to natural environments and birth outcomes in 11 birth cohorts across nine European countries. This study, part of the LifeCycle project, was based on a total sample size of 69,683 newborns with harmonised data. For each participant, we calculated seven indicators of residential exposure to natural environments: surrounding greenspace in 100m, 300m, and 500m using Normalised Difference Vegetation Index (NDVI) buffers, distance to the nearest green space, accessibility to green space, distance to the nearest blue space, and accessibility to blue space. Measures of birth weight and small for gestational age (SGA) were extracted from hospital records. We used pooled linear and logistic regression models to estimate associations between exposure to the natural environment and birth outcomes, controlling for the relevant covariates. We evaluated the potential effect modification by socioeconomic status (SES) and region of Europe and the influence of ambient air pollution on the associations. In the pooled analyses, residential surrounding greenspace in 100m, 300m, and 500m buffer was associated with increased birth weight and lower odds for SGA. Higher residential distance to green space was associated with lower birth weight and higher odds for SGA. We observed close to null associations for accessibility to green space and exposure to blue space. We found stronger estimated magnitudes for those participants with lower educational levels, from more deprived areas, and living in the northern European region. Our associations did not change notably after adjustment for air pollution. These findings may support implementing policies to promote natural environments in our cities, starting in more deprived areas.

1. Introduction

The global population living in urban areas is constantly increasing. In 2018, 55 % of the total population lived in urban areas, and this is expected to reach two thirds by 2050 (United Nations. World Urbanization Prospects, 2018). Urbanisation, if poorly planned, may lead to a reduction in the availability, accessibility, and quality of natural environments, e.g., green (vegetation) and blue (water) space for city dwellers (Regional Office for Europe WHO, 2021). This is problematic, as human contact with the natural environments has been reported to benefit many aspects of health. For example, increased exposure to green spaces has been associated with improved mental health (Gianfredi et al., 2021), well-being (Gianfredi et al., 2021), pregnancy outcomes (Hu et al., 2021), and reduced risk for cardiometabolic diseases (Yang et al., 2021), and all-cause mortality (Rojas-Rueda et al., 2019). Additionally, greater exposure to blue spaces is associated with improvements in mental health and well-being (Gascon et al., 2017). The positive association between health and exposure to nature may be because humans are innately attracted and connected to nature, and the loss of this connection results in a loss of quality of life (Kellert and Wilson, 1993). In addition to the innate connection with nature and its resulting stress recovery and attention restoration (Huang et al., 2021), other mechanisms have been proposed to underlie the association between nature and health, including encouraging physical activity, reducing stress and exposure to environmental stressors (e.g., air pollution, road traffic, industrial and construction noise, and heat), facilitating social interactions, and enriching the environmental microbiota (Markevych et al., 2017).

Through most of the aforementioned mechanisms, exposure to natural environments during pregnancy could influence fetal growth. Ensuring healthy fetal growth is essential to preventing many adverse health outcomes early and later in life. For example, babies with low weight at birth (LBW, birth weight $< 2{,}500$g) or small for gestational age (SGA, birth weight less than or equal to the 10th percentile for gestational age and sex) (American College of Obstetricians and Gynecologists, 2019) have a higher risk of stunting, lower intelligence quotient, and death in childhood; and obesity, cardiovascular disease, and diabetes in adulthood (Blencowe et al., 2019).

An increasing number of studies have reported associations between maternal exposure to green space and increased birth weight (Hu et al., 2021; Akaraci et al., 2020; Zhan et al., 2020), reduced risk of LBW (Hu et al., 2021; Zhan et al., 2020), and SGA (Akaraci et al., 2020; Zhan et al., 2020), although other studies concluded partial or limited evidence for an association (Abelt and McLafferty, 2017; Anabitarte et al., 2020; Glazer et al., 2018; Eriksson et al., 2019). Most of these studies were performed in specific populations, and effect estimates differed from one region to another (Yang et al., 2021), possibly due to different measurements of exposures and outcomes or true differences in associations between regions. Further, evidence about the magnitude for particular groups with different socioeconomic statuses (SES) remains mixed (Hu et al., 2021; Blencowe et al., 2019; Zhan et al., 2020). In addition, there are very few studies that have examined blue space associations with birth outcomes. Indeed, to our knowledge, only one study found an association between living within 500m of a freshwater body and higher birth weight (Glazer et al., 2018), whereas other studies found no association (Nieuwenhuijsen et al., 2019; Richardson et al., 2018; Abelt and McLafferty, 2017). Previous studies on natural environments and birth outcomes were mainly conducted in single countries within a specific region with a certain climate and vegetation type (Gianfredi et al., 2021). The above-mentioned differences in their observed effect estimates may be a function of each study region's cultural and climate characteristics. Up to now, the absence of standardised methodologies for exposure assessment has not allowed the comparison of the associations between natural environments and birth outcomes across different countries.

The present study aims to evaluate associations of maternal exposure to green and blue space during pregnancy with birth weight and SGA, using harmonised data from a large consortium of 11 European birth cohorts located across nine countries. As secondary aims, we (i) evaluated the potential effect modification by SES and four regions of Europe and (ii) evaluated the influence of ambient air pollution on the associations between natural space and birth outcomes.

2. Materials and methods

2.1. Study population and design

This study was conducted as part of the European Union-funded project LifeCycle (Fig. 1). The LifeCycle project aims to study early-life stressors that influence health throughout the life cycle by establishing the EU Child Cohort Network, a long-term and open Europe-wide network of birth cohort studies with harmonised data of more than 250,000 children and parents (more information on the project can be found elsewhere) (Jaddoe et al., 2020; Pinot de Moira et al., 2021). Data from the LifeCycle project allows researchers to use standardised methodologies and increased sample sizes. The large sample sizes achieved through this consortium promote higher statistical power, which is needed for increased accuracy of estimates and obtaining more robust findings. The LifeCycle geographic coverage spans much of Northern, Western, Central, and Southern Europe. In the present study, we included 11 cohorts that had the necessary available harmonised data on urban environment stressors during pregnancy, birth outcomes, and relevant individual and neighbourhood covariates, namely ABCD (Amsterdam Born Children and their Development, the Netherlands, period of enrolment: 2013) (van Eijsden et al., 2011), ALSPAC (Avon Longitudinal Study of Parents and Children, the United Kingdom, 1991–1992) (Fraser et al., 2013), BiB (Born in Bradford, the United Kingdom, 2007–2011) (Wright et al., 2013), DNBC (Danish National Birth Cohort, Denmark, 1996–2003) (Olsen et al., 2001), EDEN (Etude des Déterminants du développement et de la santé de l'Enfant, France, 2003–2006) (Heude et al., 2016), Generation R (the Generation R Study, the Netherlands, 2002–2006) (Kooijman et al., 2016), INMA (Infancia y Medio Ambiente, Spain, 2003–2008) (Guxens et al., 2012), KANC (Kaunas Birth Cohort, Lithuania, 2007–2009) (Grazuleviciene et al., 2009), MoBA (the Norwegian Mother, Father and Child Cohort Study, Norway, 1999–2008) (Magnus et al., 2016), NINFEA (Nascita e INFanzia: gli Effetti dell'Ambiente, Italy, 2005–2016) (Richiardi et al., 2007), and RHEA (Rhea Mother & Child Cohort Study, Greece, 2007–2008) (Chatzi et al., 2017). Before study enrolment, a signed consent form was obtained from all the participants in accordance with each centre's ethics committee. The harmonised data are kept within each institution and analysed remotely through DataSHIELD (Data Aggregation Through Anonymous Summary- statistics from Harmonised Individual-level Databases), a privacy-preserving federated data analysis platform. Under this infrastructure, relevant national and international data protection regulations are followed.

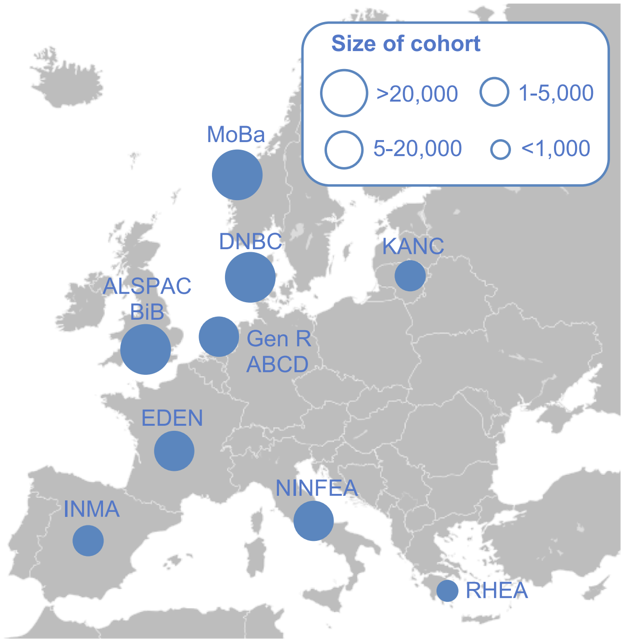

Figure adapted from: https://lifecycle-project.eu/for-scientists/the-eu-child-cohort-network/

Fig. 1. Map of cohorts and number of participants involved in the study. Figure . adapted from: https://lifecycle-project.eu/for-scientists/the-eu-child-cohort-network/

2.2. Exposure to natural environments

The assessment of natural environments was conducted at the mother's residential address during pregnancy following a standardised protocol for harmonised urban environment stressor data across all cohorts developed in the Lifecycle project (available online: https://lifecycle-project.eu/wp-content/uploads/2021/07/Protocol_v4_2021_06_25.pdf). We obtained five indicators of exposure to greenspace (i.e., residential surrounding greenspace, residential distance to green space, and accessibility to green space) and two indicators of exposure to blue space (i.e., residential distance to blue space and accessibility to blue space) during pregnancy for each participant.

2.2.1. Indicators of exposure to greenspace

Residential surrounding greenspace was abstracted as the average Normalised Difference Vegetation Index (NDVI) in buffers of 100m, 300m, and 500m around the participant's residential address at the time of pregnancy. NDVI is a widely used index to quantify vegetation by measuring the difference between near-infrared light (reflected by vegetation) and red light (absorbed by vegetation) (Geological Survey, 2022). The values vary from −1 to 1, with higher values indicating more photosynthetic capacity and thus more vegetation. We used cloud-free images from Landsat 4–5 Thematic Mapper (TM) and Landsat 7 Enhanced Thematic Mapper Plus (ETM +) within 30x30m resolution to develop the NDVI maps (Supplementary Materials, Table S1). One or more images were selected for each cohort/city to cover the entire study period. Water was not removed but negative values in the images have been reclassified to null values previously.

Residential distance to green space was calculated using the Urban Atlas (European Environment Agency. Data and maps 2022) generated by European Environmental Protection Agency (except for INMA-Gipuzkoa and MoBa, where maps from the European Nature Information System (EUNIS) (EUNIS, 2022) and the Norwegian Mapping Authority (The Norwegian Mapping Authority. Kartkatalogen., 2022) were used, respectively) (Supplementary Materials, Table S1). Residential distance to green space consisted of the Euclidean distance in metres from the residential address to the nearest green space $\geq$ 5,000m^2 (i.e., major green space) (The WHO Regional Office for Europe, 2017). Accessibility to greenspace around residential address was defined as living within 300m of a public major green space (yes/no) (The WHO Regional Office for Europe, 2017).

2.2.2. Indicators of exposure to blue space

Residential distance to blue space was calculated as the Euclidean distance in metres from the residential address to the nearest blue space $\geq$ 5,000m^2. This size was given by the area extension of each polygon in the Urban Atlas layer (European Environment Agency. Data and maps 2022). Accessibility to blue space around residential address was the presence (yes/no) of a blue space $\geq$ 5,000m^2 in 300m from home. Both indicators were calculated based on the Urban Atlas (European Environment Agency. Data and maps 2022) (except for INMA-Gipuzkoa and

MoBA, where maps from EUNIS (EUNIS, 2022) and the Norwegian Mapping Authority (The Norwegian Mapping Authority. Kartkatalogen., 2022) were used).

2.3. Birth outcomes

We used birth weight (continuous, grams) and small for gestational age (SGA, binary, yes/no) as our outcomes of interest because of their clinical relevance. Birth weight was obtained from hospital records in all cohorts. Gestational age at birth was obtained using each cohort's best clinical judgement: a) using the last menstrual period if the difference from ultrasound measurement was less than seven days or if ultrasound was not available, b) using ultrasound if the difference between last menstrual period and ultrasound was more than seven days or if last menstrual period was not available, c) using maternal report if none of them was available. SGA was defined using the WHO fetal growth charts (Kiserud et al., 2017) as being below the 5th percentile for gestational age and sex. The 5th percentile was chosen as this is more indicative of significant impaired fetal growth compared to the 10th percentile which is more frequently used (Onald et al., 1999). A child was classified as SGA if their birth weight was below the 5th percentile for gestational age and sex. SGA data was not available for KANC.

2.4. Covariates

We selected a set of covariates *a priori* based on previous literature: maternal age (continuous, year), parity (binary, nullipara/multipara), gestational age at birth (continuous, days), sex of the child (binary, boy/girl), maternal education level (categorical, low/medium/high), residential area-level deprivation index (categorical, low deprivation/medium deprivation/high deprivation), a multidimensional evaluation of an area's socioeconomic conditions, and maternal smoking during pregnancy (binary, yes/no). Data on parity was obtained from birth medical registry data in all cohorts. The maternal level of education was based on the highest ongoing or completed education at the time of delivery. This categorization followed the International Standard Classification of Education 97/2011 (ISCED-97/2011); mapping tools for specific countries can be found here: https://uis.unesco.org/en/isced-mappings. Country specific indices of deprivation were used to create the area-level deprivation index (more information in Supplementary Materials, Table S2).

2.5. Statistical analyses

2.5.1. Main analyses

Statistical analyses were conducted through DataSHIELD, a data infrastructure with series of R packages, that enables a remote federated analysis, without the need of physically transferring, pooling, sharing, or disclosing the individual-level data across the cohorts participating in the LifeCycle consortium (Wilson et al., 2017). We first described the main characteristics of our study participants for each cohort separately and then for all cohorts combined. Our main analyses utilized a full-likelihood-based individual person data analysis (often called "pooled" or 1-stage analysis) which generates the same results as if the data from all cohorts were physically transferred to a central warehouse and analysed jointly. We used pooled linear and logistic regressions models to investigate associations of exposure to each natural environment indicator with difference in mean birth weight and odds ratios (OR) of SGA, respectively. The models were adjusted for the individual and neighbourhood level covariates described above as well as for cohort as a categorical variable. In the models including SGA as our outcome, we did not further adjust for gestational age at birth and sex of the child. The effect estimates were calculated per one- interquartile range (1-IQR) increase in each continuous indicator of green and blue space exposure and a category difference in each categorical indicator (accessibility to green space and accessibility to blue space, Yes/No, reference: No). Each regression analysis has been performed on the complete cases of the variables for each specific model.

2.5.2. Sensitivity analyses

We further adjusted our main models for maternal ethnicity (not available for NINFEA, MoBa, DNBC, RHEA, and KANC) and alcohol consumption during pregnancy (not available for ABCD). Ethnicity (binary, Western/Non-western or mixed) and alcohol consumption (binary, yes/no) were obtained mainly through questionnaires. Some cohorts, including BiB, Generation R, and ABCD, had a significant representation of other ethnic groups than Western.

To investigate the influence of ambient air pollution on the associations, we further adjusted our main models by the following indicators of air pollution during pregnancy: NO_2 (nitrogen dioxide, $\mu g/m^3$) and $PM_{2.5}$ (particulate matter with an aerodynamic diameter<2.5 μm, $\mu g/m^3$). Air pollutants were estimated at the residential addresses of participants as average levels during the entire pregnancy. The levels of air pollutants were calculated based on the land-use regression (LUR) models developed in the European Study of Cohorts for Air Pollution Effects (ESCAPE) project, including most of the cohorts participating in this study (Beelen et al., 2013; Eeftens et al., 2012). For those cohorts for which ESCAPE local models were not available, models developed within the Effects of Low-Level Air Pollution: A Study in Europe (ELAPSE) project (de Hoogh et al., 2018) were used (more information in Supplementary Materials, Table S1).

2.5.3. Stratified analyses

To assess the potential effect modification by SES, we stratified our main models by maternal education level (low/medium/high), an indicator of household SES, and by residential area-level deprivation index (low deprivation/medium deprivation/high deprivation). In addition, we stratified our models to assess potential regional differences in associations. We categorised the regions as Western Europe (ABCD, EDEN, and Generation R), Northern Europe (ALSPAC, BiB, DNBC, KANC, and MoBA), and Southern Europe (INMA, NINFEA, and RHEA).

3. Results

3.1. Study population

After limiting the participants to those from mothers with singleton pregnancies and removing participants with missing data on the study exposure and outcomes, we included a total of 69,683 liveborn singletons in the analysis (see flowchart in Fig. 2). The description of the pregnancy and maternal sociodemographic and lifestyle characteristics of the study participants are shown in Table 1. Mothers had a median age of 29.5 years (IQR= 6.2), and most of the mothers had high education level (48 %) and were of Western ethnicity (66 %), lived in highly deprived areas (45 %), and did not smoke during pregnancy (80 %). However, there was substantial variation by cohort. The offspring had a median birth weight of 3,422 g, with 6.6 % being classified as SGA.

3.2. Natural environments

The description of exposure to natural environments indicators during pregnancy is presented in Table 1. The NDVI values varied from a median of 0.14 (IQR = 0.08) in RHEA (Greece) to 0.52 (0.15) in MoBA (Norway). The median residential distance to green and blue space was 177m (IQR = 232m) and 937m (IQR = 1000m), respectively. 73 % of the participants had a green space accessible from the residential address, whereas only 22 % of the participants had accessibility to blue space. Participants from ABCD and Generation R (the Netherlands) had the highest accessibility to blue space (88 % for ABCD and 53 % for Generation R) compared to participants of the other cohorts. The correlations were high among the three NDVI buffers of residential surrounding greenspace exposure (correlation coefficients: 0.84–0.97)

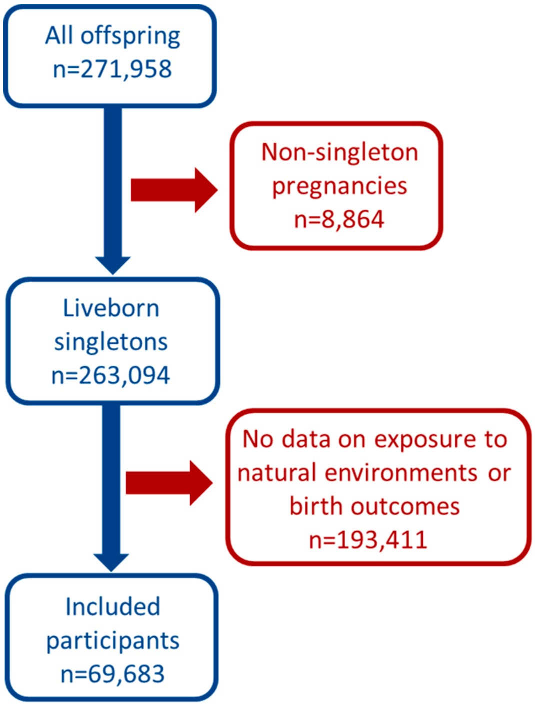

Fig. 2. Selection of study participants flowchart.

(Figure S1). Moreover, the residential distance to green space was negatively correlated with residential surrounding greenspace.

3.3. *Main analyses*

3.3.1. *Birth weight*

Table 2 summarizes the estimates of linear regression models for associations between exposure to natural environments during pregnancy and birth weight. Higher maternal exposure to residential surrounding greenspace during pregnancy was associated with higher birth weight. Specifically, we found that an IQR increase of NDVI in 100m, 300m, and 500m buffers was associated with 16.9g (95% confidence interval (CI): 12.0g, 21.8g), 17.5g (95% CI: 12.4g, 22.6g), and 18.5g (95% CI: 13.3g, 23.7g) increase in the average of birth weight. Moreover, a longer residential distance to a major green space was associated with lower birth weight [-8.4g (95% CI: −13.1g, −3.8g)]. For accessibility to green space, the estimates were not conclusive. Similarly, we did not find clear statistically significant associations in the two indicators of exposure to blue space and birth weight.

3.3.2. *Small for gestational age*

Table 3 summarises the odds ratios (ORs) of the associations between exposure to natural environments and SGA. Overall, we found a consistent pattern of associations in the same direction as we observed for birth weight. An IQR increase in residential surrounding greenspace across buffers of 100m, 300m, and 500m, was associated with respective odds ratios of 0.87 (95% CI: 0.83, 0.92), 0.87 (95% CI: 0.82, 0.91), and 0.86 (95% CI: 0.81, 0.90) for SGA. An IQR increase in residential distance to green space was associated with an odds ratio of 1.07 (95% CI: 1.02, 1.12) for SGA. Associations between accessibility to green space, residential distance to blue space, and accessibility to blue space with reduced SGA were close to null.

3.4. *Sensitivity analyses*

After further adjustment of our main models for ethnicity and alcohol consumption, we observed an attenuation of the association estimates for both birth weight and SGA (Supplementary Materials, Tables S3 and S4). In terms of statistical significance, associations between residential distance to green space and both outcomes lost their significance after further adjustment for ethnicity and alcohol consumption. In addition, we did not observe a notable change in the magnitude of coefficient estimates (changes $\leq$ 10 %) after further adjustment of our models for NO$_2$ and PM$_{2.5}$ (Supplementary Materials Tables S5 and S6).

3.5. *Stratified analyses*

The associations between exposure to the natural environment and birth weight and SGA across strata of maternal education level, area-level deprivation index, and region of Europe are presented in Figures S2, S3, and S4 in Supplementary Materials. In general, we observed some evidence of stronger associations between residential surrounding greenspace and birth weight and SGA for those participants with the lowest education level and those living in the most deprived areas. After stratification by region, we also found some indications for potentially stronger associations for those participants living in the northern region.

4. Discussion

We investigated the associations between seven metrics of exposure to natural environments during pregnancy and birth weight and SGA probability. Capitalising on data from 11 birth cohorts from across Europe enabled us to evaluate, for the first time, this association across different countries and shed light on the role of region on this association. We found that more residential surrounding greenspace and shorter residential distance to green space were associated with higher birth weight and lower odds of SGA after controlling for individual and neighbourhood covariates. There was some evidence that these associations were stronger for people from lower SES groups and those living in the northern parts of Europe. Our findings for accessibility to green space, residential distance to blue space, and accessibility to blue space were close to null. Similarly, we did not find indications that ambient air pollution with NO$_2$ and PM$_{2.5}$ could influence the association between exposure to natural environments and birth outcomes.

4.1. *Interpretation of results*

Our main findings are consistent with prior studies (Dadvand et al., 2012; Dadvand et al., 2014; Markevych et al., 2014; Nieuwenhuijsen et al., 2019). The study by *Nieuwenhuijsen et al.,* (Nieuwenhuijsen et al., 2019) evaluating the pregnancy urban exposome and birth weight in six European cohorts, found an IQR increase in NDVI averages across buffers of 100m, 300m, and 500m was associated with an increase of 30.2g (95% CI: 21.7g, 38.7g), 30.7g (22.5g, 38.9g), and 29.6g (21.6g, 37.5g). A study using the *Born in Bradford* birth cohort (United Kingdom) found an IQR increase in exposure in NDVI in 100m and 500m buffer was associated with an increase of 15.8g (1. g, 30.6g) and 15.8g (0.9g, 30.7g) in birth weight, respectively (Dadvand et al., 2014). Similarly, in Germany, an IQR increase of residential surrounding greenspace in a 500m buffer was positively associated with an increase in average birth weight of 17.6g (95% CI: 0.5g, 34.6g) (Markevych et al., 2014). In Spain, higher exposure to residential surrounding greenspace was associated with an average increased birth weight of 44g (95% CI: 20.2g, 68.2g) in 500m NDVI buffer (Dadvand et al., 2012). In addition, our study adds that an IQR increase in residential distance to green space was associated with −8.4g (95% CI: −13.1g, −3.8g) in birth weight. These findings were consistent with two previous studies where residential distance to green space was negatively associated with birth weight, with estimates of −12.8g (95% CI: −19.2g, −6.3g) (Nieuwenhuijsen et al., 2019) and −13.4 g (95% CI: −78.9g, 48.0g) (Torres Toda et al., 2020). Contrary to our findings, in Atlanta, the absence of parks within a distance of 800 m

Table 1
Description of pregnancy, sociodemographic, lifestyle, natural environment (green and blues space), and air pollution variables.

Variables	All cohorts (n= 69,683)	ABCD (n= 7,183)	ALSPAC (n= 11,261)	BiB (n= 13,172)	DNBC (n= 10,548)	EDEN (n= 1,417)	GenR (n= 8,180)	INMA (n= 1,973)	KANC (n= 4,041)	MoBa (n= 8,899)	NINFEA (n= 2,149)	RHEA (n= 860)
Pregnancy and maternal												
Maternal age (years) (median, IQR)	29.5 (6.2)	32 (6)	28 (6)	27 (8)	30 (5)	29 (6)	31 (7)	32 (6)	28 (7)	31 (5)	34 (5)	29 (6)
Parity (n, %)												
Multipara	25,029 (46%)	2,567 (46%)	4,419 (55%)	5,681 (59%)	2,087 (29%)	770 (56%)	2,967 (45%)	823 (45%)	2,072 (51%)	2,940 (36%)	484 (25%)	219 (57%)
Nullipara	29,845 (54%)	3,003 (54%)	3,679 (45%)	3,950 (41%)	5,059 (71%)	615 (44%)	3,656 (55%)	1,023 (55%)	1,957 (49%)	5,340 (64%)	1,399 (75%)	164 (43%)
Gestational age (weeks) (median, IQR)	40.2 (1.8)	40 (2)	40 (2)	40 (2)	40 (2)	39 (1)	41 (2)	40 (2)	40 (1)	40 (2)	40 (2)	38 (1)
SGA (n, %)												
Yes	3,977 (6.6%)	328 (5%)	625 (6%)	1,404 (11%)	302 (3%)	104 (7%)	546 (7%)	151 (8%)	–	323 (4 %)	146 (7%)	48 (6%)
No	56,531 (93.4%)	6,221 (95%)	9,512 (94%)	11,135 (89%)	8,987 (97%)	1,262 (93%)	6,986 (93%)	1,746 (92%)	–	7,984 (96%)	1,934 (93%)	764 (94%)
Birth weight (g) (median, IQR)	3,422 (652)	3,460 (670)	3,430 (650)	3,240 (680)	3,570 (650)	3,280 (630)	3,430 (685)	3,275 (570)	3,500 (640)	3,550 (642)	3,270 (580)	3,170 (548)
Sex of the child (n, %)												
Boy	27,944 (51%)	2,793 (50%)	4,127 (51%)	4,920 (51%)	3,687 (51%)	708 (51%)	3,331 (50%)	949 (51%)	2,067 (51%)	4,210 (51%)	954 (51%)	198 (52%)
Girl	26,930 (49%)	2,777 (50%)	3,971 (49%)	4,711 (49%)	3,459 (49%)	677 (49%)	3,292 (50%)	897 (49%)	1,962 (49%)	4,070 (49%)	929 (49%)	185 (48%)
Sociodemographic												
Maternal education level (n, %)												
High	24,513 (48%)	2,975 (53%)	1,134 (14%)	2,656 (27%)	4,991 (70%)	748 (54%)	2,861 (43%)	639 (35%)	2,144 (53%)	7,082 (85%)	1,318 (70%)	109 (28%)
Medium	15,822 (31%)	1,527 (27%)	5,552 (68%)	1,519 (16%)	1,078 (15%)	538 (39%)	3,044 (46%)	756 (41%)	522 (13%)	1,120 (13%)	496 (26%)	192 (50%)
Low	10,510 (21%)	1,068 (19%)	1,412 (17%)	5,456 (57%)	1,077 (15%)	99 (7%)	718 (11%)	451 (24%)	1,363 (34%)	78 (1%)	69 (4%)	82 (22%)
Maternal ethnicity (n, %)												
Western	21,833 (66%)	3,279 (59%)	7,877 (99%)	3,975 (41%)	–	1,163 (99%)	3,772 (57%)	1,767 (96%)	–	–	–	–
Non-Western or mixed	10,948 (33%)	2,260 (41%)	119 (1%)	5,648 (59%)	–	5 (1%)	2,842 (43%)	74 (4%)	–	–	–	–
Area-level deprivation index (n, %)												
Low deprived area	17,992 (33%)	1,218 (22%)	2,382 (29%)	290 (3%)	3,925 (55%)	530 (38%)	998 (15%)	903 (49%)	1,085 (27%)	2,794 (34%)	736 (39%)	187 (49%)
Medium deprived area	12,293 (22%)	592 (11%)	2,748 (34%)	1,193 (12%)	1,766 (25%)	353 (25%)	1,384 (21%)	713 (38%)	2,037 (51%)	2,771 (33%)	641 (33%)	132 (35%)
High deprived area	24,589 (45%)	3,760 (67%)	2,968 (37%)	8,148 (85%)	1,455 (20%)	502 (36%)	4,241 (64%)	230 (12%)	907 (22%)	2,715 (33%)	506 (27%)	64 (16%)
Lifestyle												
Maternal smoking during pregnancy (n, %)												
No	43,953 (80%)	4,961 (89%)	6,062 (75%)	8,036 (83%)	5,111 (72%)	1,013 (73%)	4,924 (74%)	1,268 (69%)	3,736 (93%)	6,866 (83%)	1,732 (92%)	244 (64%)
Yes	10,921 (20%)	609 (11%)	2,036 (25%)	1,595 (17%)	2,035 (28%)	372 (27%)	1,699 (26%)	578 (31%)	293 (7%)	1,414 (17%)	151 (8%)	139 (36%)
Maternal alcohol consumption (n, %)												
No	20,481 (50%)	–	1,585 (22%)	1,018 (35%)	2,907 (41%)	703 (51%)	3,017 (48%)	1,420 (78%)	3,775 (94%)	4,690 (57%)	1,190 (67%)	176 (46%)
Yes	20,586 (50%)	–	5,512 (78%)	1,858 (65%)	4,229 (59%)	682 (49%)	3,267 (52%)	407 (22%)	254 (6%)	3,578 (43%)	596 (33%)	203 (54%)
Natural environment												
Residential surrounding greenspace (median, IQR)												
NDVI 100m	0.37 (0.14)	0.35 (0.15)	0.38 (0.10)	0.40 (0.17)	0.27 (0.13)	0.43 (0.16)	0.36 (0.14)	0.18 (0.14)	0.49 (0.10)	0.52 (0.18)	0.20 (0.12)	0.14 (0.08)

(*continued on next page*)

Table 1 (*continued*)

Variables	All cohorts (n= 69,683)	ABCD (n= 7,183)	ALSPAC (n= 11,261)	BiB (n= 13,172)	DNBC (n= 10,548)	EDEN (n= 1,417)	GenR (n= 8,180)	INMA (n= 1,973)	KANC (n= 4,041)	MoBa (n= 8,899)	NINFEA (n= 2,149)	RHEA (n= 860)
NDVI 300m	0.39 (0.13)	0.37 (0.15)	0.40 (0.09)	0.43 (0.16)	0.30 (0.12)	0.48 (0.16)	0.37 (0.14)	0.23 (0.19)	0.48 (0.08)	0.52 (0.15)	0.23 (0.09)	0.16 (0.09)
NDVI 500m	0.40 (0.13)	0.38 (0.15)	0.41 (0.09)	0.44 (0.17)	0.31 (0.11)	0.50 (0.17)	0.37 (0.15)	0.25 (0.22)	0.49 (0.08)	0.52 (0.15)	0.24 (0.08)	0.16 (0.10)
Residential distance to green space (median m, IQR)	177 (232)	209 (255)	161 (214)	168 (217)	216 (242)	88 (144)	164 (186)	119 (163)	130 (181)	202 (350)	163 (183)	178 (273)
Accessibility to green space (n, %)												
No	18,702 (27%)	2,356 (33%)	2,704 (24%)	3,223 (24%)	3,595 (34%)	179 (13%)	1,722 (21%)	274 (14%)	708 (17%)	3,238 (36%)	435 (20%)	268 (31%)
Yes	50,981 (73%)	4,827 (67%)	8,557 (76%)	9,949 (76%)	6,953 (66%)	1,238 (87%)	6,458 (79%)	1,699 (86%)	3,333 (83%)	5,661 (64%)	1,714 (80%)	592 (69%)
Residential distance to blue space (median m, IQR)	937 (1,000)	148 (186)	1,329 (1,232)	1,603 (1,718)	685 (837)	992 (1,542)	279 (344)	1,103 (2,147)	936 (836)	851 (619)	1,138 (1,448)	1,387 (1,954)
Accessibility to blue space (n, %)												
No	54,116 (78%)	1,307 (12%)	10,500 (93%)	12,829 (97%)	8,604 (81%)	1,186 (84%)	3,825 (47%)	1,478 (75%)	3,598 (89%)	8,096 (91%)	1,916 (89%)	777 (90%)
Yes	15,567 (22%)	5,876 (88%)	761 (7%)	343 (3%)	1,944 (19%)	231 (16%)	4,355 (53%)	495 (25%)	443 (11%)	803 (9%)	233 (11%)	83 (10%)
Air pollution												
NO$_2$ (median µg/m^3, IQR)	30.77 (8.25)	36.53 (8.67)	27.31 (5.07)	23.06 (5.10)	47.26 (7.56)	22.01 (14.18)	38.36 (7.29)	27.21 (24.22)	17.94 (4.60)	20.74 (11.46)	49.33 (19.73)	11.49 (4.37)
PM$_{2.5}$ (median µg/m^3, IQR)	15.57 (2.67)	18.47 (2.25)	13.36 (1.03)	10.42 (1.48)	18.19 (2.95)	17.34 (2.88)	19.66 (3.83)	14.73 (3.04)	23.32 (4.43)	10.79 (2.89)	24.37 (7.34)	14.25 (4.02)

Table 2

Pooled linear regression models for exposure to natural environments and difference in the average of birth weight (g) and corresponding 95% confidence interval (CI). Regression estimates are represented per 1-IQR increase in each continuous indicator of exposure to natural environment and as a 1-category difference in each categorical indicator (accessibility to green space and blue space, No/Yes, reference: No).

	Unadjusted$^{(a)}$		Adjusted $^{(a),(b)}$	
	Beta Coefficient (95 % CI)	**P value**	**Beta Coefficient (95 % CI)**	**P value**
Residential surrounding greenspace				
NDVI 100m buffer	24.1 (18.5, 29.6)	**<0.01**	16.9 (12.0, 21.8)	**<0.01**
NDVI 300m buffer	26.6 (20.9, 32.3)	**<0.01**	17.5 (12.4, 22.6)	**<0.01**
NDVI 500m buffer	28.8 (22.9, 34.6)	**<0.01**	18.5 (13.3, 23.7)	**<0.01**
Residential distance to green space (m)	−9.1 (-14.4, −3.8)	**<0.01**	−8.4 (-13.1, −3.8)	**<0.01**
Accessibility to green space (ref. No)	2.1 (-7.0, 11.3)	0.64	−3.1 (-11.3, 5.1)	0.45
Residential distance to blue space (m)	−5.7 (-10.2, −1.1)	**0.01**	−1.2 (-5.4, 3.00)	0.56
Accessibility to blue space (ref. No)	13.9 (1.8, 26.1)	**0.02**	−6.2 (-16.9, 4.4)	0.25

(a) The models were adjusted for cohort.

(b) The models were further adjusted for: maternal age, parity, gestational age, sex of the child, maternal education level, area-level deprivation index, and maternal smoking during pregnancy.

Table 3

Pooled logistic regression models for exposure to natural environments and SGA represented by odds ratios (OR) and corresponding 95% CI. Regression estimates are represented per 1-IQR increase in each continuous indicator of exposure to natural environment and as a 1-category difference in each categorical indicator (accessibility to green space and blue space, No/Yes, reference: No).

	Unadjusted$^{(a)}$		**Adjusted**$^{(a),(b)}$	
	Odds Ratio (95 % CI)	**P value**	**Odds Ratio (95 % CI)**	**P value**
Residential surrounding greenspace				
NDVI 100m buffer	0.86 (0.82, 0.89)	**<0.01**	0.87 (0.83, 0.92)	**<0.01**
NDVI 300m buffer	0.84 (0.81, 0.88)	**<0.01**	0.87 (0.82, 0.91)	**<0.01**
NDVI 500m buffer	0.83 (0.79, 0.87)	**<0.01**	0.86 (0.81, 0.90)	**<0.01**
Residential distance to green space (m)	1.07 (1.02, 1.11)	**0.02**	1.07 (1.02, 1.12)	**0.02**
Accessibility to green space (ref. No)	1.00 (0.93, 1.08)	0.87	1.03 (0.95, 1.13)	0.38
Residential distance to blue space (m)	1.03 (0.99, 1.06)	0.06	1.03 (0.99, 1.06)	0.06
Accessibility to blue space (ref. No)	0.99 (0.90, 1.10)	0.95	1.02 (0.90, 1.14)	0.74

(a) The models were adjusted for cohort.

(b) The models were further adjusted for: maternal age, parity, maternal education level, area-level deprivation index, and maternal smoking during pregnancy.

from the participant's home was significantly associated with higher birth weights (Yin et al., 2019). In another study in Spain, lower residential distance and greater residential amount of greenspace were associated with higher birth weight only in the participants belonging to the lowest SES groups (Dadvand et al., 2012). Similar to the study by *Dadvand. P et al.,* (Dadvand et al., 2014) we did not observe any association between residential accessibility to green space (i.e., green space greater than 5,000m^2 in a distance of 300m from home) and birth weight.

After adjusting for individual and neighbourhood covariates, we did not observe any association between exposure to blue space during pregnancy and birth weight. Available studies on the association between exposure to blue space and birth outcomes are still scarce, with only one study reporting that living within 500m of a freshwater body was associated with a higher birth weight of 10.1g (95% CI: 2.0g, 18.2g) in fully adjusted models (Glazer et al., 2018). The other studies assessing the association between exposure to blue space and pregnancy did not find strong evidence for an association (Nieuwenhuijsen et al., 2019; Richardson et al., 2018; Abelt and McLafferty, 2017).

In our study, we found that higher residential surrounding greenspace and shorter residential distance to green spaces were associated with a reduced risk of SGA. These findings are in line with those of previous studies from various regions worldwide (Dzhambov et al., 2019; Fong et al., 2018; Lee et al., 2021; Villeneuve et al., 2022). In the Alps (Tyrol region), higher average NDVI in a 500m buffer around the maternal residential address was associated with lower odds for LBW and SGA (Dzhambov et al., 2019). In a population-based study in Canada, an IQR increase in the average NDVI within a buffer of 250m was associated with an odds ratio of 0.94 (95% CI: 0.93, 0.95) for SGA (Villeneuve et al., 2022). In Massachusetts, the United States, residential surrounding greenspace was associated with lower odds of SGA [(0.98 (95% CI: 0.97, 0.99)] (Fong et al., 2018). A recent study (Lee et al., 2021) found associations between first-trimester exposure to residential surrounding greenspace and reduced SGA. In contrast, in a study in Beijing (China), although the authors found an increased z-score for some parameters of fetal growth associated with higher residential greenspace, they did not observe significant associations with birth weight, LBW and SGA (Lin et al., 2020).

We observed attenuation of the associations after further adjusting our analyses for alcohol consumption and ethnicity and a part of this attenuation could be explained by a potential residual SES confounding that was partly surrogated by these variables. In addition, we are aware of two previous studies that also reported an attenuation in the estimates after controlling for these two covariates (Cusack et al., 2017; Yin et al., 2019).

Our findings of the stratified analyses based on SES were consistent with several studies that found greater benefits of greenspace exposure for birth outcomes for the participants from lower SES groups (Agay-Shay et al., 2019; Cusack et al., 2017; Dadvand et al., 2012; Dzhambov et al., 2019; Markevych et al., 2014). People from lower SES may be more prone to benefit from exposure to residential greenspace because of poorer health conditions and fewer opportunities to move (Dadvand et al., 2012; Torres Toda et al., 2020). Contrary to our results, other studies found benefits regardless of SES (Villeneuve et al., 2022) or more benefits for participants belonging to the highest SES groups (Fong et al., 2018; Yin et al., 2019).

We also found indications for stronger associations for the participants living in Northern Europe. This pattern was more evident for exposure to residential surrounding greenspace than accessibility to green space (i.e., living within 300m of public major green space). This study is the first to evaluate the potential effect modification by region of Europe, so we could not compare our findings with other studies. A potential explanation of our findings may rely on multiple causes and might be complex to disentangle. Cultural preferences in the use of natural environments and different vegetation types could be one of the reasons behind them. Moreover, there is less vegetation in Southern cities. Another possibility is a non-linear dose–response function with successive increments of greenspace providing greater increments of protection. In our study, the average of 100m buffer NDVI in Northern Europe was 0.41 (0.13) compared to 0.17 (0.11) in Southern Europe. We are aware of one study using non-linear models to assess greenspace exposure and birth weight (Fong et al., 2018). They found stronger positive associations in the lower range of greenspace (0.25–0.50 NDVI value in 250m buffer). However, their lower range is comparable to our values of NDVI in Northern Europe. Alternatively, it could be due to differences in the built environment that could influence the exposure to the natural environment. Apartment living is more common in Southern Europe (Eurostat. , 2020) than in northern countries. Living in a single-family home would allow more easily interaction with greenspace than living in an apartment.

4.2. Potential underlying mechanisms

Various mechanisms, including improved mental health, promoted physical activity, reduced air pollution, and enhanced social contacts, have been proposed to explain associations of natural environments and health. However, our findings do not support a mediatory role for air pollution, although a formal mediation analysis was not carried out. In other studies, higher exposure to air pollution during pregnancy has been associated with impaired fetal growth (Gong et al., 2022). Air pollutants can enter the systemic circulation through the pulmonary epithelium, induce inflammatory responses, and increase oxidative stress, leading to a loss of placenta function and fetal growth impairment (Hung et al., 2021). Higher residential surrounding greenspace has been associated with lower exposure to air pollution among pregnant women (Dadvand et al., 2012). In the literature, some evidence for a mediatory role of air pollution can be found in several studies (Dadvand et al., 2012; Laurent et al., 2019; Lee et al., 2021). We could not explore other potential mechanisms in our study, but each indicator of exposure to the natural environment could be more relevant to different mechanisms. For example, urban trees may better reflect a potential reduction in air pollution and noise, public parks may represent enhanced physical activity and social contact, and surrounding greenspace at home may relate to stress recovery and attention restoration. Lakes and rivers may promote physical activity, whereas a promenade may enhance stress recovery and physical activity.

4.3. Limitations

Our study faced some limitations that warrant consideration. First, we assessed the exposure for the residential address at delivery. Therefore, there could have been exposure misclassification for the participants who have moved during pregnancy. However, given that a large proportion did not move during pregnancy, (Pedersen et al., 2013) the effect of such exposure misclassification could have been minimal. Although we controlled our models for neighbourhood and household SES variables, the strong confounding by such factors, due to families with higher SES tend to have healthier lifestyles, such as not smoking in pregnancy, and hence healthier infants that those with lower SES, and these families tend to live in affluent neighbourhoods, meant that we cannot rule out some residual confounding. Our findings indicated that exposure to residential greenspace was more beneficial among low SES families, implying those high SES families may already be taking advantage of their SES regardless of the amount of residential greenspace. Gestational age at birth was assessed under the recommendations of the Developing a Child Cohort Research Strategy for Europe (CHICOS) project (Stoltenberg et al., 2022), using each cohort's best clinical judgement. We prioritised ultrasound measurements, but we also relied on the last menstrual period and maternal report, if necessary. Misclassification of gestational age might bias our findings in either direction depending on if it was systematic in relation to birth weight (and hence to derivation of SGA) and further in relation to the green/blue-space exposures. Although NDVI offers a standardised way to measure greenspace across different regions, it cannot differentiate vegetation types. Exposure to different green space types (i.e., grass, trees, shrubs, and flowers) could be relevant for underlying mechanisms. For instance, a study in Denmark explored how different areas with several vegetation types could promote more the psychological restoration of the participants (Stigsdotter et al., 2017). They found that participants preferred areas of beech forest over pine forest for restoration, and serene forest, rich in species, and with a refuge feeling (Stigsdotter et al., 2017). Moreover, our measures of exposure to natural environments did not consider quality aspects of the environments. Quality characteristics such as aesthetics, amenities, biodiversity, and safety, could be relevant for our evaluated associations. For example, participants with unsafe or impassable green spaces near their homes may not visit them regardless of the proximity of these spaces. Exposure to different blue space types (i.e., rivers, canals, sea, or lakes) could also be relevant for determining underlying mechanisms. For instance, different blue space types could be promoting different amounts of psychological restoration. A previous study by Pearson et al., found that visibility of oceanic blue spaces had a larger and positive association with lower psychological distress than inland blue spaces. However, the study did not find associations between visibility of green space and lower psychological distress, and they theorised that blue space may be more significant in their study area than green space due to the country's island geography (Hipp et al., 2014). Furthermore, different blue space types could be disadvantageous for social cohesion. Hipp et al., found that increasing the length of a river had a negative association on social cohesion. To finalise, further replication of this study and evidence of causality is needed.

4.4. Conclusions

We found that greater residential surrounding greenspace and shorter residential distance to green spaces during pregnancy were associated with higher birth weight and lower risk for SGA in nine countries across Europe. We observed indications for stronger associations among participants from lower SES and those living in Northern Europe. Findings for accessibility to green space, distance to blue space, and accessibility to blue space were inconclusive. We recommend that future studies improve the exposure assessment by, for example, including data on the quality of natural environments and the use of these spaces while shedding light on the underlying mechanisms. Continued allocation of accessible natural environments in our cities could benefit our children's health from before birth and onwards and should be considered by urban designers.

CRediT authorship contribution statement

Maria Torres Toda: Conceptualization, Investigation, Methodology, Formal analysis, Visualization, Writing – original draft. **Demetris Avraam:** Data curation, Formal analysis, Methodology, Software, Writing – review & editing. **Timothy James Cadman:** Formal analysis, Project administration, Writing – review & editing. **Serena Fossati:** Project administration, Writing – review & editing. **Montserrat De Castro:** Data curation, Visualization, Methodology, Writing – review & editing. **Audrius Dedele:** Funding acquisition, Writing – review & editing. **Geoffrey Donovan:** Conceptualization, Writing – review & editing. **Ahmed Elhakeem:** Funding acquisition, Project administration, Writing – review & editing. **Marisa Estarlich:** Funding acquisition, Project administration, Writing – review & editing. **Amanda Fernandes:** Formal analysis, Methodology, Validation, Writing – review & editing. **Romy Gonçalves:** Writing – review & editing. **Regina Grazuleviciene:** Funding acquisition, Writing – review & editing. **Jennifer R. Harris:** Funding acquisition, Project administration, Writing – review & editing. **Margreet W Harskamp-van Ginkel:** Funding acquisition, Project administration, Writing – review & editing. **Barbara Heude:** Funding acquisition, Project administration, Writing – review & editing. **Jesús Ibarluzea:** Funding acquisition, Project administration, Writing – review & editing. **Carmen Iñiguez:** Funding acquisition, Project administration, Writing – review & editing. **Vincent WV Jaddoe:** Funding acquisition, Project administration, Writing – review & editing. **Deborah Lawlor:** Funding acquisition, Project administration, Writing – review & editing. **Aitana Lertxundi:** Funding acquisition, Project administration, Writing – review & editing. **Johanna Lepeule:** Funding acquisition, Project administration, Writing – review & editing. **Rosemary McEachan:** Funding acquisition, Project administration, Writing – review & editing. **Giovenale Moirano:** Funding acquisition, Project administration, Writing – review & editing. **Johanna LT Nader:** Project administration, Writing – review & editing. **Anne-Marie Nybo Andersen:** Funding acquisition, Project administration, Writing – review & editing. **Marie Pedersen:** Funding acquisition, Project administration, Writing – review & editing. **Costanza Pizzi:** Funding acquisition, Project administration, Writing – review & editing. **Theano Roumeliotaki:** Data curation, Software, Writing – review & editing. **Susana Santos:** Project administration, Writing – review & editing. **Jordi Sunyer:** Funding acquisition, Project administration, Writing – review & editing. **Tiffany Yang:** Project administration, Writing – review & editing. **Marina Vafeiadi:** Funding acquisition, Project administration, Writing – review & editing. **Tanja GM Vrijkotte:** Funding acquisition, Project administration, Writing – review & editing. **Mark Nieuwenhuijsen:** Funding acquisition, Project administration, Writing – review & editing. **Martine Vrijheid:** Funding acquisition, Project administration, Conceptualization, Writing – review & editing. **Maria Foraster:** Funding acquisition, Project administration, Investigation, Conceptualization, Validation, Supervision, Writing – review & editing. **Payam Dadvand:** Funding acquisition, Project administration, Investigation, Conceptualization, Validation, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary material

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