HHS Public Access

Author manuscript

Environ Res. Author manuscript; available in PMC 2024 January 01.

Published in final edited form as:

Environ Res. 2023 January 01; 216(Pt 3): 114760. doi:10.1016/j.envres.2022.114760.

Assessing associations between residential proximity to greenspace and birth defects in the National Birth Defects Prevention Study

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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.

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Kari Weber**: Conceptualization, Methodology, Software, Writing-original draft, Project administration.**Wei Yang**: Conceptualization, Methodology, Software, Formal analysis, Writing-review and editing.**Suzan Carmichael**: Conceptualization, Resources, Writing-review and editing.**R. Thomas Collins**: Conceptualization, Writing-review and editing.**Thomas Luben**: Conceptualization, Writing-review and editing.**Tania Desrosiers**: Conceptualization, Resources, Writing-review and editing.**Tabassum Insaf**: Conceptualization, Resources, Writing-review and editing.**Mimi Le**: Conceptualization, Resources, Writing-review and editing.**Shannon Evans**: Conceptualization, Resources, Writing-review and editing.**Paul Romitti**: Conceptualization, Resources, Writing-review and editing.**Mahsa Yazdy**: Conceptualization, Resources, Writing-review and editing.**Wendy Nembhard**: Conceptualization, Resources, Writing-review and editing.**Gary Shaw**: Conceptualization, Resources, Writing-review and editing.**NBDPS**: Investigation, Resources, Funding acquisition.**

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.114760.

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Abstract

Background: Residential proximity to greenspace is associated with various health outcomes.

Objectives: We estimated associations between maternal residential proximity to greenspace (based on an index of vegetation) and selected structural birth defects, including effect modification by neighborhood-level factors.

Methods: Data were from the National Birth Defects Prevention Study (1997–2011) and included 19,065 infants with at least one eligible birth defect (cases) and 8925 without birth defects (controls) from eight Centers throughout the United States. Maternal participants reported their addresses throughout pregnancy. Each address was systematically geocoded and residences around conception were linked to greenspace, US Census, and US Department of Agriculture data. Greenspace was estimated using the normalized difference vegetation index (NDVI); average maximum NDVI was estimated within 100 m and 500 m concentric buffers surrounding geocoded addresses to estimate residential NDVI. We used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals comparing those in the highest and lowest quartiles of residential NDVI and stratifying by rural/urban residence and neighborhood median income.

Results: After multivariable adjustment, for the 500 m buffer, inverse associations were observed for tetralogy of Fallot, secundum atrial septal defects, anencephaly, anotia/microtia, cleft lip ± cleft palate, transverse limb deficiency, and omphalocele, (aORs: 0.54–0.86). Results were similar for 100 m buffer analyses and similar patterns were observed for other defects, though results were not significant. Significant heterogeneity was observed after stratification by rural/urban for hypoplastic left heart, coarctation of the aorta, and cleft palate, with inverse associations only among participants residing in rural areas. Stratification by median income showed heterogeneity for atrioventricular and secundum atrial septal defects, anencephaly, and anorectal atresia, with inverse associations only among participants residing in a high-income neighborhood (aORs: 0.45–0.81).

Discussion: Our results suggest that perinatal residential proximity to more greenspace may contribute to a reduced risk of certain birth defects, especially among those living in rural or high-income neighborhoods.

Keywords

Greenspace; Birth defects; Neighborhood; NDVI; Pregnancy

1. Introduction

Structural birth defects are a leading cause of infant death (Parker et al., 2010). While there are some chromosomal syndromes or mono-genic causes, very little is known about the

etiologies of birth defects. It is probable that most human birth defects have multiple and complex causes. As such, it is necessary to seek novel measures to capture the combinations of exposures experienced by pregnant women and the developing fetus to improve our understanding of the etiology of birth defects.

One relatively novel area of environmental research that may capture a combination of exposures is residential proximity to greenspace, such as parks, trees, or other types of vegetation. Greenspace, owing to its numerous health related qualities, has been inversely associated with a variety of adverse pregnancy outcomes, including preterm birth and infant birth weight (Twohig-Bennett and Jones, 2018); and we previously observed inverse associations between greater exposure to greenspace and preeclampsia (Weber et al., 2020). Some aspects potentially contributing to the benefits of greenspace include decreased exposure to noise, heat, and air pollution, more physical activity, and reduced maternal stress (Markevych et al., 2017). These same aspects have also been associated with certain birth defects, although not consistently (Watkins et al., 2003; Ren et al., 2018; Haghighi et al., 2021; Carmichael et al., 2017). Studies of these exposures often evaluate each one individually without taking other environmental co-exposures into account. Assessing greenspace may estimate the effects of combinations of these exposures or how they may modify each other. In addition to the importance of investigating greenspace in combination with other environmental exposures, studies that also investigate manifold lifestyle and demographic factors with such environmental exposures are lacking.

We analyzed greenspace, alone and in combination with other exposures such as neighborhood and maternal lifestyle factors, and their associations with select birth defect phenotypes. To our knowledge, this is the first study to examine these associations. This work was performed using one of the largest population-based, case-control studies of birth defects ever conducted in the United States (US), the National Birth Defects Prevention Study (NBDPS).

2. MATERIALS and METHODS

This study included participants from the Arkansas (AR), California (CA), Georgia (GA), Iowa (IA), Massachusetts (MA), North Carolina (NC), New York (NY), and Texas (TX) Centers of the NBDPS for which detailed methods have been described (Reefhuis et al., 2015). NBDPS is a multi-center, case-control study of over 30 major birth defects for births with date of delivery from October 1, 1997 to estimated date of delivery December 31, 2011. Medical records of infants and fetuses diagnosed with a birth defect were identified at each Center by trained staff and entered into the NBDPS database. Cases in the database were reviewed by clinical geneticists with birth defect expertise, classified as eligible for NBDPS according to defect-specific criteria and further classified as isolated, multiple, or complex. (Rasmussen et al., 2003). Case infants with a documented chromosomal abnormality were ineligible. Approximately 100 live-born control infants without a birth defect were randomly selected per year by each Center in the same geographic areas as case infants using vital records (AR [2000–2011], GA [2001–2011], IA, MA, NC) or birth hospitals (AR [1997–1999], CA, GA [1997–2000], NY, TX).

Mothers of case and control infants were invited to complete a standardized questionnaire via a computer-assisted telephone interview. Interviews were conducted in English or Spanish and took place from 6 weeks to 24 months after the estimated delivery date. Among eligible case and control mothers, participation from the Centers included in this analysis was 66% and 63%, respectively. Participants answered questions regarding maternal and paternal demographics, maternal behaviors, health and medical history, occupation, and dietary intake. Median time from date of delivery to interview was 10 months for case infants (interquartile range, 8 months) and 7 months for control infants (interquartile range, 7 months). The Institutional Review Board of each Center provided approval for NBDPS, and participants provided verbal consent to participate in the interview.

As part of the questionnaire, participants were asked to report complete residential information from 3 months before conception (B3–B1) through the end of their pregnancy (P1–P9). All addresses were geocoded by the Agency for Toxic Substances and Disease Registry's Geographic Research, Analysis and Services Program, and geocodes were returned to their respective Centers where they were linked with the full participant records (Reefhuis et al., 2015).

Residential greenspace was estimated for each geocoded address using the normalized difference vegetation index (NDVI) and proximity was estimated by calculating the average maximum NDVI within 100 m and 500 m concentric buffers surrounding each participant's address. NDVI is calculated by normalizing the difference between the visible and near-infrared region (NIR) wavelengths of sunlight reflected by the Earth's surface.

$$NDVI = \frac{NIR - Red}{NIR + Red}$$

The values range from −1 to 1 with values closer to 1 corresponding to denser vegetation or greenness (Tucker, 1978). According to the U.S. Geological Survey, landscape such as sand or rock would have NDVI values close to 0, values below 0 correspond to water, and a forest at peak vegetation would have NDVI values between approximately 0.6 to 0.9.

NDVI was estimated using Google Earth Engine images over 3-year periods for efficiency: 1997–1999, 2000–2002, 2003–2005, 2006–2008, 2009–2011 (Gorelick et al., 2017). As cloud cover and resulting shadows can decrease estimation accuracy, and seasonal changes may cause greenspaces, such as agriculture or tree canopy, to not be "green", cloud-masked images were used to determine maximum NDVI for each pixel by determining the "greenest" image. This image would be from the point during the time-period with peak vegetation, most likely during late spring or summer. Maximum NDVI images were created at 30 m spatial resolution using Landsat 5 images (Collection 1, Tier 1 top of atmosphere reflectance) for years 1997–1999, 2003–2011 and Landsat 7 images (Collection 1, Tier 1 top of atmosphere reflectance) for years 2000–2002 courtesy of the U.S. Geological Survey (Williams et al., 2006).

For each study center and time-period, images from Google Earth Engine were linked with geocoded participant addresses using ArcGIS (ESRI, Release 10.8.1. Redlands, CA). The

time-period image used was based on the estimated date of conception which would be during the etiologic time window rather than at the time of delivery. NDVI values were assigned to each participant based on the address they resided at for greater than 2/3, or more than 67 days of the B1–P2 exposure window, as this is believed to be the relevant etiologic exposure window for the birth defects included in this analysis. Quartiles of NDVI were determined among control estimates across all centers for the 100 m and 500 m residential buffers.

We included as potential cases, infants affected by major birth defects of the following systems: cardiovascular, musculoskeletal, digestive, genitourinary, neural tube, ear, craniofacial, and respiratory defects. Birth defect phenotypes within system groupings were analyzed individually. Phenotypes were only included if they contained at least 50 “exposed” infants (those in the highest quartile of NDVI (highest vegetation)). Because hypospadias is only diagnosed in male infants, analyses for hypospadias were restricted to male control infants. Women who reported having pregestational diabetes were excluded from this analysis given the association between diabetes and birth defects (Correa et al., 2008). Sensitivity analyses were done restricting the dataset to simple isolated congenital heart defects and isolated non-cardiac defects to exclude cases with accompanying malformations (with at least one additional, unrelated major malformation). The term “unrelated” refers to defects in different body parts or systems and not a part of a sequence (Rasmussen et al., 2003; Botto et al., 2007).

Distributions of maternal and infant characteristics were determined among cases and controls. Using logistic regression, odds ratios (OR) and 95% confidence intervals (CI) were estimated comparing those in the highest quartiles of residential NDVI to the lowest quartile separately for each birth defect phenotype and residential buffer. Given the large amount of data and the small range of NDVI values, only results comparing the highest to lowest quartile are presented. Analyses were adjusted for maternal variables believed *a priori* to be potential confounders: age at delivery, race/ethnicity/nativity (White non-Hispanic, Hispanic Foreign-Born, Hispanic US-Born, Black non-Hispanic, Other), season of conception (winter, spring, summer, fall), and periconceptional (B1–P2) lifestyle factors - use of a multivitamin containing folic acid (yes/no), cigarette smoking (yes/no), alcohol intake (yes/no), employed during pregnancy (yes/no).

Potential effect modifiers were statistically evaluated by adding an interaction between NDVI and each factor to the multivariable logistic regression model and statistical significance was evaluated using the Wald test. Analyses were stratified by whether the participant resided in a census block with a median annual income greater than the Center-specific median (high-income). These data were derived from the 2000 US Census (Manson et al., 2021) and medians used were Center-specific due to variability among the Centers. Additional neighborhood socioeconomic variables were explored such as percentage of residents living below the federal poverty level but results were similar to median income analyses and thus are not reported. Residence in “rural” or “urban” areas was derived using the 2000 Rural-Urban Commuting Area Codes from the US Department of Agriculture, Economic Research Service data. Additional stratified analyses included stratification by pre-pregnancy maternal obesity based on self-reported height and weight

(≥30 kg/m^2/<30 kg/m^2), and women who reported “high stress”, indicated by answering “yes” to experiencing three or more stressful life events such as a death of someone close, legal/-financial problems, or being the victim of violence or crime (see Appendix A for the full list of questions). Information on major life stressors was available for years 2006–2011 and each previously described analysis was performed on this subset of data.

To assess potential quality control issues, analyses were done excluding participants with less than 25% of the possible pixels calculated from NDVI images. The maximum number of pixels available for calculation of maximum average NDVI was 50 for the 100 m buffer and 1200 for the 500 m buffer resulting in exclusion of about 1% and 10% of the participants, respectively. All analyses were completed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

Of the 37,091 interviewed participants, there were 35,309 (95% of cases and 96% of controls) with valid geocoded addresses. Residential greenspace was successfully estimated for 34,777 (98% of cases and 99% of controls). Of those with a residential greenspace estimation, 33,254 (94% among both cases and controls) had a greenspace estimation for the relevant exposure window (B1–P2) and 32,672 (92% of cases and 93% of controls) lived at the addresses for greater than two-thirds of the relevant exposure window. About 6% of case mothers and 5.7% of control mothers were excluded because they reported living at an NDVI-measured address but did not report move in/out dates or reported dates were out of B1–P2 exposure window. We further excluded 684 case and 68 control infants whose mothers had pregestational diabetes. The dataset included 22,995 cases (92%) and 8925 controls (93%).

NDVI values for control infants across all study centers ranged from 0.04 to 0.83 for 100 m and 0 to 0.82 for 500 m residential buffers, respectively (Supplemental Table 1). The highest quartile of NDVI for the 100 m buffer was >0.61 and for the 500 m buffer was >0.64, as determined among controls. Inclusion of defects with at least 50 “exposed” cases resulted in 19,065 case infants throughout the phenotypic subsets in the final analytic dataset, including congenital heart defects, neural tube defects, clefts, abdominal defects, and other defects.

Characteristics of cases and controls did not substantially differ. There were slightly more reports of maternal periconceptional cigarette smoking, conceptions during the winter months, and pre-pregnancy obesity among case compared to control mothers (Table 1).

Associations between greenspace and congenital heart and non-cardiac defects are presented in Table 2. Inverse associations (i.e., more greenspace with lower odds) were observed for tetralogy of Fallot, total anomalous pulmonary venous return (TAPVR), and secundum atrial septal defects, although the associations were less precise for TAPVR after adjustment. For non-cardiac defects, results were similar for the 100 m and 500 m buffers. Inverse associations were observed for anencephaly, anotia/microtia, cleft lip ± cleft palate, transverse limb deficiency, and omphalocele, before and after adjustment. There were also suggestive associations observed between greenspace and spina bifida, diaphragmatic

hernia, and gastroschisis. Conversely, there were higher odds of coarctation of the aorta, craniosynostosis, hypospadias and esophageal atresia for those living in greener areas; however, these results were attenuated after adjustment and no longer statistically precise.

After stratification by whether each mother lived in a “rural” or “urban” area, the same patterns remained for tetralogy of Fallot, TAPVR, and secundum atrial septal defect. Significant heterogeneity was observed in the 500 m buffer for hypoplastic left heart and coarctation of aorta with inverse associations between greenspace and the respective defect observed only among those living in a rural area (Table 3). For the non-cardiac defects (Table 3), there was suggestive heterogeneity with stronger inverse associations among those in rural areas for cleft lip ± cleft palate, diaphragmatic hernia, and omphalocele. There was significant heterogeneity observed only in the 500 m buffer for cleft palate where the inverse association was observed among those in rural areas and for anencephaly in the 100 m buffer, though the inverse association was observed for urban areas.

The income distribution across Centers ranged from a median of approximately $27,000 to $55,500 per year (Supplemental Table 2). After stratification for residence in a neighborhood with a median income above or below the overall Center-specific median, significant heterogeneity was observed for the association between greenspace and atrioventricular septal defects and secundum atrial septal defects, anencephaly, and anorectal atresia. The inverse association was among those in high-income neighborhoods. Similarly, suggestive heterogeneity was observed for aortic stenosis in the 500 m buffer, and anotia/microtia, and cleft lip ± cleft palate in the 100 m buffer (p-value < 0.1) with an inverse association among those in a high-income neighborhood (Table 4).

Heterogeneity was also observed between greenspace and trans-position of the great vessels in the 100 m buffer with an inverse association among women reporting being obese pre-pregnancy. For the non-cardiac defects, for greenspace in a 500 m buffer, heterogeneity was observed for cleft palate (Table 5).

Restricting to only isolated cases as described above, results were very similar to those using the full sample for congenital heart defects and non-cardiac defects though less precise due to the smaller sample size (Supplemental Tables 3 and 4).

Stratification by life stressors yielded inconsistent results with higher odds observed for only some defects and greenspace proximity among those reporting “high stress” (Supplemental Table 5). Additional analyses for quality control restricting to participants with NDVI for over 25% of available pixels in their residential buffers yielded similar results to the main analysis (results not shown).

4. Discussion

In this analysis of one of the largest population-based, case-control study of major birth defects in the US, we observed inverse associations between greenspace and many of the selected defects, as well as some heterogeneity by the additional factors explored. For congenital heart defects, observed associations reflected reduced odds for tetralogy of Fallot and secundum atrial septal defects. After stratification by residential area

factors, heterogeneity was observed for certain defects and additional inverse associations were generally observed among participants residing in rural areas and in high-income neighborhoods. For non-cardiac defects, residential greenspace was associated with reduced odds of anencephaly, anotia/microtia, cleft lip ± cleft palate, transverse limb deficiencies, and omphalocele, generally in both the 100 m and 500 m buffers. Similar to findings for the heart defects, where heterogeneity was observed, the pattern tended to be consistent among those residing in rural and high-income neighborhoods. For the few defect phenotypes where heterogeneity was observed by pre-pregnancy obesity, the inverse associations tended to be among those who were obese.

Analyses of different buffers and stratified analyses were performed to investigate what might be contributing to the observed benefits of greenspace. For example, a previous study estimated the average speed pregnant women walk and a median time of 37 min per day based on their sample and determined that 500 m would be a reasonable distance for a pregnant woman to travel on foot (Dadvand et al., 2012). If estimates were notably different between the 100 m and 500 m buffers, it could indicate that use of a walkable neighborhood park offered the greatest benefit or vice versa. In this study, estimates were similar which may indicate multiple explanations for the observed benefit.

One such potential benefit is that more greenspace within a 100 m buffer of one's residence may indicate more tree canopy or being further from major roadways which could result in less noise and air pollution. Both noise and air pollution have been observed to be associated with birth defects, although results are inconsistent. A systematic review of noise from aircraft, road traffic and birth outcomes reported suggestive evidence of an association between noise from aircraft and birth defects (Nieuwenhuijsen et al., 2017). Studies have also observed associations between higher exposure to air pollutants ($PM_{2.5}$, PM_{10} and NO_2) and various birth defect phenotypes (Ren et al., 2018; Hu et al., 2020; Choi et al., 2019; Stingone et al., 2014). As noise and air pollution often co-occur with each other as well as other environmental and socioeconomic factors, our initial greenspace results may suggest that more work examining greenspace with these co-exposures and birth defects is warranted. Such underlying factors may also contribute to the explanation of our results observed in rural versus urban areas if the participants were less exposed to major sources of noise and pollution like airports and major roadways.

A possible mechanism that may relate to both residential and community greenspace is extreme heat mitigation. Greenness may alleviate extreme heat through tree canopy providing shade and by providing protection against urban heat islands (Tiwari et al., 2021). Some studies have reported associations between extreme heat and certain birth defect phenotypes (Haghighi et al., 2021; Van Zutphen et al., 2012; Stingone et al., 2019; Simmons et al., 2022; Lin et al., 2018). Like noise and air pollution, our results suggest that examining extreme heat and potential risk abatement through greenspace is justified.

Biologically, greenspace and its attendant co-exposures are a plausible new direction to determine the etiology and potential prevention of birth defects. Many lifestyle and environmental exposures may cause oxidative stress which may, in turn, cause abnormal placental development (Al-Gubory, 2014). Certain defects for which we observed

associations with greenspace, such as gastroschisis, limb defects, and some congenital heart defects, have been proposed to have a vascular origin through possible hypoxia, vasoconstriction, or vascular disruption (Sadler and Rasmussen, 2010). Certain heart defects have also been hypothesized to be caused by placental dysfunction and abnormal angiogenesis (Sliwa and Mebazaa, 2014). Similar mechanisms have been proposed for preeclampsia, which we have observed to be inversely associated with greenspace (Weber et al., 2020) and to be associated with certain birth defects (Weber et al., 2018). Vascular mechanisms may jointly explain both birth outcomes and help explain potential benefits of greenspaces which have been observed to be associated with lower blood pressure, reduced incidence of stroke and cardiovascular mortality in other studies (Twohig-Bennett and Jones, 2018).

A potential decrease in obesity due to an increased opportunity for physical activity is a major proposed benefit of neighborhood greenspace (e.g., parks, trails). Maternal obesity has been associated with various birth defects including spina bifida, omphalocele, and certain heart defects (Watkins et al., 2003). In a review of greenspace and obesity, the majority of studies reported an association between greenspace and less obesity or obesity-related health outcomes (Lachowycz and Jones, 2011). However, these findings were not all consistent and use of greenspace may be a factor in those inconsistencies. One study, for example, observed that individuals in lower SES neighborhoods were less likely to use recreational facilities compared to higher SES neighborhoods despite being closer to the facilities (Giles-Corti and Donovan, 2002).

As we observed, the findings suggesting greenspace may decrease the risks of select birth defects were among those living in “high-income” neighborhoods. Greenspace quality and safety may be a concern in “low-income” neighborhoods and prevent their use or negate their benefits. One study in Portugal found that greenspaces in more deprived areas had more damage, fewer amenities, and more safety concerns (Hoffimann et al., 2017) and a study in Baltimore observed lower park quality in lower income neighborhoods (Engelberg et al., 2016) which may lead to less utilization or fewer benefits. A study of gender differences in park use in Los Angeles found women in high-poverty neighborhoods were less likely to use parks than their male counterparts (Derose et al., 2018). Future work may help inform if greenspace promotes physical activity in pregnant women and if mediation through physical activity may explain part of our observed associations between greenspace and birth defects.

Our analysis of stress in relation to greenspace and birth defects yielded some results counter to our hypothesis. However, these analyses were done on a subset of data with less power and were also based on major life stressors such as the death of a loved one, serious legal issues, or being the victim of abuse. While this information is relevant, these questions do not necessarily characterize chronic stress or other periods of acute stress. One study found urban parks to generally improve “wellbeing” (Larson et al., 2016) so greenspace may provide a more general benefit that does not align with major stressor abatement.

This study has many strengths. To the best of our knowledge, this is the first study to explore the potential association between greenspace and numerous birth defect phenotypes.

The NBDPS is one of the largest population-based, case-control studies of birth defects in the US with detailed demographic, health, and lifestyle data available. The inclusion of multiple states provided a diverse study population from various regions. The combination of urban and rural ascertainment locations provides a unique opportunity to parse out beneficial contributions that may be gleaned from types of greenspaces like an urban park for recreation versus a forested area to reduce noise pollution. Specific residential address data for the beginning of pregnancy provided the opportunity to estimate proximity to greenspace, the ability to link with other sources like the US Census and USDA, and the ability to center our analyses on the critically relevant time-period for the development of birth defects. Availability of data from sources beyond NBDPS allowed analyses of heterogeneity by relevant neighborhood and residential area variables which may help estimate type, utilization, and potential benefits of greenspaces.

This study also has some limitations. Our estimation of greenspace was based solely on NDVI and therefore cannot specifically differentiate between types of greenspace such as a park or an agricultural field. However, in this initial look at birth defects, the ability to stratify our data by urban and rural areas allowed us to estimate greenspace type and we aimed to gain additional insight by looking at different buffers and stratifying by other variables that could indicate the beneficial types of greenspace. Now that we have observed associations that support our hypotheses regarding the benefits of greenspace in birth defects, future work can explore other measures such as proximity to specific types of land use (i.e., parks) or residential tree canopy. Information for maternal physical activity was only available in this dataset from 2009 to 2011 and due to the smaller sample size, estimates could not be calculated or were highly imprecise. Future work can incorporate physical activity as more data become available and associations between access to greenspaces and physical activity in this population can be explored. There may also be some exposure misclassification given that NDVI was estimated for the participants' residences, and they may spend much of their time away from their homes. However, we would not expect this to differ between cases and controls, resulting in attenuation of any results. We also did not do separate estimates for each year, but it is unlikely that significant changes in greenness would occur between two 3-year time-periods based on the ranges of NDVI we observed.

Overall, our results support the hypothesis that greenspace is beneficial and may help reduce the risk of certain birth defects, potentially through multiple pathways. The financial toll of birth defects is substantial, with hospital costs for common birth defects like congenital heart defects estimated to be $6 billion annually (Arth et al., 2017). Investigation of potential interventions, such as additional or higher quality neighborhood greenspace or additional tree canopy, that are both cost-effective and equitable is a worthwhile endeavor. Given the great societal costs of birth defects and that there are few known causes, future work may help inform the types of greenspace that are most beneficial and determine their potential as cost-effective prevention measures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This project was supported through Centers for Disease Control and Prevention (CDC) cooperative agreements under PA #96043, PA #02081, FOA #DD09-001, FOA #DD13-003, and NOFO #DD18-001 to the Centers for Birth Defects Research and Prevention participating in the National Birth Defects Prevention Study (NBDPS) and/or the Birth Defects Study To Evaluate Pregnancy exposureS (BD-STEPS). This project was supported by the CDC's Environmental Public Health and Emergency Response Program, NYS Unique Federal Award Number NUE1EH001341 (NYS Environmental Public Health Tracking Network Maintenance and Enhancement to Accommodate Sub-County Indicators). The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the New York State Department of Health. The research described in this article has been reviewed by the Center for Public Health and Environmental Assessment, US EPA, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Agency, nor does the mention of trade names of commercial products constitute endorsement or recommendation for use.

Data sharing

The datasets generated and/or analyzed during the current study are not publicly available to guarantee the confidentiality of participants and to ensure that data are used in accordance with their consented purposes but are available from the corresponding author on reasonable request. The study questionnaires and process for accessing the data used in this study are described at https://www.cdc.gov/ncbddd/birthdefects/nbdps-public-access-procedures.html. The code book and analytic code may be made available upon request.

Data availability

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Table 1

Descriptive characteristics of cases of selected birth defects and non-malformed controls, National Birth Defects Prevention Study, 1997–2011.

	Cases(n = 19,065)	Controls (n = 8925)
	n (%)[a]	*n* (%)[a]
Maternal race/ethnicity		
White non-Hispanic	11,098 (58.2)	5032 (56.4)
Hispanic foreign-born	2563 (13.4)	1226 (13.7)
Hispanic US-born	2036 (10.7)	930 (10.4)
Black non-Hispanic	1925 (10.1)	1046 (11.7)
Other	1282 (6.7)	594 (6.7)
Missing	161 (0.8)	97 (1.1)
Maternal education		
<High school	3324 (17.4)	1502 (16.8)
High school graduate	4780 (25.1)	2092 (23.4)
College graduate	10,605 (55.6)	5152 (57.7)
Missing	356 (1.9)	179 (2.0)
Number of previous pregnancies that ended in a live birth		
0	8278 (43.4)	3583 (40.2)
1	5961 (31.3)	2952 (33.1)
2	2999 (15.7)	1546 (17.3)
>2	1810 (9.5)	836 (9.4)
Missing	17 (<0.1)	8 (<0.1)
Birth status		
Live birth	18,339 (96.2)	8923 (100)
Stillbirth (Fetal Death ≥ 20 Weeks)	315 (1.7)	-
Induced Abortion	394 (2.1)	-
Missing	17 (<0.1)	2 (<0.1)
Maternal intake of folic acid-containing vitamin supplements[b]		
No	4281 (22.5)	2021 (22.6)
Yes	14,445 (75.8)	6746 (75.6)
Missing	339 (1.8)	158 (1.8)
Maternal cigarette smoking[b]		
No	14,874 (78.0)	7140 (80.0)
Yes	3899 (20.5)	1640 (18.4)
Missing	292 (1.5)	145 (1.6)
Maternal alcohol intake[b]		
No	11,503 (60.3)	5333 (59.8)
Yes	7209 (37.8)	3420 (38.3)
Missing	353 (1.9)	172 (1.9)
Maternal occupation[c]		

	Cases(n = 19,065)	Controls (n = 8925)
	***n* (%)[a]**	***n* (%)[a]**
No	6161 (32.3)	2841 (31.8)
Yes	12,587 (66.0)	5916 (66.3)
Missing	317 (1.7)	168 (1.9)
Season of conception		
Winter (Dec-Feb)	5003 (26.2)	2199 (24.6)
Spring (March-May)	4714 (24.7)	2224 (24.9)
Summer (June-Aug)	4595 (24.1)	2219 (24.9)
Fall (Sep-Nov)	4753 (24.9)	2283 (25.6)
Pre-pregnancy body mass index (kg/m^2)		
Non obese <30	14,543 (76.3)	6930 (77.7)
Obese ≥30	3679 (19.3)	1591 (17.8)
Missing	843 (4.4)	404 (4.5)
Residing in rural or urban area [d]		
Urban	15,256 (80.0)	7162 (80.2)
Rural	3770 (19.8)	1739 (19.5)
Missing	39 (0.2)	24 (0.3)
Household annual income below Center-specific median [e]		
No	9571 (50.2)	4455 (49.9)
Yes	9449 (49.6)	4443 (49.8)
Missing	45 (0.2)	27 (0.3)
Maternal stress score[f](2006–2011)		
N	6744	3372
0–2 “low stress”	5787 (85.8)	2965 (87.9)
3–7 “high stress”	957 (14.2)	407 (12.1)
Maternal age at delivery, years (Mean ± SD)	27.75 ± 6.29	27.75 ± 6.13
NDVI mean 100m buffer (Median, 25th – 75th percentile)	0.52 (0.40–0.61)	0.53 (0.41–0.61)
NDVI mean 500m buffer (Median, 25th – 75th percentile)	0.55 (0.44–0.63)	0.56 (0.45–0.64)

NDVI: normalized difference vegetation index; SD: standard deviation.

[a] Percentages may not equal 100 owing to rounding.

[b] Refers to the period 1 month before through 2 months after conception.

[c] Refers to the period 1 month before through 1 month after conception.

[d] Derived using 2000 Rural-Urban Commuting Area Codes from the US Department of Agriculture, Economic Research Service data.

[e] Derived using 2000 US Census at the block group level.

[f] Indices reflect the number of questions that had a “yes” response. Questions can be found in Appendix A.

Table 2

Associations between greenspace (average NDVI) within 100 m and 500 m participant residential buffers and selected birth defects, comparing the highest to lowest quartile of NDVI, National Birth Defects Prevention Study, 1997–2011.

		100 m		500 m	
	No. of Cases[a]	**OR (95% CI)[b]**	**aOR (95% CI)[c]**	**OR (95% CI)[b]**	**aOR (95% CI)[c]**
Congenital heart defects					
Tetralogy of Fallot	898	0.76 (0.62,0.92)	0.71 (0.57,0.87)	0.74 (0.60,0.90)	0.70 (0.56,0.86)
Transposition of great vessels	569	1.03 (0.81,1.31)	0.86 (0.66,1.11)	1.02 (0.80,1.29)	0.86 (0.67,1.12)
Atrioventricular septal defect	271	1.16 (0.82,1.65)	0.94 (0.65,1.37)	1.24 (0.87,1.77)	1.02 (0.70,1.48)
Total anomalous pulmonary venous return	211	0.68 (0.47,0.99)	0.81 (0.54,1.21)	0.62 (0.42,0.90)	0.71 (0.47,1.07)
Hypoplastic left heart	465	0.99 (0.76,1.27)	0.92 (0.70,1.21)	0.88 (0.68,1.14)	0.81 (0.61,1.07)
Coarctation of the aorta	812	1.07 (0.88,1.31)	0.95 (0.76,1.18)	1.28 (1.04,1.58)	1.18 (0.94,1.47)
Aortic stenosis	327	1.23 (0.90,1.68)	0.94 (0.67,1.30)	1.10 (0.79,1.52)	0.84 (0.60,1.19)
Pulmonary valve stenosis	1057	1.08 (0.89,1.30)	1.02 (0.83,1.25)	1.10 (0.91,1.33)	1.04 (0.85,1.27)
Perimembranous ventricular septal defects	1298	1.14 (0.97,1.35)	1.09 (0.91,1.30)	1.01 (0.85,1.19)	0.96 (0.80,1.15)
Secundum atrial septal defect	1706	0.85 (0.73,0.98)	0.96 (0.81,1.12)	0.75 (0.65,0.87)	0.83 (0.71,0.98)
Non-cardiac defects					
Anencephaly	470	0.64 (0.50,0.84)	0.79 (0.59,1.05)	0.61 (0.47,0.79)	0.73 (0.55,0.97)
Spina bifida	922	0.76 (0.63,0.92)	0.85 (0.69,1.04)	0.73 (0.60,0.89)	0.82 (0.66,1.01)
Hydrocephaly	367	0.91 (0.68,1.21)	0.90 (0.66,1.22)	1.03 (0.77,1.39)	1.04 (0.75,1.43)
Anotia/microtia	475	0.43 (0.34,0.56)	0.76 (0.57,1.00)	0.40 (0.31,0.53)	0.71 (0.53,0.94)
Cleft palate	1197	1.00 (0.84,1.19)	0.90 (0.75,1.08)	0.95 (0.80,1.13)	0.86 (0.71,1.03)
Cleft lip with or without cleft palate	2298	0.77 (0.67,0.87)	0.79 (0.69,0.91)	0.83 (0.73,0.94)	0.86 (0.75,0.99)
Esophageal atresia	531	1.36 (1.07,1.73)	1.18 (0.91,1.53)	1.35 (1.05,1.73)	1.19 (0.91,1.56)
Anorectal atresia	747	0.83 (0.67,1.02)	0.99 (0.79,1.25)	0.78 (0.63,0.97)	0.93 (0.74,1.18)
Hypospadias[d]	1657	1.63 (1.37,1.92)	1.05 (0.88,1.26)	1.59 (1.34,1.87)	1.05 (0.88,1.26)
Longitudinal limb deficiency	316	0.73 (0.54,0.99)	0.76 (0.55,1.05)	0.77 (0.56,1.05)	0.82 (0.58,1.14)
Transverse limb deficiency	490	0.68 (0.53,0.87)	0.73 (0.56,0.96)	0.66 (0.51,0.86)	0.71 (0.54,0.94)
Craniosynostosis	1066	1.43 (1.19,1.71)	1.09 (0.90,1.33)	1.44 (1.20,1.73)	1.13 (0.93,1.38)
Diaphragmatic hernia	619	0.76 (0.60,0.96)	0.75 (0.58,0.96)	0.82 (0.65,1.03)	0.80 (0.63,1.03)
Omphalocele	317	0.79 (0.57,1.08)	0.73 (0.51,1.03)	0.59 (0.42,0.81)	0.54 (0.38,0.76)

		100 m		500 m	
	No. of Cases[a]	**OR (95% CI)[b]**	**aOR (95% CI)[c]**	**OR (95% CI)[b]**	**aOR (95% CI)[c]**
Gastroschisis	983	0.59 (0.49,0.71)	0.91 (0.73,1.13)	0.55 (0.46,0.67)	0.82 (0.66,1.01)

aOR: adjusted odds ratio; CI: confidence interval; NDVI: normalized difference vegetation index; OR: odds ratio.

[a]Number of cases with no missing covariates.

[b]Each quartile was compared to the lowest quartile (reference group). Due to the large amount of data and range of NDVI, only the highest quartile to lowest comparison is shown.

[c]Adjusted for maternal race/ethnicity (White non-Hispanic, Hispanic foreign-born, Hispanic US-born, Black non-Hispanic, Other), vitamin use b1-p2 (Yes vs. No), smoking b1-p2 (Yes vs. No), alcohol intake b1-p2 (Yes vs. No), maternal occupation during b1-p1 (Yes vs. No), season of conception (winter, spring, summer, fall), and maternal age at delivery (continuous).

[d]Compared with male controls.

Table 3

Associations between greenspace (average NDVI) within 100 m and 500 m participant residential buffers and selected birth defects, comparing the highest to lowest quartile of NDVI, by **rural/urban** residential area, National Birth Defects Prevention Study, 1997–2011.

	aOR (95% CI)[a]					
	100 m			500 m		
	Rural	Urban	Interaction *P* value[b]	Rural	Urban	Interaction *P* value[b]
Congenital heart defects						
Tetralogy of Fallot	0.59 (0.35,1.02)	0.75 (0.58,0.96)	0.25	0.62 (0.36,1.08)	0.72 (0.56,0.93)	0.60
Transposition of great vessels	0.64 (0.32,1.28)	0.91 (0.67,1.23)	0.17	0.80 (0.40,1.57)	0.88 (0.65,1.19)	0.38
Atrioventricular septal defect	2.36 (0.78,7.18)	0.82 (0.52,1.28)	0.27	2.65 (0.76,9.18)	0.88 (0.55,1.39)	0.33
Total anomalous pulmonary venous return	0.54 (0.18,1.62)	0.91 (0.57,1.45)	0.31	0.59 (0.21,1.64)	0.86 (0.52,1.42)	0.50
Hypoplastic left heart	0.50 (0.27,0.94)	1.11 (0.80,1.56)	0.11	0.35 (0.18,0.71)	1.03 (0.74,1.44)	0.03
Coarctation of the aorta	0.61 (0.36,1.05)	1.06 (0.82,1.38)	0.12	0.67 (0.38,1.20)	1.37 (1.05,1.79)	0.02
Aortic stenosis	2.22 (0.76,6.55)	0.90 (0.62,1.32)	0.47	0.63 (0.26,1.55)	1.03 (0.68,1.56)	0.32
Pulmonary valve stenosis	0.94 (0.56,1.58)	1.08 (0.85,1.38)	0.50	0.85 (0.50,1.44)	1.13 (0.88,1.45)	0.41
Perimembranous ventricular septal defects	1.39 (0.84,2.30)	1.07 (0.86,1.32)	0.27	1.07 (0.64,1.80)	0.99 (0.80,1.24)	0.57
Secundum atrial septal defect	0.92 (0.61,1.39)	0.90 (0.75,1.10)	0.69	0.66 (0.44,0.99)	0.80 (0.65,0.97)	0.74
Non-cardiac defects						
Anencephaly	1.07 (0.55,2.08)	0.68 (0.47,0.99)	0.04	0.89 (0.45,1.73)	0.62 (0.42,0.91)	0.13
Spina bifida	0.86 (0.54,1.39)	0.84 (0.65,1.09)	0.33	0.78 (0.47,1.30)	0.82 (0.62,1.08)	0.68
Hydrocephaly	0.87 (0.42,1.80)	0.83 (0.57,1.21)	0.64	0.69 (0.31,1.51)	1.21 (0.81,1.81)	0.72
Anotia/microtia	0.80 (0.43,1.49)	0.70 (0.50,1.00)	0.91	0.76 (0.38,1.50)	0.65 (0.45,0.93)	0.79
Cleft palate	0.86 (0.54,1.38)	0.96 (0.77,1.20)	0.24	0.59 (0.38,0.93)	0.93 (0.74,1.16)	0.04
Cleft lip with or without cleft palate	0.66 (0.47,0.93)	0.82 (0.69,0.97)	0.41	0.56 (0.40,0.79)	0.89 (0.75,1.06)	0.17
Esophageal atresia	1.81 (0.88,3.72)	1.04 (0.77,1.42)	0.96	1.36 (0.65,2.82)	1.13 (0.81,1.56)	0.80
Anorectal atresia	1.69 (0.92,3.10)	0.86 (0.65,1.14)	0.12	1.02 (0.54,1.93)	0.79 (0.59,1.06)	0.58
Hypospadias[c]	1.46 (0.80,2.66)	1.02 (0.83,1.26)	0.13	1.46 (0.80,2.66)	1.05 (0.85,1.29)	0.38
Longitudinal limb deficiency	0.63 (0.29,1.36)	0.83 (0.55,1.23)	0.93	1.13 (0.45,2.87)	0.82 (0.54,1.25)	0.56
Transverse limb deficiency	0.56 (0.30,1.05)	0.73 (0.53,1.02)	0.60	0.76 (0.39,1.51)	0.63 (0.44,0.89)	0.63
Craniosynostosis	1.13 (0.67,1.89)	1.15 (0.91,1.44)	0.28	1.22 (0.70,2.13)	1.13 (0.89,1.43)	0.72
Diaphragmatic hernia	0.55 (0.30,1.00)	0.84 (0.62,1.14)	0.06	0.54 (0.30,0.98)	0.89 (0.65,1.20)	0.09

	aOR (95% CI)[a]					
	100 m			500 m		
	Rural	Urban	Interaction *P* value[b]	Rural	Urban	Interaction *P* value[b]
Omphalocele	0.51 (0.20,1.28)	0.82 (0.55,1.24)	0.31	0.39 (0.16,0.99)	0.63 (0.42,0.95)	0.19
Gastroschisis	0.97 (0.59,1.60)	0.87 (0.66,1.14)	0.37	0.54 (0.33,0.89)	0.86 (0.64,1.14)	0.51

aOR: adjusted odds ratio; CI: confidence interval; NDVI: normalized difference vegetation index.

[a]Adjusted for maternal race/ethnicity (White non-Hispanic, Hispanic foreign-born, Hispanic US-born, Black non-Hispanic, Other), vitamin use b1-p2 (Yes vs. No), smoking b1-p2 (Yes vs. No), alcohol intake b1-p2 (Yes vs. No), maternal occupation during b1-p1 (Yes vs. No), season of conception (winter, spring, summer, fall), and maternal age at delivery (continuous).

[b]*P* value for interaction was from Wald Chi-square test.

[c]Compared with male controls.

Table 4

Associations between greenspace (average NDVI) within 100 m and 500 m participant residential buffers and selected birth defects, by **neighborhood median household income**, National Birth Defects Prevention Study, 1997–2011.

	aOR (95% CI)[a]					
	100 m			500 m		
	Above or equal to the median	Below the median	Interaction *P* value[b]	Above or equal to the median	Below the median	Interaction *P* value[b]
Congenital heart defects						
Tetralogy of Fallot	0.75 (0.54,1.04)	0.74 (0.54,1.01)	0.60	0.68 (0.48,0.94)	0.82 (0.59,1.13)	0.35
Transposition of great vessels	0.86 (0.60,1.24)	0.72 (0.47,1.10)	0.58	0.79 (0.55,1.16)	0.90 (0.60,1.34)	0.92
Atrioventricular septal defect	0.73 (0.43,1.24)	1.37 (0.76,2.47)	0.04	0.70 (0.40,1.22)	1.68 (0.93,3.05)	0.01
Total anomalous pulmonary venous return	0.72 (0.40,1.30)	0.85 (0.45,1.61)	0.71	0.58 (0.31,1.09)	0.95 (0.51,1.75)	0.81
Hypoplastic left heart	0.78 (0.52,1.15)	1.26 (0.81,1.96)	0.19	0.71 (0.48,1.05)	0.95 (0.59,1.53)	0.76
Coarctation of the aorta	0.85 (0.62,1.17)	1.11 (0.79,1.56)	0.29	1.08 (0.77,1.51)	1.28 (0.91,1.81)	0.29
Aortic stenosis	0.73 (0.46,1.16)	1.31 (0.77,2.23)	0.22	0.65 (0.39,1.07)	1.50 (0.87,2.58)	0.07
Pulmonary valve stenosis	1.01 (0.73,1.40)	1.16 (0.86,1.57)	0.87	1.32 (0.92,1.89)	1.10 (0.82,1.47)	0.31
Perimembranous ventricular septal defects	1.05 (0.80,1.38)	1.22 (0.93,1.59)	0.37	0.93 (0.70,1.24)	1.13 (0.86,1.48)	0.30
Secundum atrial septal defect	0.75 (0.59,0.96)	1.15 (0.90,1.46)	0.02	0.72 (0.56,0.92)	0.90 (0.70,1.15)	0.10
Non-cardiac defects						
Anencephaly	0.50 (0.32,0.77)	1.37 (0.90,2.10)	0.002	0.45 (0.29,0.70)	1.29 (0.83,1.99)	0.003
Spina bifida	0.84 (0.61,1.14)	0.96 (0.70,1.32)	0.41	0.76 (0.54,1.05)	1.00 (0.72,1.39)	0.11
Hydrocephaly	0.94 (0.59,1.50)	0.77 (0.49,1.23)	0.36	1.07 (0.64,1.77)	1.24 (0.77,2.02)	0.97
Anotia/microtia	0.54 (0.36,0.82)	0.98 (0.64,1.50)	0.09	0.54 (0.35,0.84)	0.80 (0.51,1.25)	0.26
Cleft palate	0.84 (0.64,1.11)	1.07 (0.81,1.43)	0.26	0.73 (0.56,0.97)	1.04 (0.78,1.38)	0.16
Cleft lip with or without cleft palate	0.74 (0.60,0.92)	0.88 (0.71,1.09)	0.09	0.79 (0.64,0.98)	0.93 (0.75,1.15)	0.21
Esophageal atresia	1.13 (0.76,1.66)	1.32 (0.88,1.97)	0.76	1.18 (0.77,1.79)	1.31 (0.87,1.98)	0.71
Anorectal atresia	0.81 (0.57,1.14)	1.24 (0.88,1.76)	0.02	0.65 (0.45,0.93)	1.16 (0.81,1.65)	0.002
Hypospadias[c]	1.17 (0.88,1.54)	1.03 (0.79,1.36)	0.63	1.34 (1.00,1.79)	0.92 (0.70,1.20)	0.15
Longitudinal limb deficiency	0.67 (0.41,1.09)	0.89 (0.54,1.47)	0.36	0.74 (0.43,1.26)	1.00 (0.61,1.64)	0.29
Transverse limb deficiency	0.61 (0.41,0.92)	0.85 (0.56,1.28)	0.24	0.57 (0.37,0.86)	0.82 (0.53,1.25)	0.26

	aOR (95% CI)[a]					
	100 m			500 m		
	Above or equal to the median	Below the median	Interaction *P* value[b]	Above or equal to the median	Below the median	Interaction *P* value[b]
Craniosynostosis	1.01 (0.76,1.34)	1.35 (1.00,1.84)	0.40	1.22 (0.89,1.65)	1.22 (0.89,1.65)	0.93
Diaphragmatic hernia	0.94 (0.64,1.38)	0.67 (0.45,0.99)	0.10	0.84 (0.57,1.24)	0.86 (0.58,1.26)	0.44
Omphalocele	0.77 (0.46,1.29)	0.67 (0.38,1.16)	0.62	0.50 (0.30,0.84)	0.63 (0.37,1.08)	0.33
Gastroschisis	0.80 (0.56,1.14)	1.04 (0.77,1.41)	0.20	0.87 (0.60,1.27)	0.86 (0.63,1.16)	0.71

aOR: adjusted odds ratio; CI: confidence interval; NDVI: normalized difference vegetation index.

[a]Adjusted for maternal race/ethnicity (White non-Hispanic, Hispanic foreign-born, Hispanic US-born, Black non-Hispanic, Other), vitamin use b1-p2 (Yes vs. No), smoking b1-p2 (Yes vs. No), alcohol intake b1-p2 (Yes vs. No), maternal occupation during b1-p1 (Yes vs. No), season of conception (winter, spring, summer, fall), and maternal age at delivery (continuous).

[b]P value for interaction was from Wald Chi-square test.

[c]Compared with male controls.

Table 5

Associations between greenspace (average NDVI) within 100 m and 500 m participant residential buffers and selected birth defects, by **maternal pre-pregnancy obesity**, National Birth Defects Prevention Study, 1997–2011.

	aOR (95% CI)[a]					
	100 m			500 m		
	Non obese	Obese	Interaction *P* value[b]	Non obese	Obese	Interaction *P* value[b]
Congenital heart defects						
Tetralogy of Fallot	0.73 (0.56,0.94)	0.67 (0.41,1.09)	0.98	0.78 (0.60,1.01)	0.62 (0.37,1.02)	0.74
Transposition of great vessels	0.92 (0.68,1.24)	0.39 (0.19,0.81)	0.04	0.91 (0.67,1.23)	0.62 (0.32,1.23)	0.33
Atrioventricular septal defect	0.93 (0.59,1.46)	0.85 (0.36,2.03)	0.97	0.98 (0.62,1.54)	1.26 (0.49,3.27)	0.20
Total anomalous pulmonary venous return	0.89 (0.54,1.45)	0.54 (0.20,1.46)	0.25	0.87 (0.53,1.43)	0.57 (0.20,1.62)	0.48
Hypoplastic left heart	0.95 (0.67,1.34)	0.88 (0.48,1.62)	0.80	0.85 (0.60,1.20)	0.87 (0.46,1.63)	0.95
Coarctation of the aorta	0.96 (0.74,1.25)	0.94 (0.53,1.67)	0.25	1.18 (0.90,1.55)	1.35 (0.76,2.41)	0.63
Aortic stenosis	0.97 (0.64,1.46)	0.87 (0.42,1.84)	0.86	1.02 (0.66,1.58)	1.00 (0.47,2.14)	0.74
Pulmonary valve stenosis	1.13 (0.87,1.45)	1.00 (0.63,1.61)	0.45	1.22 (0.94,1.57)	0.91 (0.56,1.50)	0.28
Perimembranous ventricular septal defects	1.10 (0.89,1.35)	1.18 (0.71,1.95)	0.34	1.02 (0.82,1.27)	1.06 (0.65,1.73)	0.42
Secundum atrial septal defect	0.96 (0.79,1.16)	0.78 (0.53,1.15)	0.44	0.84 (0.69,1.02)	0.75 (0.50,1.11)	0.99
Non-cardiac defects						
Anencephaly	0.92 (0.64,1.31)	0.54 (0.27,1.07)	0.41	0.81 (0.56,1.16)	0.87 (0.44,1.72)	0.50
Spina bifida	0.99 (0.76,1.29)	0.68 (0.43,1.07)	0.43	0.98 (0.75,1.30)	0.64 (0.39,1.05)	0.54
Hydrocephaly	0.85 (0.59,1.25)	0.97 (0.48,1.98)	0.87	1.30 (0.86,1.96)	0.81 (0.39,1.68)	0.67
Anotia/microtia	0.65 (0.45,0.92)	1.30 (0.61,2.77)	0.08	0.70 (0.49,1.01)	0.62 (0.27,1.42)	0.91
Cleft palate	1.01 (0.81,1.26)	0.72 (0.44,1.18)	0.12	0.97 (0.77,1.21)	0.50 (0.32,0.80)	0.04
Cleft lip with or without cleft palate	0.79 (0.67,0.94)	0.88 (0.61,1.26)	0.79	0.90 (0.76,1.06)	0.76 (0.53,1.10)	0.42
Esophageal atresia	1.18 (0.87,1.62)	1.25 (0.62,2.51)	0.60	1.26 (0.91,1.76)	1.26 (0.63,2.53)	0.81
Anorectal atresia	1.09 (0.81,1.46)	0.77 (0.45,1.30)	0.20	0.98 (0.73,1.31)	0.59 (0.34,1.02)	0.15
Hypospadias[c]	1.14 (0.92,1.42)	0.80 (0.52,1.23)	0.29	1.16 (0.93,1.43)	0.73 (0.47,1.13)	0.17
Longitudinal limb deficiency	0.85 (0.57,1.26)	0.55 (0.23,1.29)	0.15	0.87 (0.58,1.31)	0.80 (0.34,1.89)	0.30
Transverse limb deficiency	0.72 (0.52,1.01)	0.59 (0.30,1.16)	0.68	0.73 (0.52,1.02)	0.62 (0.32,1.22)	0.79
Craniosynostosis	1.06 (0.84,1.34)	1.37 (0.83,2.27)	0.46	1.12 (0.88,1.43)	1.23 (0.75,2.01)	0.50
Diaphragmatic hernia	0.82 (0.61,1.12)	0.67 (0.36,1.24)	0.52	0.84 (0.62,1.14)	1.01 (0.56,1.84)	0.95

	aOR (95% CI)[a]					
	100 m			500 m		
	Non obese	Obese	Interaction *P* value[b]	Non obese	Obese	Interaction *P* value[b]
Omphalocele	0.84 (0.54,1.32)	0.60 (0.30,1.22)	0.74	0.54 (0.35,0.85)	0.65 (0.32,1.32)	0.34
Gastroschisis	0.92 (0.72,1.17)	1.00 (0.41,2.43)	0.95	0.85 (0.66,1.09)	0.67 (0.26,1.74)	0.42

aOR: adjusted odds ratio; CI: confidence interval; NDVI: normalized difference vegetation index.

[a]Adjusted for maternal race/ethnicity (White non-Hispanic, Hispanic foreign-born, Hispanic US-born, Black non-Hispanic, Other), vitamin use b1-p2 (Yes vs. No), smoking b1-p2 (Yes vs. No), alcohol intake b1-p2 (Yes vs. No), maternal occupation during b1-p1 (Yes vs. No), season of conception (winter, spring, summer, fall), and maternal age at delivery (continuous).

[b]P value for interaction was from Wald Chi-square test.

[c]Compared with male controls.