Original Research Article

ENVIRONMENTAL EPIDEMIOLOGY

OPEN

Residential proximity to green space and preeclampsia in California

Kari A. Weber[a], Evan Lyons[b], Wei Yang[a], Charlotte Stevenson[c], David K. Stevenson[a], Gary M. Shaw[a]

Background: We investigated whether residing near more green space might reduce the risk of preeclampsia.
Methods: Participants were women who delivered a live, singleton birth between 1998 and 2011 in eight counties of the San Joaquin Valley in California. There were 7276 cases of preeclampsia divided into mild, severe, or superimposed on preexisting hypertension. Controls were 197,345 women who did not have a hypertensive disorder and delivered between 37 and 41 weeks. Green space was estimated from satellite data using Normalized Difference Vegetation Index (NDVI), an index calculated from surface reflectance at the visible and near-infrared wavelengths. Values closer to 1 denote a higher density of green vegetation. Average NDVI was calculated within a 50 m, 100 m, and 500 m buffer around each woman's residence. Odds ratios and 95% confidence intervals were estimated comparing the lowest and highest quartiles of mean NDVI to the interquartile range comparing each preeclampsia phenotype, divided into early (20–31 weeks) and late (32–36 weeks) preterm birth, to full-term controls.
Results: We observed an inverse association in the 500 m buffer for women in the top quartile of NDVI and a positive association for women in the lowest quartile of NDVI for women with superimposed preeclampsia. There were no associations in the 50 and 100 m buffers.
Conclusion: Within a 500 m buffer, more green space was inversely associated with superimposed preeclampsia. Future work should explore the mechanism by which green space may protect against preeclampsia.

Keywords: Preeclampsia; Hypertension; Green space; Preterm birth; NDVI; Pregnancy

Introduction

Residential proximity or access to green space, which can include trees, grass or other type of vegetation, has been positively associated with various health outcomes.[1,2] Proposed potential mechanisms include reduced stress, less exposure to noise, reduction in heat, physical activity opportunities, and air pollution abatement.[3] Studies of pregnancy health and offspring outcomes have observed mixed results.[4–11] Few studies, however, have examined the association of green space with preeclampsia, a major cause of maternal and neonatal mortality and a substantial contributor to preterm birth.[12,13]

In the United States, 3%–5% of pregnant women are diagnosed with preeclampsia, a hypertensive disorder of pregnancy, traditionally defined as a combination of high blood pressure and proteinuria after 20 weeks of pregnancy.[13,14] Preeclampsia is known to be associated with characteristic placental pathology, but etiologies are not fully understood.[15] There are few known risk factors besides obesity, preexisting hypertension, diabetes mellitus, and preeclampsia in a previous pregnancy.[13,15] One causal theory for preeclampsia is that abnormal placentation produces vascular compromise resulting in placental ischemia and oxidative stress.[16] Exposure to green space as a direct effect (e.g., decreased air pollution) or as a proximal effect (e.g., reduced stress or more physical activity) may be an important factor that could potentially be modified to alter the population burden of preeclampsia.

Using a unique geographical area in the San Joaquin Valley of California, with a large and diverse population, we sought to determine if residential proximity to more green space may reduce the risk of preeclampsia.

[a]Department of Pediatrics, Division of Neonatal and Developmental Medicine, Stanford University School of Medicine, Stanford, California; [b]Department of Earth System Science, Stanford University, Stanford, California; and [c]Freelance Science Writer, Sun Valley, Idaho.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of the article.

The results reported herein correspond to specific aims of grant F32HD096754 to investigator KAW from the Eunice Kennedy Shriver National Institute of Child Health & Human Development. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health. This work was also supported by the March of Dimes Prematurity Research Center at Stanford University.

The data are publicly available from the Office of Statewide Health Planning and Development (OSHPD). The data are not available for replication because specific approvals from OSHPD and the California Committee for the Protection of Human Subjects must be obtained in order to access them.

SDC *Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.environepidem.com).*

**Correspondence Author. Address: Department of Pediatrics, Stanford University School of Medicine, 1265 Welch Road x1C21, Stanford, CA 94305, USA. E-mail: kaweber@stanford.edu (K.A. Weber)*

Environmental Epidemiology (2020) 4:e120

Received: 17 June 2020; Accepted 15 September 2020

Published online 21 October 2020

DOI: 10.1097/EE9.0000000000000120

What this study adds

Health benefits of living near green space are being discovered. Few studies have explored such benefits for pregnancy health. We identified a lower odds of a specific preeclampsia phenotype for women residing near a higher density of green space. This work adds to the evidence of the potential benefits of green space interventions, especially for pregnant women and the developing fetus.

Methods

Study population

Data were from 892,088 live births delivered in California between 1998 and 2011 to women who resided in the eight counties of the San Joaquin Valley (Fresno, Kern, Kings, Madera, Merced, San Joaquin, Stanislaus, and Tulare). After excluding births not consistent with eligibility criteria (singleton, 20–41 weeks gestational age, and birth weights between 500 and 5000 g), there were 771,416 births. A case–control study of preterm births in this population was performed previously.[17] In that study, for analytic efficiency, all 78,421 preterm births (<37 weeks gestation) were selected along with a randomly selected subset of 235,263 term births (>37 weeks gestation). Maternal residential addresses for these 313,684 births were obtained from birth certificates and geocoded using the REST API Geocode Service at the California Department of Public Health Information Technology Services Division. After addresses were standardized, verified, and corrected, 295,387 maternal residences were successfully geocoded (94%).

The geocoded residences were additionally linked with maternal and infant hospital discharge data from the Office of Statewide Health and Planning, and linkage was successful for 293,044 records (99%). The data included maternal and infant demographic data, as well as clinical data from the delivery for nearly all inpatient live births in California. The linkage algorithm has been validated and described previously.[18,19]

A subset of the case–control dataset was further used to specifically investigate preeclampsia among the women who delivered preterm.[20] That is, only women who delivered a preterm infant and were diagnosed with preeclampsia were included as cases. Women diagnosed with preeclampsia who delivered at term were excluded from the study (2% of the controls). Preeclampsia was identified from hospitalization records using the *International Classification of Diseases, 9th Revision, Clinical Modification* codes. Women were classified into three preeclampsia phenotypes: mild preeclampsia (642.4), severe preeclampsia/eclampsia (642.5, 642.6), and preeclampsia or eclampsia superimposed on preexisting hypertension (642.7). Women with multiple codes for a hypertensive disorder were reclassified to create mutually exclusive groups. Women with a preexisting hypertension code (401–405, 642.0, 642.1, 642.2, 642.9) and a preeclampsia code were reclassified as having preeclampsia superimposed on preexisting hypertension and those with multiple preeclampsia codes were reclassified as having the most severe condition. Within these phenotypic groups, women were further stratified by gestational age at delivery into early preterm (20–31 weeks) and late preterm (32–36 weeks). These phenotypic subgroups were specified owing to potential etiologic differences by severity of preeclampsia and gestational age at delivery. Women who delivered in the study period who did not have diabetes (gestational or preexisting), did not have any hypertensive disorder, and who delivered between 37 and 41 weeks served as the reference population. After exclusion of women missing green space or pesticide data, the final sample included 7276 cases and 197,345 controls (Figure 1).

Green space estimation

Green space was estimated using the Normalized Difference Vegetation Index (NDVI). NDVI is the normalized difference between visible and near-infrared region (NIR) wavelengths reflected by the earth's surface and ranges from −1 to 1, with values closer to 1 denoting a higher density of green.[21]

$$\text{NDVI} = (\text{NIR} - \text{Red}) / (\text{NIR} + \text{Red})$$

We used Google Earth Engine[22] to create images of annual maximum NDVI from cloud-masked Landsat images at 30 m spatial resolution. We used Landsat 7 Enhanced Thematic Mapper Plus (ETM+) Collection 1 Tier 1 top of atmosphere reflectance for the years 2000–2002 (SLC-on) and Landsat 5 TM Collection 1 Tier 1 top of atmosphere reflectance for all other study years, courtesy of the US Geological Survey.[23] We then calculated the average maximum NDVI with 30 m resolution separately for each year and assigned values based on year of conception. Maximum NDVI was obtained from Google Earth Engine by masking pixels obstructed by cloud cover and using the image with peak vegetation, the "greenest" time of that year. Participants were assigned NDVI values based on the estimated date of conception of their infant.

Using ArcGIS (ESRI, Release 10.6.1. Redlands, CA), we then linked each birth with the corresponding file from Google Earth Engine for the year of conception using the geocoded addresses. For each maternal residence, average NDVI was calculated within a 50, 100, and 500 m concentric buffer. For example, for a woman's home, an NDVI value would be assigned for the greenness within a circle with a 500 m radius from it. Within that circle, there would be two additional circles, one with a 100 m radius and one with a 50 m radius within that. There may be different values if, for example, there was a large park or forest further than 100 m away but within the 500 m buffer and not much greenness very close to the woman's home. Then the 500 m buffer NDVI may be much higher than the 50 m buffer. US Geological Survey considers an NDVI of 0.6–0.9 to be high or the equivalent of living in a forest at peak growth.

Statistical analysis

Distributions of maternal and infant characteristics were examined by case/control status, and cases were further divided into preeclampsia phenotype. The range of average green space within the three residential buffers was also determined separately for controls and each case phenotype. For each buffer (50, 100, and 500 m), the average NDVIs were divided into quartiles with cutoff values determined among controls. Using logistic regression, odds ratios and 95% confidence intervals were estimated comparing the lowest and highest quartiles to the interquartile range and comparing the highest quartile to the lowest quartile. Odds ratios and 95% confidence intervals were calculated comparing each preeclampsia phenotype, divided into early (20–31 weeks) and late (32–36 weeks) preterm birth, to full-term controls. Odds ratios were also calculated combining early and late preterm for each preeclampsia phenotype. The average NDVI for each buffer was examined in continuous form, with odds ratios and 95% confidence intervals representing change in odds for one interquartile range (interquartile region) change in density of green space, and *P* trends were calculated. Finally, a sensitivity analysis was performed comparing those residing within buffers with greater than a 0.6 average NDVI to those with less than 0.6. Analyses were unadjusted and adjusted for covariates determined a priori to be potential confounders. Covariates included maternal age (years), race/ethnicity (white non-Hispanic, US-born Hispanic, foreign-born Hispanic, black, other), education (less than high school, high school diploma, more than high school), parity (1, ≥2), insurance payer type for the delivery (Medi-Cal, private, other), and season of conception (winter, spring, summer, fall). We used complete case analysis, and women missing one of the covariates adjusted for were excluded from analysis.

Pesticide data were available from the larger case–control study from which this analysis derives.[17] Thus, as an additional exploratory analysis, we included these data as covariates in some specific analyses. Briefly, pesticide data included 543 chemicals and 69 physiochemical groupings that were applied at >100 lb and considered potential reproductive toxicants based on Environmental Protection Agency's risk assessment and California Proposition 65 list or were classified as endocrine disruptors.[24] Case and control women's exposure was assigned using the California Environmental Health Tracking Program Pesticide Linkage Tool, a custom-developed Java application

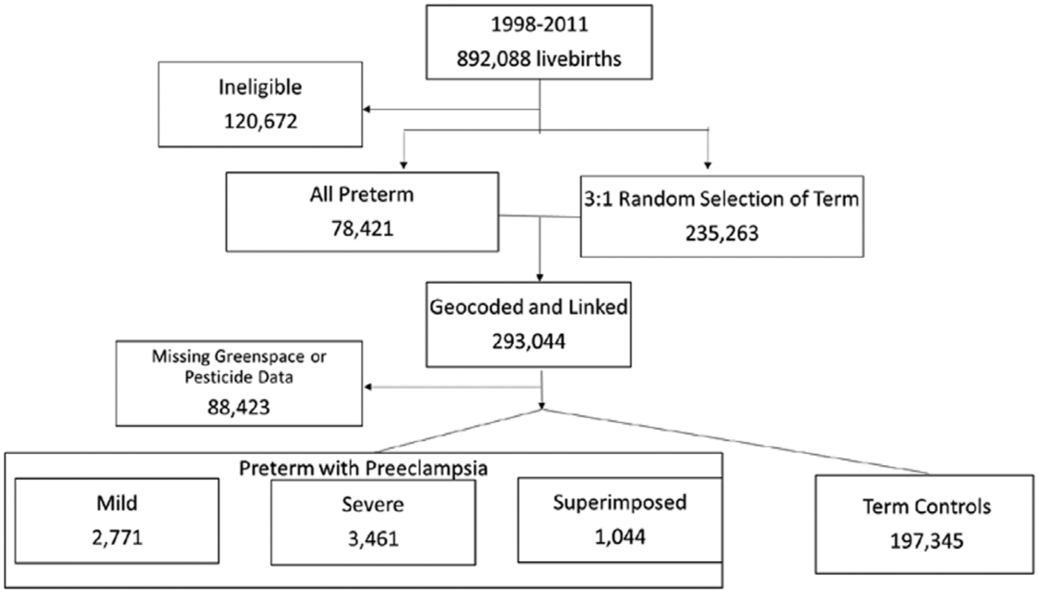

Figure 1. Sampling procedure.

(Oracle, Redwood Shores, CA), within a 500 m radius of each residence.

For the exploratory analysis, we estimated potential modification of the association between green space and preeclampsia by exposure to pesticides. Pesticide exposure was divided into 0 vs. ≥1 for the sum of total number of chemicals based on our previous analysis.[20] Using NDVI results from the 500 m buffer, for those in the lowest 25th percentile and those in the highest 75th percentile, we stratified by any exposure to a pesticide.

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

This study was approved by the Stanford University Institutional Review Board and the California State Committee for the Protection of Human Subjects.

Results

Characteristics of cases and controls are presented in Table 1. Among the 7276 cases, 2771 were considered to have mild, 3461 severe, and 1044 to have superimposed preeclampsia. Among those with preeclampsia, women were more likely to be older than 35 years, and women with superimposed preeclampsia were more likely to be aged 30 years and older and less likely to be younger than 25 years compared with controls. Cases were less likely to be foreign-born Hispanic but more likely to be US-born Hispanic or black compared to controls. Cases with mild or severe preeclampsia were more likely to be nulliparous than controls and case women with superimposed preeclampsia tended to have more education than controls. There was not much variation by payer type or season of conception except slightly more fall conceptions among women with superimposed preeclampsia.

For all cases and controls, the median average NDVI was roughly 0.3 for all buffer sizes. As shown in Table 2, minimum NDVIs ranged from 0.04 to 0.1, with the 25th percentile value of about 0.25 for each case phenotypic group as well as for controls. In the 50th and 75th percentiles, there was more variation. Among each 50, 100, or 500 m buffer, controls had a higher average NDVI than did cases (Table 2). Among controls, average NDVIs within the 50 and 100 m buffers were strongly correlated (r = 0.9) and average NDVIs within 100 and 500 m were moderately correlated (r= 0.7) as well as 50 and 500 m (r = 0.6; results not shown).

Table 1.

Descriptive characteristics (percentages)[a] of 7276 women with preeclampsia (cases) who delivered preterm (20–36 weeks) and 197,345 women (controls)[b] who delivered full term (37–41 weeks), California, 1998–2011

	Cases by sub-phenotype			
	Mild (n = 2,771)	Severe (n = 3,461)	Superimposed (n = 1,044)	Controls (n = 197,345)
Age (y)				
<20	17	17	3	14
20–24	27	27	16	30
25–29	24	24	24	28
30–34	18	18	30	18
≥35	14	14	28	10
Missing	<0.1	0.0	0.0	<0.1
Race/ethnicity				
White, non-Hispanic	29	25	25	29
US-born Hispanic	34	35	33	28
Foreign-born Hispanic	23	25	19	29
Black, non-Hispanic	6.4	5.9	12	4.5
Other	7.5	8.5	10	8.6
Missing	0.7	0.8	1.1	0.6
Education				
Less than high school	29	29	24	33
High school	33	32	30	32
More than high school	37	37	44	34
Missing	2.0	2.3	2.1	1.6
Parity				
1	53	57	32	35
≥2	47	43	68	65
Missing	0.1	0.1	0.1	0.1
Payer type for delivery				
Medi-Cal	58	57	55	57
Private	38	39	41	40
Other	3.0	4.2	3.5	3.2
Missing	0.3	0.2	0.2	0.2
Season of conception				
Winter (Dec–Feb)	24	25	24	26
Spring (March–May)	26	24	25	25
Summer (June–Aug)	25	26	22	24
Fall (Sep–Nov)	25	25	29	25

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

[b]Defined as women who delivered in the study period who did not have diabetes (gestational or preexisting), did not have any hypertensive disorder, and delivered between 37 and 41 weeks.

Association between average NDVI within the 50, 100, and 500 m buffers and each preeclampsia phenotype is presented in Table 3. Odds ratios for unadjusted models (Model 1), those adjusted for season of conception (Model 2), and those additionally adjusted for maternal age, race/ethnicity, education, parity, and payer source for care (Model 3) were similar, thus only results from Model 3 were presented to include all a priori confounders. Overall, associations for the 50 and 100 m buffers were essentially null when comparing lowest or highest quartiles to the interquartile range and comparing the lowest to the highest quartiles. There were also no significant trends though the trend for the late preterm superimposed cases approached significance. We did observe associations in the 500 m buffer for cases with superimposed preeclampsia and for late preterm mild and severe preeclampsia cases. For superimposed preeclampsia, we observed an inverse association for early preterm births for women in the top 75% of NDVI compared to the middle 50% as well and for later preterm births for women with mild and severe preeclampsia. When comparing the highest to the lowest quartile, we observed similar associations and significant *P* trends for the later preterm births for all phenotypes and early preterm births for superimposed preeclampsia. When comparing women living in a buffer with an NDVI greater than 0.6 to less than 0.6, there were lower odds of both severe and superimposed preeclampsia in all , though the results only reached significance for severe preeclampsia in the 500 m buffer and superimposed in the 100 m buffer (results not show). When combining early and late preterm births comparing the lowest to the highest quartile of NDVI, patterns were similar with slight inverse associations for all phenotypes and significant trends for all phenotypes in the 500 m buffer (results not shown).

We investigated whether residential proximity characterized by pesticide exposures altered the observed green space results. Supplemental Table 1 (http://links.lww.com/EE/A108) presents adjusted odds ratios for preeclampsia phenotypes and average NDVI in a 500 m buffer around a woman's residence by exposure to any chemical group of pesticide. For women exposed to more chemicals, there were somewhat higher odds of mild preeclampsia and early preterm birth. The protective pattern of green space for superimposed preeclampsia and early preterm birth also remained, regardless of the presence of pesticides. Overall, we did not observe many differences in the associations between green space and preeclampsia by differences in exposure to pesticides.

Discussion

For green space within a 500 m buffer, as hypothesized, we observed an inverse association for superimposed preeclampsia and slight inverse associations for the mild and severe phenotypes. That is, having a higher percentage of green space surrounding their residences was inversely associated with preeclampsia. We did not observe these associations within smaller buffers and only modest associations for milder forms for preeclampsia, which may indicate the relevant mechanisms. We did observe potential effect modification of the association between pesticide exposure and mild preeclampsia by the amount of surrounding green space in the direction we expected, that is, odds were higher for those exposed to lower amounts of green space.

A previous study of green space and preeclampsia did not observe an association.[10] However, that study combined all potentially heterogeneous preeclampsia phenotypes as a single outcome—here we observed the strongest associations among the superimposed preeclampsia phenotype. Given that our results may be driven by preexisting hypertension in the superimposed cases, it is possible that the underlying connection could be an association with blood pressure. Studies have examined the relationship between green space and blood pressure with conflicting results, although a meta-analysis reported an inverse association between green space and diastolic blood pressure.[1]

We did observe slightly different results for different buffer sizes. The proportion of green space in various buffers would seem to measure different aspects of what could be posited as different mechanisms. For example, the 500 m buffer was based on a previous study that observed a median walking time of 37 minutes/day and found pregnant women to walk roughly 4 km/hour.[25] A review of green space and physical activity studies found that buffer sizes between 500 and 1999 m were the best predictors of physical health based on being able to cover 2000 m walking at a moderate pace for 20 minutes.[26] This would suggest that larger buffers are better measures for the effects of physical activity, and this may point to a potential explanation for the observed association here. Studies have also observed health effects within smaller buffers as well, but with different measures of green space. One study observed a reduction in small-for-gestational age infants with an increase in tree canopy within a 50 m buffer.[27] Using tree canopy as a measure may point to possible mechanisms like heat or noise abatement. While we did not observe significant associations in our study, it is possible that other measures of green space beyond NDVI, such as tree canopy or proximity to specific land use or amenities like parks, may offer different results and warrants further research. An additional consideration is that overlapping buffers

Table 2.

Distribution of average NDVI among women with each preeclampsia phenotype and controls, by buffer distance surrounding participant residences, California, 1998–2011

	Buffer (m)	Minimum	25th Percentile	50th Percentile	75th Percentile	Maximum
Cases						
Superimposed	50	0.07	0.24	0.29	0.35	0.84
	100	0.08	0.25	0.30	0.35	0.64
	500	0.10	0.27	0.32	0.37	0.74
Severe	50	0.06	0.24	0.30	0.35	0.97
	100	0.08	0.26	0.30	0.36	0.77
	500	0.08	0.28	0.32	0.38	0.75
Mild	50	0.04	0.25	0.30	0.35	0.87
	100	0.05	0.26	0.30	0.36	0.73
	500	0.09	0.28	0.32	0.38	0.74
Controls	50	0.04	0.25	0.30	0.35	0.99
	100	0.05	0.26	0.31	0.36	0.85
	500	0.08	0.28	0.33	0.39	0.80

NDVI, normalized difference vegetation index.

Table 3.

Adjusted[a] odds ratios and 95% confidence intervals for the association between density of green space (average NDVI) within 50, 100, and 500 m buffers surrounding participant residences and preeclampsia phenotypes, California, 1998–2011

	Mild (20–31 weeks) (n = 190)	Mild (32–36 weeks) (n = 2512)	Severe (20–31 weeks) (n = 792)	Severe (32–36 weeks) (n = 2576)	Superimposed (20–31 weeks) (n = 257)	Superimposed (32–36 weeks) (n = 759)
50 m buffer	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
≤0.25	1.0 (0.72, 1.5)	1.0 (0.91, 1.1)	0.94 (0.79, 1.1)	1.0 (0.94, 1.1)	0.93 (0.69, 1.3)	1.1 (0.91, 1.3)
0.25–≤0.35	Reference	Reference	Reference	Reference	Reference	Reference
>0.35	1.1 (0.79, 1.6)	0.92 (0.83, 1.0)	0.85 (0.72, 1.0)	0.94 (0.85, 1.0)	0.90 (0.67, 1.2)	0.89 (0.74, 1.1)
>75% vs. ≤25%	1.1 (0.73, 1.6)	0.91 (0.82, 1.0)	0.91 (0.74, 1.1)	0.91 (0.82, 1.0)	0.97 (0.68, 1.4)	0.83 (0.67, 1.0)
Continuous, 1 IQR[b]	0.98 (0.84, 1.1)	0.98 (0.94, 1.0)	0.96 (0.89, 1.0)	0.98 (0.94, 1.0)	0.97 (0.85, 1.1)	0.93 (0.86, 1.0)
P trend	0.8	0.3	0.4	0.3	0.7	0.07
100 m buffer						
≤0.26	0.89 (0.62, 1.3)	1.0 (0.94, 1.1)	1.0 (0.86, 1.2)	0.97 (0.88, 1.1)	1.0 (0.78, 1.4)	1.08 (0.91, 1.3)
0.26–≤0.36	Reference	Reference	Reference	Reference	Reference	Reference
>0.36	0.95 (0.67, 1.4)	0.94 (0.85, 1.0)	1.00 (0.84, 1.2)	0.95 (0.86, 1.0)	0.84 (0.61, 1.2)	0.97 (0.81, 1.2)
(>75% vs. ≤25%)	1.1 (0.71, 1.6)	0.90 (0.81, 1.0)	0.98 (0.80, 1.2)	0.98 (0.88, 1.1)	0.81 (0.57, 1.2)	0.90 (0.73, 1.1)
Continuous, 1 IQR[b]	0.99 (0.85, 1.2)	0.96 (0.92, 1.0)	0.98 (0.90, 1.1)	0.97 (0.93, 1.0)	0.89 (0.77, 1.0)	0.93 (0.85, 1.0)
P trend	0.9	0.1	0.6	0.2	0.1	0.06
500 m buffer						
≤0.28	0.98 (0.69, 1.4)	1.1 (0.98, 1.2)	1.0 (0.86, 1.2)	1.0 (0.92, 1.1)	0.83 (0.62, 1.1)	1.4 (1.2, 1.6)
0.28–≤0.39	Reference	Reference	Reference	Reference	Reference	Reference
>0.39	1.0 (0.71, 1.4)	0.90 (0.82, 1.0)	0.91 (0.76, 1.1)	0.91 (0.83, 1.0)	0.48 (0.33, 0.69)	1.0 (0.85, 1.2)
(>75% vs. ≤25%)	1.0 (0.69, 1.6)	0.84 (0.75, 0.94)	0.89 (0.73, 1.1)	0.90 (0.81, 1.0)	0.58 (0.38, 0.88)	0.74 (0.61, 0.90)
Continuous, 1 IQR [b]	0.99 (0.83, 1.2)	0.94 (0.90, 0.99)	0.93 (0.86, 1.0)	0.93 (0.89, 0.98)	0.81 (0.69, 0.95)	0.86 (0.78, 0.94)
P trend	0.9	0.01	0.1	0.003	0.01	0.0009

CI, confidence interval; NDVI, normalized difference vegetation index; OR, odds ratio.

[a]Adjusted for maternal age (years), race/ethnicity (non-Hispanic White, US-born Hispanic, foreign-born Hispanic, non-Hispanic Black, other), education (less than high school, high school, more than high school), parity 1, and ≥2, payer source for care (Medi-Cal, private, other), season of conception (Winter, Spring, Summer, Fall).

[b]ORs represent change in odds for a 1-IQR change in density of green space.

cannot be directly compared since they are not mutually exclusive,[26] and if the purpose of future work is to examine associations comparing different buffers, nested analyses would need to be undertaken.

We also performed an exploratory analysis building upon our investigation for risks of preeclampsia phenotypes with residential pesticide exposure.[20] Our previous analyses, overall, did not reveal positive associations. We did observe some enigmatic inverse associations with greater exposure to pesticides, especially among cases with superimposed preeclampsia. We hypothesized that this may have been due to unobserved fetal loss or "depletion of susceptibles," meaning that fetuses exposed to the highest levels of harmful substances may be miscarried before they are able to be born preterm. In this project, we explored the possibility that a previously unmeasured factor may alternatively explain those results, that is, residential proximity to green space. Our results did not explain the seemingly protective nature of pesticides because where a protective association was observed, it did not differ by pesticide exposure. However, these results should be interpreted with caution given the small numbers in many cells.

This study was performed in a very large and diverse population in California. The eight counties in the San Joaquin Valley encompass a variety of terrains including many rural and urban areas of varying socioeconomic status. Additionally, we were able to link many of the abundant registry resources in California with our green space measurements. Despite our large sample size, many of our outcomes are very rare, and thus we were unable to calculate some of our results, specifically in our exploratory analysis. Much of our data were from satellites and registries where spatial extrapolation was necessary to determine exposure indirectly. Additionally, depending on the proposed mechanism of green space benefit, we cannot determine direct exposure or utilization of green space, just proximity. For example, physical activity benefits of a park only exist if one uses the park for exercise. However, for these beginning stages of research into the potential effects of green space on preeclampsia, our work can generate hypotheses into the potential mechanisms by which green space may alter the population burden of preeclampsia.

The United Nations estimates that 68% of the world's population will live in an urban setting by the year 2050, a sharp increase since 1950 when just 30% was urban.[28] While our population resided in both urban and rural settings, in the rapidly changing landscape of human life, it is necessary to evaluate the health impacts of various aspects of the modern natural and built environments people currently occupy. According to The Trust for Public Land, a US-based nonprofit organization, 100 million Americans do not have a green space within a 10-minute walk from home.[29] However, even within dense urban environments, creative solutions are arising from collaboration between cities, nonprofits, and health advocates. For example, in 2015, the City of Chicago completed a collaborative project called "The 606," which converted three miles of unused rail line into a greenway with attached parks and trails. With more precise data on the nature of the relationship between green space and preeclampsia, future urban green space projects could take these data and parameters into account. In this changing landscape, pregnant women and their developing fetuses are a particularly vulnerable population that deserves attention. Future work in this area should be multidisciplinary and expand to different types of green space, different terrains and climates, and additional methods to determine the mechanism of green space that may protect against preeclampsia.

Acknowledgments

We thank Dr. Paul English and the California Environmental Health Tracking Program for the scientific contributions on pesticide exposure assessment.

Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

References

1. Twohig-Bennett C, Jones A. The health benefits of the great outdoors: a systematic review and meta-analysis of greenspace exposure and health outcomes. Environ Res. 2018;166:628–637.
2. Urban Green Spaces and Health. Copenhagen, Denmark: WHO Regional Office for Europe; 2016.
3. Markevych I, Schoierer J, Hartig T, et al. Exploring pathways linking greenspace to health: theoretical and methodological guidance. Environ Res. 2017;158:301–317.
4. Banay RF, Bezold CP, James P, Hart JE, Laden F. Residential greenness: current perspectives on its impact on maternal health and pregnancy outcomes. Int J Womens Health. 2017;9:133–144.
5. Agay-Shay K, Peled A, Crespo AV, et al. Green spaces and adverse pregnancy outcomes. Occup Environ Med. 2014;71:562–569.
6. Casey JA, James P, Rudolph KE, Wu CD, Schwartz BS. Greenness and birth outcomes in a range of Pennsylvania communities. Int J Environ Res Public Health. 2016;13:311.
7. Dadvand P, Wright J, Martinez D, et al. Inequality, green spaces, and pregnant women: roles of ethnicity and individual and neighbourhood socioeconomic status. Environ Int. 2014;71:101–108.
8. Ebisu K, Holford TR, Bell ML. Association between greenness, urbanicity, and birth weight. Sci Total Environ. 2016;542(pt A):750–756.
9. Hystad P, Davies HW, Frank L, et al. Residential greenness and birth outcomes: evaluating the influence of spatially correlated built-environment factors. Environ Health Perspect. 2014;122:1095–1102.
10. Laurent O, Wu J, Li L, Milesi C. Green spaces and pregnancy outcomes in Southern California. Health Place. 2013;24:190–195.
11. Kihal-Talantikite W, Padilla CM, Lalloué B, Gelormini M, Zmirou-Navier D, Deguen S. Green space, social inequalities and neonatal mortality in France. BMC Pregnancy Childbirth. 2013;13:191.
12. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet. 2008;371:75–84.
13. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. Lancet. 2016;387:999–1011.
14. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. BMJ. 2013;347:f6564.
15. Redman CW, Sargent IL. Immunology of pre-eclampsia. Am J Reprod Immunol. 2010;63:534–543.
16. Redman CW, Sargent IL, Staff AC. IFPA senior award lecture: making sense of pre-eclampsia - two placental causes of preeclampsia? Placenta. 2014;35(suppl):S20–S25.
17. Shaw GM, Yang W, Roberts EM, et al. Residential agricultural pesticide exposures and risks of spontaneous preterm birth. Epidemiology. 2018;29:8–21.
18. Herrchen B, Gould JB, Nesbitt TS. Vital statistics linked birth/infant death and hospital discharge record linkage for epidemiological studies. Comput Biomed Res. 1997;30:290–305.
19. Lyndon A, Lee HC, Gilbert WM, Gould JB, Lee KA. Maternal morbidity during childbirth hospitalization in California. J Matern Fetal Neonatal Med. 2012;25:2529–2535.
20. Shaw GM, Yang W, Roberts EM, et al. Residential agricultural pesticide exposures and risks of preeclampsia. Environ Res. 2018;164:546–555.
21. Tucker CJ. Red and Photographic Infrared Linear Combinations for Monitoring Vegetation. United States: NASA Center for Aerospace Information (CASI); 1978.
22. Gorelick N, Hancher M, Dixon M, Ilyushchenko S, Thau D, Moore R. Google earth engine: planetary-scale geospatial analysis for everyone. Remote Sensing Environ. 2017;202:18–27.
23. Williams DL, Goward S, Arvidson T. Landsat: yesterday, today, and tomorrow. Photogramm Eng Remote Sensing. 2006;72:1171–1178.
24. European-Commission. Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption. 10 November 2000. Available at: https://ec.europa.eu/environment/archives/docum/pdf/bkh_main.pdf. Accessed 3 January 2020.
25. Dadvand P, de Nazelle A, Figueras F, et al. Green space, health inequality and pregnancy. Environ Int. 2012;40:110–115.
26. Browning M, Lee K. Within what distance does "Greenness" best predict physical health? A systematic review of articles with GIS buffer analyses across the lifespan. Int J Environ Res Public Health. 2017;14:675.
27. Donovan GH, Michael YL, Butry DT, Sullivan AD, Chase JM. Urban trees and the risk of poor birth outcomes. Health Place. 2011;17:390–393.
28. United Nations, Department of Economic and Social Affairs, Population Division. World Urbanization Prospects:The 2018 Revision (ST/ESA/SER.A/420). New York, NY: United Nations; 2019.
29. The Trust for Public Land. 2018 City Park Facts. 2018. Available at: www.tpl.org/cityparkfacts. Accessed 3 January 2020.