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## Early Life Exposure to Green Space and Insulin Resistance: An Assessment from Infancy to Early Adolescence

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### Abstract

**Background:** Recent studies suggest that greater exposure to natural vegetation, or “green space” is associated with lower diabetes risk, possibly through increasing physical activity. However, there is limited research on green space and insulin resistance in youth. We hypothesized greater green space at early-life sensitive time periods would be associated with lower insulin resistance in youth.

**Methods:** We used data from Project Viva (N=460), a pre-birth cohort study that recruited pregnant women in eastern Massachusetts, 1999–2002, and followed offspring into adolescence. We defined residential green space exposure at infancy (median age - 1.1 years), early childhood (3.2 years), mid-childhood (7.7 years), and early adolescence (12.8 years), using 30m resolution Landsat satellite imagery to estimate the Normalized Difference Vegetation Index [NDVI]. Our main outcome was early adolescence estimated insulin resistance (HOMA-IR). We used multiple imputation to account for missing data and multiple linear regression models adjusted for age, sex, race/ethnicity, parental education, household income, and neighborhood median household income.

**Results:** The highest green space tertile had the highest percentage of white participants (85%), college-educated mothers (87%) and fathers (85%), and households with income higher than US \$70,000 (86%). Unadjusted models showed that participants living in the highest green space

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tertile at infancy had a 0.15 unit lower HOMA-IR (95% CI: -0.23, -0.06) in early adolescence, than those living in the lowest tertile. However, in adjusted models, we did not observe evidence of associations between green space from infancy to early adolescence and HOMA-IR in early adolescence, although some point estimates were in the hypothesized direction. For example, participants in the highest green space tertile in infancy had 0.03 units lower HOMA-IR (95% CI: -0.14, 0.08) than those living in the lowest tertile.

**Conclusions:** Exposure to green space at early life sensitive time periods was not associated with HOMA-IR in youth. Early-life longitudinal studies across diverse populations are needed to confirm or refute our results.

### Keywords

Longitudinal data; Green space; Environmental Epidemiology; Insulin Resistance; Sensitive Periods; Children's Health

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### Introduction

Globally, 55% of the population lives in urban areas, a proportion that is expected to increase to 68% by 2050.<sup>1</sup> Within the US, according to the 2010 Census Bureau, 81% of the population lives in urban areas.<sup>2</sup> Living in urban areas offers many benefits such as good education and access to health care, but it also limits access to green space. Natural environmental features, including green spaces, have been associated with better health and wellbeing. For example, higher levels of green space exposure have been linked to increased physical activity,<sup>3-7</sup> lower levels of hypertension<sup>8,9</sup> and depression,<sup>10-14</sup> and lower risk of mortality,<sup>15</sup> likely because these settings reduce exposure to noise and air pollution, and provide opportunities for physical activity, social connection and psychological restoration. These mechanisms may be especially pertinent during early life periods as times of rapid development.

Cross-sectional studies have reported green space as a protective factor against the risk of diabetes among adults.<sup>16-21</sup> Also, a recent study reported that higher levels of residential green space were associated with lower maternal glucose levels, decreased risks of incident impaired glucose intolerance and gestational diabetes mellitus.<sup>22</sup> However, few studies have considered the association between green space and glycemic-related traits in children and adolescents and most of the research on green space and health has been cross-sectional, therefore unable to evaluate the most etiologically relevant time window of exposure. One cross-sectional study of 3,844 Iranian schoolchildren aged 7-18 years reported inverse associations between time spent in green spaces and fasting blood glucose levels,<sup>23</sup> and another of 837 15-year old German adolescents reported that an increase in green space exposure was associated with a lower insulin resistance.<sup>24</sup> However, no studies have evaluated green space exposure at different time windows throughout early life in association with insulin resistance. We hypothesized that children are more sensitive to environmental exposures particularly during critical windows of susceptibility. This analysis aimed to evaluate the association between early life exposure to green space and insulin resistance and assess life-periods from infancy to early adolescence in which individuals might be more susceptible to their surroundings.

## SUBJECTS AND METHODS

### Study Population

We used data from Project Viva, a longitudinal pregnancy and birth cohort. From April 1999 through November 2002, pregnant women were recruited at eight urban and suburban practices of Atrius Harvard Vanguard Health Medical Associates, a multi-specialty group practice in eastern Massachusetts, United States.<sup>25</sup> Of 2,128 live singleton births, 603 participants provided data on HOMA-IR in early adolescence. From the 603 participants with outcome data, 560 participants had complete data on green space exposure at infancy (median age 1.1 years), early childhood (median 3.2 years), mid-childhood (median 7.7 years), and early adolescence in-person visits (median 12.8 years). Of the 560 participants with outcome and exposure data, 460 had complete data on the covariates (Supplementary Figure 1). The institutional review board of Harvard Pilgrim Health Care approved this study and all procedures were in accordance with the ethical standards for human experimentation established by the Declaration of Helsinki. All mothers provided written informed consent at enrollment and at each postpartum in-person visit, and children provided verbal assent at the early adolescence visit.

### Exposure

Normalized Difference Vegetation Index (NDVI) values were used to estimate the amount of green vegetation around the residential address of Project Viva participants. We computed NDVI for every in-person visit at infancy, early childhood, mid-childhood, and early adolescence, at 3 different buffer sizes (90, 270, and 1,230 m). The NDVI is the most widely used satellite-derived indicator of the quantity of green vegetation on the ground (ranging between -1 and 1). Negative values (approaching -1) correspond to water, values around zero correspond to barren areas of rock or sand, and positive values represent grassland, a value of 1 indicates the highest vegetation index (Supplementary Figure 2). NDVI has been used as a marker for exposure to green spaces in numerous previous epidemiological studies.<sup>15,26,27</sup> For this study, we used Landsat satellite data at 30m resolution for each geocoded address (X-Y geographical coordinates) from July 1999 to 2017, since NDVI reaches its maximum and highest level of geographic variation during the height of the summer. We used the estimate for July of the specific year of follow-up (Supplementary Figure 3B). We used the focal function in the R raster package version 3.4.0. to estimate the area-weighted average at the different buffer sizes (e.g. average NDVI of all the pixels around the home in a 90, 270, and 1,230 m buffers).

### Outcome

Our main outcome of interest was the homeostatic model assessment to estimate insulin resistance (HOMA-IR) at early adolescence (mean  $\pm$  SD: 13.1  $\pm$  0.7 years old). A phlebotomist performed fasting blood draw in willing participants using standardized techniques. Children fasted for at least eight hours before the time of the blood draw. Plasma fasting insulin was measured using an electro-chemiluminescence immunoassay on the Roche Modular system and fasting glucose was measured enzymatically using Roche Diagnostics reagents. We estimated insulin resistance using the homeostatic model assessment (HOMA-IR; (glucose in mg/dL x insulin in  $\mu$ U/mL) / 405).<sup>28,29</sup> Higher values of

HOMA-IR indicate higher insulin resistance, and therefore higher diabetes risk. To normalize its distribution, HOMA-IR was log-transformed (Supplementary Figure 3A).

### Covariates

At enrollment during the first trimester of pregnancy (median 9.9 weeks), women reported their education level and household income. We obtained child's sex from the delivery interview and mothers reported their child's race/ethnicity at the early childhood (3-year) visit. We abstracted residential census tract median annual household income at the time of delivery from 2000 US Census data.

In each model, we adjusted for the following covariates selected a priori: child characteristics [age at early adolescence visit (continuous), sex (female or male), mother's race/ethnicity (white, black, Asian, Hispanic, or other), parental characteristics [maternal education level (%  $\geq$ college graduate), paternal education level (%  $\geq$ college graduate)], household income (%  $>$ 70,000/year US\$), neighborhood income [census tract median household income at enrollment (continuous)]. Air pollution exposure at infancy was included as a potential confounder in sensitivity analysis. Daily particulate air pollutants with an aerodynamic diameter less than 2.5 $\mu$ m (PM<sub>2.5</sub>) levels in a 1 $\times$ 1 km grid were estimated using published and validated air pollution prediction models based on land use, chemical transport modeling, and satellite remote sensing data. Further details on particulate matter has been published elsewhere.<sup>30</sup>

Further, air pollution, physical activity and obesity measured at early childhood were analyzed as potential mediators. Physical activity was self-reported by the mother as a response to the question "In the past month, on average, how many hours a day is your child involved in active play (such as running, jumping, climbing)?" Trained research assistants collected measures at an in-person research visit in early childhood.<sup>25</sup> Child weight and height were measured, from which we calculated BMI and age- and sex-specific BMI z-scores using Centers for Disease Control and Prevention 2000 reference data.<sup>31</sup>

### Statistical Analysis

We used multiple linear regression models to assess the association between NDVI during each age period (infancy, early childhood, mid-childhood, and early adolescence), and HOMA-IR measured in early adolescence. For each age period, we adjusted for covariates described above, as well as exposure to green space at each time point, and in all preceding age-periods, but not in subsequent age periods.<sup>34</sup> Thus, model 1 assesses exposure to green space at infancy adjusting for covariates, model 2 assesses exposure to green space at early childhood adjusting for covariates as well as exposure to green space at infancy, model 3 assesses exposure to green space at mid-childhood adjusting for covariates as well as for exposure to green space at early childhood and infancy, and so on. We also evaluated the presence of non-linear relationships between early life exposure to green space and HOMA-IR at early adolescence using restricted cubic splines, but there was no indication of non-linearity (non-linearity p-values were  $>$ 0.05) so spline terms were not included in our final models. Additionally, we tested for effect modification of the relationship between green space at each time point and HOMA-IR by child's sex, mother's race/ethnicity (white: yes/

no), parental socio-economic status (maternal and paternal education level) and neighborhood socio-economic status, as suggested by previous research<sup>19,24</sup>. We modeled interaction terms between area-weighted average NDVI at each time point and each potential effect modifier and used likelihood ratio tests to assess statistical significance. We also obtained strata-specific effect estimates from stratified analyses. We report results for NDVI tertiles, and the linear test for trend. NDVI was assessed at 3 different buffer sizes around each participant's home at each time period: 90, 270 and 1,230 m. The main results presented are based on the 90 m buffer, but results were similar for the 270m and the 1230m buffers. Effect estimates were back-transformed from the log scale using  $[\exp(\beta) - 1]^{24}$  and are thus presented as difference of the outcome, with corresponding 95% confidence intervals (CI) and p-values, for participants with high (tertile 3) and medium (tertile 2) exposure to green space compared to participants with low exposure to green space (tertile 1). We used causal mediation analysis to test whether the association between exposure to green space and HOMA-IR was mediated by air pollution, physical activity or obesity. In general, the most effective way to ensure temporal and causal ordering is to use at least three waves of data with the exposure at wave 1, mediator at wave 2 and outcome at wave 3.<sup>32</sup> The longitudinal design of Project Viva allowed us to conduct analyses to determine potential mediation. Based on this, we used exposure to green space at baseline (infancy), mediators at early childhood, and HOMA-IR at early adolescence. We used the "mediation" package in R for this analysis. Lastly, we ran sensitivity analysis among non-movers (N=189). Statistical significance was assessed at the 0.05 level. Data were analyzed using R software version 3.4.0.

### Missing data

The proportion of participants with complete data (N=460) represented 22% of the original sample size (supplementary figure 1). We used multiple imputation by chained equations (MICE) to handle the potential selection bias originating from missingness. We used SAS 9.4 with 50 imputations and 2128 participants. Following guidelines,<sup>33</sup> the imputation model included all model variables, plus main predictors of missingness (parity, maternal pre-pregnancy BMI, maternal age at enrollment, birthweight [z-value], gestational age, parental smoking, pregnancy smoking status, BMI at early adolescence and traffic density and urbanicity at enrollment). Regression analyses were run across 50 imputed datasets, and the pooled estimates were reported. Imputed results were broadly similar to those obtained using observed values; the former are presented.

### Results

The mean age of participants at HOMA-IR assessment was 13.0 (SD 0.7) years (Table 1). Approximately 75% of participants were white, while more than two thirds had parents with a college education. More than half (67%) of participants reported having a household income over US\$70,000 per year at study enrollment. The tertile with highest residential green space at early adolescence contained a greater proportion of white participants, college degree educated parents, households with income higher than US\$70,000, and highest median household income at the census tract level (Table 1). A comparison between participants with complete and incomplete data on HOMA-IR showed that participants with

complete outcome data were more likely to be white, have parents with higher than college education, and a household income >US\$70,000 per year. Exposure to green space at infancy, early childhood, mid-childhood and early adolescence was similar between participants with missing and complete data on HOMA-IR (Supplementary Table 6).

The correlation between NDVI at infancy and early childhood was 0.8, which decreased to 0.6 between infancy and mid-childhood, and to 0.5 between infancy and early adolescence. The correlation between NDVI at early childhood and mid-childhood was 0.7, which decreased to 0.6 between early- childhood and early adolescence. The correlation between NDVI at mid-childhood and early adolescence was 0.8 (Supplementary Table 1). The correlations among green space exposures were similar between participants who moved compared to the full analytical sample.

Unadjusted models showed that those living in the highest tertile of exposure to green space at infancy had a 0.15 unit lower HOMA-IR (95% CI: -0.23, -0.06), than those living in the lowest tertile. Further, those living in the highest tertile of exposure to green space at early childhood had a 0.11 unit lower HOMA-IR (95% CI: -0.19, -0.02), while those living in the highest tertile at mid-childhood had a 0.12 unit lower HOMA-IR (95% CI: -0.21, -0.03), and those living in the highest tertile at early adolescence had a 0.12 unit lower HOMA-IR (95% CI: -0.20, -0.03), compared to those living in the lowest tertile of exposure to green space (Supplementary Table 2). However, when we adjusted for demographic variables (age, sex, race/ethnicity), this associations were attenuated towards the null (Supplementary Table 2). In fully adjusted models, we did not observe evidence for associations between residential green space at infancy, early childhood, mid-childhood or early adolescence with HOMA-IR at early adolescence. In adjusted models, we still see an inverse association between residential green space at infancy and mid-childhood, and HOMA-IR but with wide confidence intervals. For example, those living in the highest tertile of exposure to green space at infancy had a 0.03 unit lower HOMA-IR (95% CI: (-0.14,0.08, p-value for trend=0.25), compared to those in the lowest tertile at infancy, after accounting for age at early adolescence visit, sex, race/ethnicity, parental education status, HH income and neighborhood income (Table 2).

Our results also show weak positive associations with wide confidence intervals between greater residential green space at early childhood with HOMA-IR (0.08, 95% CI: (-0.09, 0.27) (Table 2). None of the above-mentioned associations reached statistical significance at any buffer area (90, 270 and 1,230 m) around each participant's residence.

### Stratified Analyses

We observed no differences in the association between green space exposure and HOMA-IR when we stratified the analyses by child's sex and race/ethnicity. Results from stratified analyses for sex and race/ethnicity are shown in Figure 1. Further, we did not find association between tertiles of green space exposure and HOMA-IR in early adolescence by parental socio-economic status and neighborhood socio-economic status (Figure 2). We did not find evidence that associations of early life green space exposure with HOMA-IR in early adolescence were modified by any of the characteristics we examined as potential effect modifiers (all green space x effect modifiers product interaction p-values = 0.1).

Sensitivity analyses of complete case analysis are shown in Supplementary Table 3. The relationship between early life exposure to green space and HOMA-IR at early adolescence was similarly null. In combined models including both air pollution and greenness, the association between greenness and HOMA-IR was not statistically significant (Supplementary Table 4). Estimates of the proportion of the association between green space and HOMA-IR that might be mediated by other factors (assuming that underlying assumptions of the mediation analyses hold) were not statistically significant for physical activity, exposure to air pollution or obesity (Supplementary Table 5). Further, results among participants who did not move across the life-course were similar (Supplementary table 7).

## DISCUSSION

In a prospective pre-birth cohort in Massachusetts, exposure to green space during infancy, early childhood, mid-childhood and early adolescence was not related to insulin resistance at early adolescence, effect sizes were close to 0 and confidence intervals consistently crossed the null. The results were consistent when focusing on the area immediately around each residence (90-m buffer) versus a larger radius (270 m and 1,230 m buffers) around each participant's home. The association between greenness and HOMA-IR did not differ by sex, race/ethnicity, parental socio-economic status, and neighborhood socio-economic status.

Overall, our findings do not support the hypothesized protective association between residential exposure to green space in early life as assessed by NDVI and insulin resistance in adolescence. Prior studies evaluating the association between NDVI and diabetes risk in adolescents and adults have been inconsistent, with some<sup>19,24</sup> but not all studies reporting a reduced risk with greater exposure. Our null findings are consistent with a longitudinal study that found no strong association between access to open space green space and type 2 diabetes mellitus risk among adults,<sup>35</sup> and another cross-sectional study that examined the association between surrounding green space at the time of delivery and incident gestational diabetes mellitus, which found a nonsignificant association.<sup>34</sup> Similarly to the study by Thiering and colleagues,<sup>24</sup> in combined models including both air pollution and greenness, the association between greenness and HOMA-IR was not statistically significant. Taken together, these findings highlight the need for further research in cohort studies to evaluate long-term exposure to green space and diabetes risk.

Stratification according to sex, race/ethnicity, parental socio-economic status and neighborhood socio-economic status did not provide any evidence to support the hypothesis that higher NDVI is associated with decreased insulin resistance. In addition, our results on effect modification by neighborhood socioeconomic circumstances are consistent with prior studies.<sup>19,24</sup> For instance, Astell-Burt et al. reported no effect modification by neighborhood socioeconomic status in the beneficial effect on diabetes risk from green space among adults.<sup>19</sup> However, Thiering et al. found that the association between HOMA-IR and green space was stronger among adolescents with lower socioeconomic status.<sup>24</sup>

The differences in our results compared to previous cross-sectional studies that have reported green space as a protective factor against the risk of diabetes among adults,<sup>16-21</sup> may be due to study design, age groups evaluated or measurements for diabetes risk



assessment. For example, the only other available longitudinal study of the association between residential surrounding greens pace and incidence of diabetes mellitus that showed a protective association, evaluated adults in the UK.<sup>37</sup> Paquet et al. (2014) also looked at adults and used HbA1c > 5.7% or fasting plasma glucose > 5.6 mmol/L as their outcome measure.<sup>35</sup> Dadvand et al (2018) evaluated children but used fasting blood glucose as the outcome.<sup>23</sup> Finally, it is also important to mention that Project Viva is predominantly composed of mother-infant pairs from mid-high socioeconomic backgrounds: at recruitment and delivery, approximately 65% of mothers had completed a college degree or more, and 84% reported annual household incomes greater than US\$40,000. Previous evidence has indicated that the association between greenness and HOMA-IR is stronger among adolescents with lower socioeconomic status and thus the effect on Project Viva participants might have been weakened due to the socio-economic characteristics.<sup>24</sup>

There are a number of limitations of this study to consider. First, the appropriate scale to measure greenness is uncertain,<sup>38</sup> and it constitutes a major challenge in spatial analyses.<sup>39</sup> In this study, we explored three geographic scales (90, 270, and 1230 m buffers) which yielded similar results (Supplementary Table 3). Second, although NDVI has been used extensively to measure exposure to greenness, it does not provide information on the quality of greenness. More work is needed to identify specific features of green space (e.g. trees v. grassy fields v. parks) that most closely drive behavior and might be related to diabetes risk. Further, while a recent validation study demonstrated that NDVI performs adequately when compared with environmental psychologists' evaluations of green spaces,<sup>40</sup> future studies should consider other measures of green space in association with diabetes risk. Third, selection into neighborhoods according to health status is a common concern in studies of geographic context and health. However, given the young age of Project Viva participants, they unlikely selected their neighborhood of residence and thus reduce confounding by neighborhood preference in the association between greenness and insulin resistance. Fourth, the strong association between residential green space and socio-economic status measures suggest potential confounding; although we adjusted for individual- and neighborhood measures of socio-economic status, residual confounding is likely. Future studies should consider socioeconomic factors as key drivers of the association between the built/natural environment and human health. Furthermore, the association between green space and insulin resistance was consistently null across different levels of individual- and neighborhood socio-economic status, which boosts confidence in our results. Fifth, missing data may result in selection bias. Although it is reassuring that early-life exposure to green space and other characteristics of included participants were generally similar to those of the excluded participants, there were small differences in some factors correlated with both exposures and outcomes (mother's education and father's education), suggesting that selection bias is possible (Supplementary Table 6). However, we used MICE as the imputation model which accounts for the process that created the missing data. The results from MICE and complete-case analysis showed similar results. Finally, insulin resistance was estimated only at early adolescence from fasting insulin and glucose levels (HOMA-IR) which is not the gold-standard for estimation of insulin resistance; yet, HOMA-IR has been shown to have high accuracy for dynamic indices of insulin resistance measured in

adolescents,<sup>41</sup> and prepubertal children.<sup>42</sup> Future studies should evaluate the change in HOMA-IR across time in association with exposure to green space.

This study also has a number of notable strengths. To our knowledge, it is the first prospective examination to evaluate green space exposure at different time windows during early childhood in association with insulin resistance. We were able to construct longitudinal measures of exposure to greenness in the area surrounding each participant's home address over 12 years of follow-up. Very few prior studies have investigated green exposure throughout early life including multiple time points to investigate their long-term effects through adolescence. Whether the null effect of green exposure with insulin resistance remains or becomes stronger during the transition from adolescence to adulthood should be investigated. Our study addresses the need for more analyses with finer spatial scale,<sup>43</sup> and the exploration of multiple buffers to evaluate the uncertain geographic context problem.<sup>39</sup> We hypothesize that smaller buffers, such as 90m, would represent the greenness within view from the home, 270 would represent greenness right around the home, and 1230 would represent greenness in the general neighborhood of the participant. Additionally, we were able to control for important confounders, and test effect modification by various factors, such as individual- and neighborhood SES.

## CONCLUSION

In this longitudinal cohort from eastern Massachusetts, we hypothesized a protective association between residential green space exposure in early life and insulin resistance in early adolescence. However, we did not find substantial evidence in support of this hypothesis. Findings were consistently null across sex, race/ethnicity, parental socio-economic status and neighborhood socio-economic status. Although additional research is required on the relationship between other measurements of exposure to green space (e.g. quality or type of green space) during early life stages and other health outcomes (e.g. mental health), these findings suggest that childhood residential exposure to green space does not have a protective effect on diabetes risk among adolescents.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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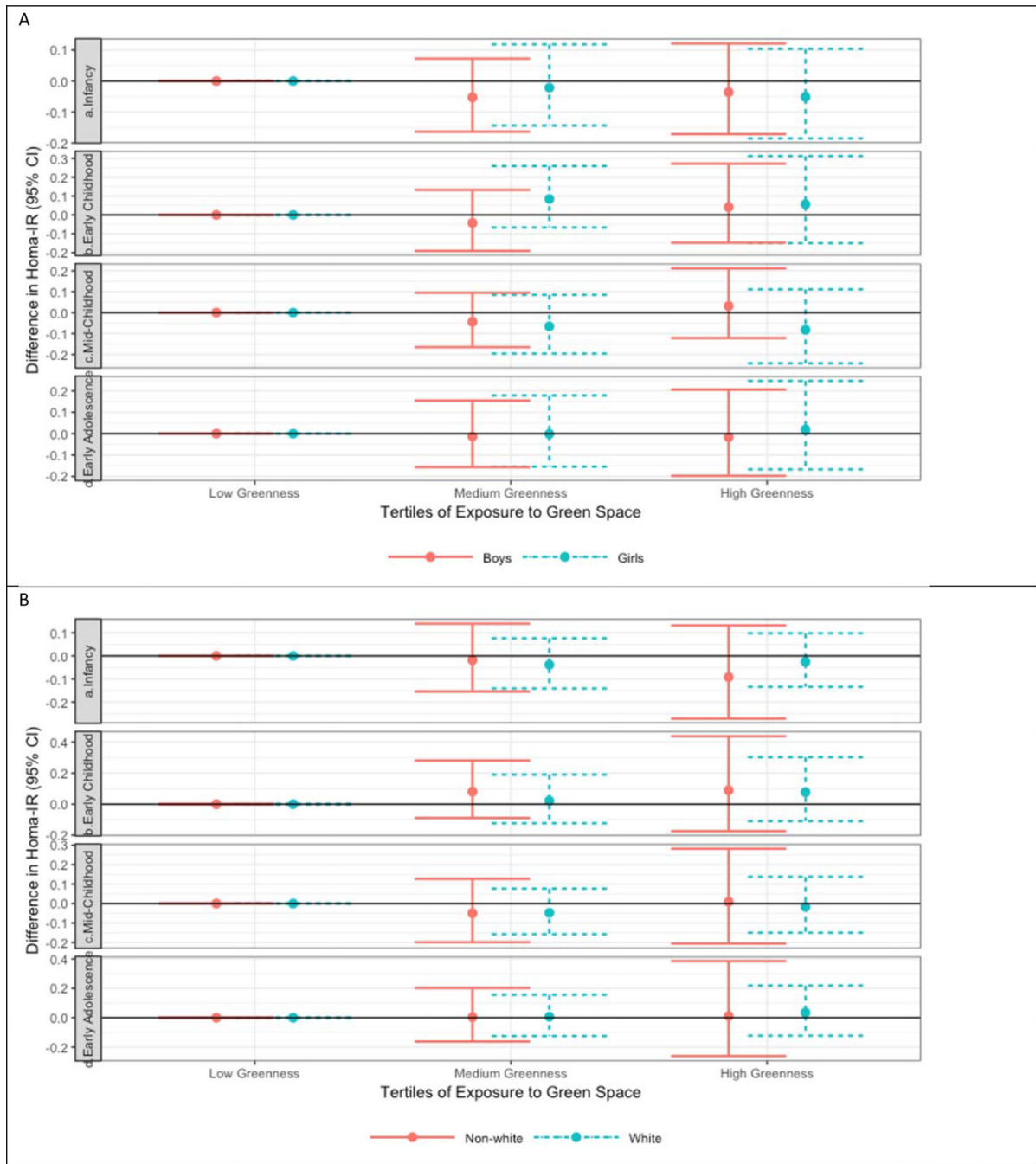
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**Figure 1.**

Fully adjusted linear regression coefficients and 95% confidence intervals for exposure to green space at infancy, early childhood, mid-childhood, and early adolescence at the 90 m buffer, and HOMA-IR at early adolescence in Project Viva stratified by (A) sex, (B) race/ethnicity <sup>c</sup>

<sup>c</sup> Race/ethnicity was classified as White (Y/N). All models adjusted for child age and sex, mother’s race/ethnicity and education, father’s education, household income and neighborhood median household income, except when stratifying variable. Later exposure

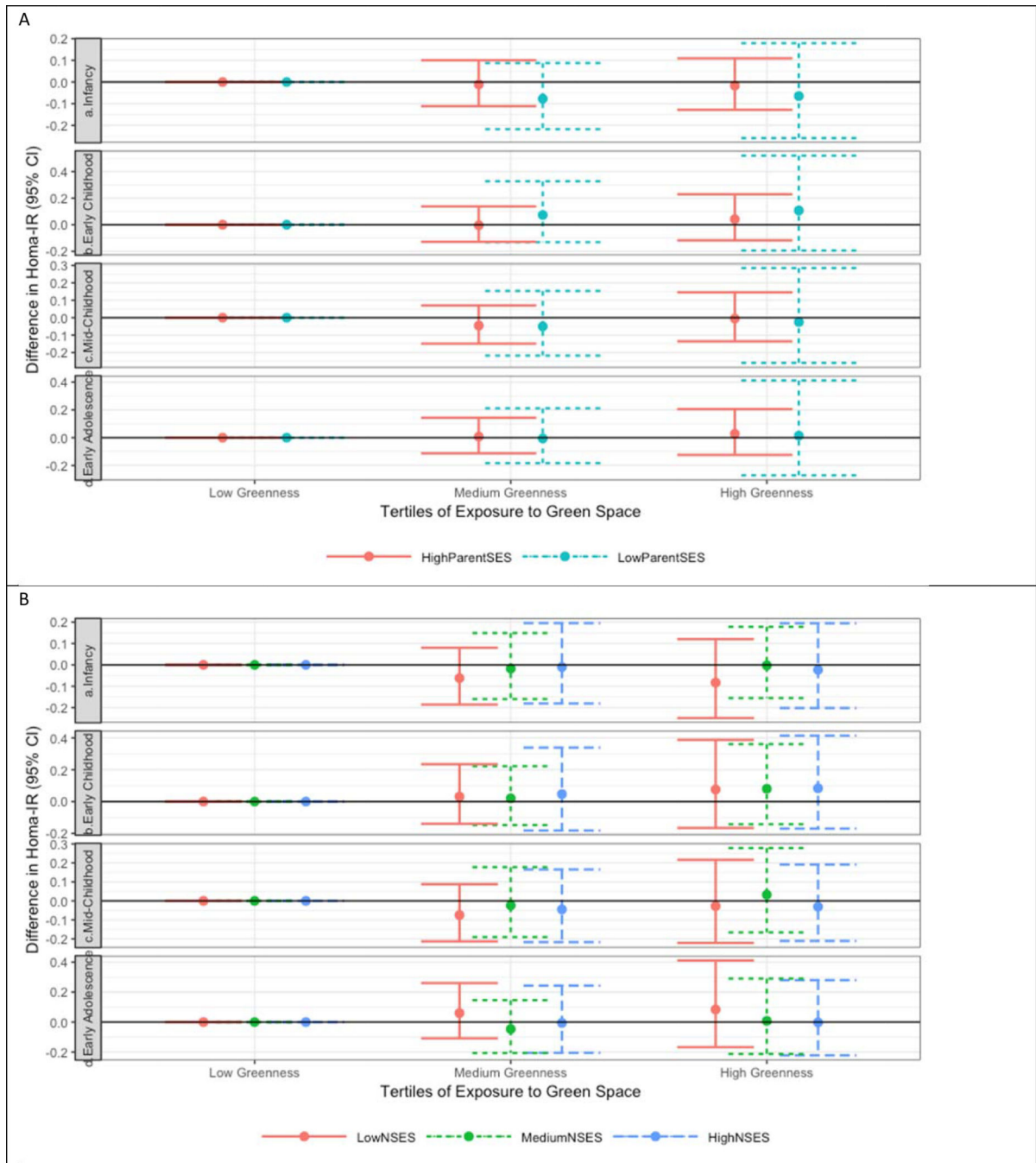
timepoints additionally adjusted for early exposure timepoints. For example, NDVI in early adolescence adjusted for NDVI in infancy, early childhood, and mid-childhood.

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**Figure 2.** Fully adjusted linear regression coefficients and 95% confidence intervals for exposure to green space at infancy, early childhood, mid-childhood, and early adolescence at the 90-m buffer, and HOMA-IR at early adolescence in Project Viva stratified by (A) parental socio-economic status<sup>d</sup> and (B) neighborhood socio-economic status<sup>e</sup>  
<sup>d</sup> High parental socio-economic status was classified if either mother or father  $\geq$  college graduate, and low parental SES otherwise.



<sup>e</sup> All models adjusted for child age and sex, mother's race/ethnicity and education, father's education, household income and neighborhood median household income, except when stratifying variable. Later exposure timepoints additionally adjusted for early exposure timepoints. For example, NDVI in early adolescence adjusted for NDVI in infancy, early childhood, and mid-childhood.

**Table 1.**

Project Viva study participant characteristics by tertiles of Normalized Difference Vegetation Index within 90 m buffer from early adolescence <sup>a</sup>

	<b>Tertile 1</b>	<b>Tertile 2</b>	<b>Tertile 3</b>	<b>Overall</b>
<b>Child's age at early adolescence visit, years (mean ± SD)</b>	13.0±0.7	13.0±0.7	13.0±0.8	13.0±0.7
<b>Child's sex % female</b>	44.1	46.5	49.7	47.0
<b>Mother's race/ethnicity % White</b>	55.2	81.0	85.1	74.6
<b>Mother's education % ≥college graduate</b>	60.1	79.6	87.4	76.5
<b>Father's education % ≥college graduate</b>	52.4	68.3	84.6	69.6
<b>Household income % &gt;US\$70,000 per year</b>	43.4	67.6	85.7	67.0
<b>Census tract median household income (US\$) (mean ± SD)</b>	45,994±15,172	62,766±17,278	68,063±22,220	59,567±20,932
<b>HOMA-IR (mean ± SD) at early adolescence</b>	3.1±1.9	2.9±1.7	3.1±2.5	3.1±2.1

<sup>a</sup>Table based on observed data (N=460).

**Table 2.**

Adjusted linear regression coefficients and 95% confidence intervals for early life exposure to NDVI within a 90 m, 270 m, and 1230 m buffers and HOMA-IR at early adolescence in Project Viva<sup>b</sup>

	<b>Infancy</b>	<b>Early childhood</b>	<b>Mid-childhood</b>	<b>Early adolescence</b>
	<b>Difference (95%CI)</b>	<b>Difference (95%CI)</b>	<b>Difference (95%CI)</b>	<b>Difference (95%CI)</b>
<b>90m Buffer</b>				
<b>Tertile 1</b> (N=36,112)	0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
<b>Tertile 2</b> (N=36,314)	-0.03 (-0.11, 0.05)	0.04 (-0.08, 0.16)	-0.04 (-0.14, 0.06)	0.01 (-0.09, 0.13)
<b>Tertile 3</b> (N=35,583)	-0.03 (-0.14, 0.08)	0.08 (-0.09, 0.27)	-0.01 (-0.13, 0.13)	0.03 (-0.11, 0.20)
<b>270m Buffer</b>				
<b>Tertile 1</b> (N=36,106)	0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
<b>Tertile 2</b> (N=35,943)	-0.02 (-0.12, 0.08)	0.00 (-0.11, 0.13)	-0.01 (-0.12, 0.11)	0.02 (-0.10, 0.15)
<b>Tertile 3</b> (N=35,960)	0.00 (-0.11, 0.12)	0.05 (-0.11, 0.23)	-0.01 (-0.15, 0.15)	0.00 (-0.15, 0.18)
<b>1230m Buffer</b>				
<b>Tertile 1</b> (N=36,079)	0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
<b>Tertile 2</b> (N=35,992)	0.01 (-0.09, 0.11)	0.02 (-0.09, 0.15)	-0.06 (-0.17, 0.06)	-0.01 (-0.13, 0.12)
<b>Tertile 3</b> (N=35,938)	0.01 (-0.10, 0.15)	0.07 (-0.10, 0.26)	-0.14 (-0.26, 0.00)	-0.02 (-0.16, 0.15)
<b>P for linear trend at 90m Buffer</b>	0.48	0.36	0.92	0.57

<sup>b</sup>All models adjusted for child age and sex, mother's race/ethnicity and education, father's education, household income and median household income. Later exposure timepoints additionally adjusted for early exposure timepoints. For example, NDVI in early adolescence adjusted for NDVI in infancy, early childhood, and mid-childhood.