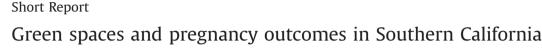
Contents lists available at ScienceDirect

Health & Place

journal homepage: www.elsevier.com/locate/healthplace



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ARTICLE INFO

Article history: Received 10 June 2013 Received in revised form 25 September 2013 Accepted 25 September 2013 Available online 9 October 2013

Keywords: Green space Greenness Premature birth Birth weight Preeclampsia

1. Introduction

In a context of rapid urbanization at the global scale, there is growing interest in the relationships between green spaces and health (Bowler et al., 2010; Lee and Maheswaran, 2011; Maas et al., 2009). Greenness exposure has been associated with reductions in risks of various health outcomes, including self-perceived health (Maas et al., 2006; Mitchell and Popham, 2007), blood pressure (Agyemang et al., 2007) and mortality (Villeneuve et al., 2012). The causal nature of these associations is not established to date (Bowler et al., 2010; Lee and Maheswaran, 2011) and the biological mechanisms potentially in play are not clear, but possible pathways include reduction of exposure to noise, air pollution (Dadvand et al., 2012b) and urban heat (Jenerette et al., 2011), as well as stress relief (Fan et al., 2011; van den Berg et al., 2010). Such an array of modifications might also be beneficial to pregnancy outcomes.

So far, the relationships between greenness and pregnancy outcomes have been investigated in only three studies (Dadvand et al., 2012a, 2012c; Donovan et al., 2011). All reported increases in birth weight associated with exposure to greenness, and no association with the length of gestation (Dadvand et al., 2012a; 2012c; Donovan et al., 2011). These pioneering findings from studies of 2000 to 8000 subjects need confirmation, ideally from larger studies. No study has examined the relation between greenness and preeclampsia so far, although exposure to green spaces has been

ABSTRACT

Little is known about the impacts of green spaces on pregnancy outcomes. The relationship between green space exposure and preeclampsia has never been studied. We used a hospital-based perinatal database including more than 80,000 births to study the relationships between greenness exposure and three pregnancy outcomes: birth weight in term born infants, preterm deliveries and preeclampsia. Greenness was characterized using the normalized difference vegetation index (NDVI) within circular buffers surrounding maternal homes. Analyses were conducted using generalized estimating equations, adjusted for potential confounders. We observed an increase in birth weight in term born infants and a reduced risk of preterm births associated with an increase in NDVI. No significant association was observed between greenness and preeclampsia. This study provides modest support for beneficial effects of greenness exposure on pregnancy outcomes and calls for confirmation in other study settings.

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associated with decreases in blood pressure (Agyemang et al., 2007) and chronic hypertension is a risk factor for preeclampsia (Hutcheon et al., 2011).

This study examines the relation between greenness exposure and three pregnancy outcomes: birth weight, preterm deliveries and preeclampsia.

2. Methods

Neonatal records from 1997 to 2006 were extracted from a perinatal research database constituted by a network of four hospitals located in Los Angeles and Orange counties, in California, United States (Wu et al., 2009). Residential addresses of mothers at delivery were geocoded with a 93% success rate. Subjects missing important covariate information used in previous studies were excluded (12%) (Wu et al., 2009), as were multiple pregnancies (5%), leaving 81,186 subjects for analysis.

The normalized difference vegetation index (NDVI) (Tucker, 1979) was used to characterize greenness exposure (Dadvand et al., 2012c; Villeneuve et al., 2012). NDVI is the ratio of the difference between the near-infrared region and red reflectance to the sum of these two measures, calculated as follows:

NDVI = (band 4-band 3)/(band 4+band 3)

where band 4 and band 3 are the surface reflectances acquired by the near infrared and red bands, respectively, of Landsat sensors. We used a set of mostly cloud-free Landsat scenes from the Global Land Survey 2005 (GLS, United States Geological Survey) dataset covering Southern California. The GLS 2005 consists of orthorectified Landsat





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5 and gap-filled Landsat 7 data at a spatial resolution of 30 m acquired during the leaf-on season for the location. The GLS 2005 has acquisition dates from 2005 and 2006. Scenes of low quality or excessive cloud cover were replaced with scenes acquired in 2004, 2007 or 2008. All the Landsat scenes were processed for atmospheric correction and converted to surface reflectance with the Landsat Ecosystem Disturbance Adaptive Processing System (LEDAPS) algorithm (Masek et al., 2012) prior to calculating the normalized difference vegetation index (NDVI). Maternal exposure to greenness was estimated by calculating the average NDVI value in circular buffers of 50, 100 and 150 m radii around homes.

As part of previous studies, several indicators of exposure to air pollution were estimated, and found to be associated with pregnancy outcomes (Wu et al., 2011). They include traffic density in proximity to maternal homes (50, 150 or 300 m) and pollutant concentration measurements from the nearest monitoring station, for nitrogen oxides (NO_x), carbon monoxide (CO), ozone (O₃) and particulate matter of less than 10 or 2.5 µm in aerodynamic diameter (PM₁₀ and PM_{2.5}). Local traffic-generated NO_x concentrations were also estimated using the CALINE4 dispersion model (Benson, 1989). Pollutant concentrations were averaged across the whole pregnancy period (details available in a freely accessible publication (Wu et al., 2011)).

We studied the relations between exposure to greenness and (1) birth weight in infants born at term (\geq 37 weeks of gestation) (2) preterm birth (< 37 weeks of gestation) and (3) preeclampsia (defined as blood pressure > 140/90 mmHg and proteinuria or hemolysis, elevated liver enzyme levels, and low platelet count (HELLP) syndrome during pregnancy), using generalized estimating equations to take into account within-hospital correlations. We estimated (1) the mean change in birth weight and (2) odds ratios for preterm birth or preeclampsia, associated with an interquartile range (IQR) increase in NDVI exposure. We also conducted similar analyses by quartile of NDVI exposure, taking the lowest

exposure quartile as a reference. Analyses were conducted using the GENMOD procedure in SAS 9.3 (SAS Institute, Cary NC).

Models were adjusted for potential confounders selected on the basis of previous knowledge and exploratory data analyses. Maternal age, poverty (defined as the percentage of population living below the federal poverty line by Census Block Group of maternal residence) and length of gestation (the latter for the birth weight analyses only) were adjusted for using both linear and quadratic terms. Other potential confounders were introduced as categorical variables: maternal race/ethnicity, insurance status (public/private), parity (first child or not), infant's gender (birth weight analyses only), pyelonephritis (preterm birth analysis only) and diabetes (preeclampsia and birth weight analyses only). To evaluate the potential influence of air pollution on the relationships between greenness and pregnancy outcomes (that might be either confounding or mediating since greenness may reduce levels of air pollution (Novak, 2000)), we assessed the impact of further adjustment of the above models for our nine complementary air pollution indicators (introduced as linear variables, one at a time).

We explored the use of multiple imputation techniques (5 simulations) to impute missing values for the variables race/ethnicity (4% missing values) and insurance status (4% missing values). Since this had no major impact on the study results, we present results based on complete-case analyses.

This study has been approved by the Institutional Review Board of the University of California, Irvine.

3. Results

Table 1 describes the characteristics of the study population, separately for all births and for term births. Supplementary Material Table S1 describes the NDVI and air pollution variables and their correlations. In term born infants, significant increases in

Table 1

Characteristics of the study population from four Southern California hospitals, 1997–2006.

Subject characteristics	Number of infants	Number of preeclampsia cases	Number of preterm birth cases (< 37 weeks of gestation)	Number of term born infants	Mean birth weight in term born infants (in grams)
Infant's gender					
Female	39,274	1162	3110	36,133	3408
Male	41,912	1280	3602	38,283	3527
Age of mothers (in years)					
Less than 20	5,059	205	492	4,565	3345
20-39	72,257	2072	5789	66,418	3476
40 or more	3,870	165	431	3,433	3503
Race/ethnicity of mothers					
African American	7,153	280	891	6,261	3330
Asian	8,012	205	648	7,358	3315
Hispanic	26,061	868	2365	23,678	3469
Caucasian	32,754	900	2175	30,548	3542
Mixed	355	11	33	322	3473
Other	3,403	88	308	3,095	3413
Missing	3,448	90	292	3,154	3462
Insurance status of mothers					
Private	54,917	1547	3990	50,880	3491
Public	23,014	778	2481	20,525	3418
Missing	3,255	117	241	3,011	3460
Diabetes in mothers					
No	76,774	2158	6097	70,622	3463
Yes	4,412	284	615	3794	3582
Parity					
First delivery	66,175	2192	5743	60,382	3458
At least second delivery	15,011	250	969	14,034	3518

mean birth weight are associated with an IQR increase in NDVI exposure within 50 m and 100 m buffers (Table 2). Significance persists for the 50 m buffer after adjustment for air pollution indicators, but disappears for the 100 m buffer after adjustment for NO_x, O_3 or CO. Analyses by exposure quartile show a significant association in the upper quartile of NDVI exposure as measured within a 50 m buffer, which persists after adjustment for air pollution (Supplementary Material Table S2).

A significantly decreased risk of preterm birth is associated with an IQR increase in NDVI within 150 m buffers (Table 3). Significance disappears after adjustment for PM_{2.5} or traffic density. Conversely, significantly decreased risks are observed for 50 m and 100 m buffers only after adjustment for NO_x or CO. Analyses by exposure quartile reveal significantly decreased risks for the two upper quartiles of NDVI within the 100 and 150 m buffers, but an increase in the second quartile for the 100 m buffer. Significant or borderline significant ($p \le 0.06$) decreased preterm birth risks are observed for the highest quartile of NDVI within 150 m of home, even after adjusting for any air pollution indicator (Supplementary Material Table S3).

There is no significant association between an IQR increase in NDVI and preeclampsia with and without adjustment for air pollution indicators (Table 4).

4. Discussion

We observed a modest increase "in" birth weight and a slightly reduced risk "of" preterm birth associated with greenness surrounding maternal homes. No consistent association was observed for preeclampsia.

Our finding of increased birth weights associated with greenness exposure is consistent with previous studies (Dadvand et al., 2012a, 2012c; Donovan et al., 2011). However, in our study the most robust findings are limited to a 50 m radius around homes, whereas Davdan et al. found increases in birth weight for NDVI up to 100 (Dadvand et al., 2012a) or 500 m (Dadvand et al., 2012c) (even after adjustment for NO₂ for the latter study). Donovan et al. (2011) reported results for a 50 m radius only, which were qualitatively similar to ours. To our knowledge our study is the first that shows a

Table 2

Change in mean birth weight per inter-quartile range increase in NDVI exposure, in term-born children (four hospitals in Southern California, 1997-2006).

	NDVI within 50 m buffers			NDVI within 10	NDVI within 100 m buffers			NDVI within 150 m buffers		
	Change in mean birth weight per IQR increase in NDVI ^c	95% Confidence interval	р	Change in mean birth weight per IQR increase in NDVI ^c	95% Confidence interval	р	Change in mean birth weight per IQR increase in NDVI ^c	95% Confidence interval	р	
Base model ^a	6.09	(3.11, 9.06)	< 0.01	1.43	(0.01, 2.84)	0.05	0.54	(-1.29, 2.38)	0.56	
Base model ^a , further adjusted for NO _x ^b	4.83	(1.93, 7.72)	< 0.01	0.68	(-0.79, 2.15)	0.36	-0.20	(-2.04, 1.64)	0.83	
Base model ^a , further adjusted for PM ₁₀ ^b	6.08	(2.95, 9.21)	< 0.01	1.66	(0.26, 3.07)	0.02	0.90	(-0.75, 2.56)	0.29	
Base model ^a , further adjusted for PM _{2.5} ^b	6.64	(3.27, 10)	< 0.01	1.82	(0.44, 3.20)	0.01	0.52	(-2.01, 3.05)	0.69	
Base model ^a , further adjusted for O_3^{b}	5.22	(2.36, 8.08)	< 0.01	0.80	(-0.59, 2.19)	0.26	0.00	(-1.91, 1.91)	1.00	
Base model ^a , further adjusted for CO ^b	5.25	(2.50, 8)	< 0.01	1.05	(-0.25, 2.35)	0.11	0.12	(-1.47, 1.71)	0.88	
Base model ^a , further adjusted for traffic density within 50 m	6.50	(3.03, 9.97)	< 0.01	1.52	(-0.05, 3.09)	0.06	0.60	(– 1.36, 2.57)	0.55	
Base model ^a , further adjusted for traffic density within 150 m	6.01	(3.19, 8.83)	< 0.01	1.25	(-0.05, 2.56)	0.06	0.39	(-1.24, 2.02)	0.64	
Base model ^a , further adjusted for traffic density within 300 m	6.19	(3.10, 9.28)	< 0.01	1.49	(-0.03, 3)	0.06	0.59	(– 1.25, 2.44)	0.53	
Base model ^a , further adjusted for CALINE4 NO _x ^b	6.22	(3.22, 9.22)	< 0.01	2.17	(0.59, 3.75)	0.01	0.59	(-1.25, 2.44)	0.53	

^a Generalized estimating equations model with identity link function including NDVI, maternal age and maternal age squared, length of gestation and length of gestation squared, poverty and poverty squared, insurance status, race/ethnicity, parity, diabetes and infant's gender as dependent variables.

^b NO_x: nitrogen oxides, PM₁₀: particulate matter of less than 10 μm, PM_{2.5}: particulate matter of less than 2.5 μm, O₃: ozone, CO: carbon monoxide. All pollutants were measured my monitoring stations, except CALINE4 NO_x that were local traffic-generated NO_x concentrations estimated using the CALINE4 dispersion model.

^c IQR stands for inter-quartile range. The inter-quartile range increase in NDVI exposure is 0.109 for 50 m buffers, 0.121 for 100 m buffer and 0.131 for 150 m buffers. Changes in birth weight are expressed in grams.

Table 3

Odds ratios for preterm birth per inter-quartile range increase in NDVI exposure (four hospitals in Southern California, 1997-2006).

	NDVI within 50 m buffers			NDVI within 1	NDVI within 100 m buffers			NDVI within 150 m buffers		
	Odds ratio per IQR ^c in NDVI exposure	95% Confidence interval	р	Odds ratio per IQR ^c in NDVI exposure	95% Confidence interval	р	Odds ratio per IQR ^c in NDVI exposure	95% Confidence interval	р	
Base model ^a	0.988	(0.970, 1.006)	0.17	0.978	(0.953, 1.005)	0.11	0.985	(0.972, 0.997)	0.02	
Base model ^a , further adjusted for NO_x^b	0.984	(0.972, 0.996)	0.01	0.976	(0.954, 0.999)	0.04	0.983	(0.973, 0.992)	< 0.01	
Base model ^a , further adjusted for PM ₁₀ ^b	0.988	(0.970, 1.006)	0.17	0.979	(0.952, 1.005)	0.12	0.985	(0.972, 0.998)	0.03	
Base model ^a , further adjusted for PM _{2.5} ^b	0.989	(0.973, 1.006)	0.21	0.977	(0.951, 1.004)	0.10	0.987	(0.972, 1.002)	0.09	
Base model ^a , further adjusted for O_3^{b}	0.990	(0.972, 1.008)	0.27	0.980	(0.955, 1.006)	0.13	0.986	(0.974, 0.998)	0.02	
Base model ^a , further adjusted for CO ^b	0.982	(0.972, 0.992)	< - 0.01	0.975	(0.954, 0.997)	0.03	0.981	(0.973, 0.990)	< 0.01	
Base model ^a , further adjusted for traffic density within 50 m	0.998	(0.970, 1.027)	0.91	0.984	(0.954, 1.015)	0.31	0.990	(0.974, 1.006)	0.20	
Base model ^a , further adjusted for traffic density within 150 m	0.994	(0.969, 1.019)	0.64	0.983	(0.952, 1.015)	0.29	0.988	(0.973, 1.005)	0.16	
Base model ^a , further adjusted for traffic density within 300 m	0.989	(0.969, 1.010)	0.31	0.980	(0.950, 1.010)	0.18	0.986	(0.970, 1.002)	0.09	
Base model ^a , further adjusted for CALINE4 NO _x ^b	0.984	(0.961, 1.007)	0.17	0.977	(0.949, 1.006)	0.13	0.984	(0.967, 1.000)	0.05	

^a Generalized estimating equations model with logit link function including NDVI, maternal age and maternal age squared, poverty and poverty squared, insurance status, race/ethnicity, parity and pyelonephritis as dependent variables.

^b NO_x: nitrogen oxides, PM₁₀: particulate matter of less than 10 μm, PM_{2.5}: particulate matter of less than 2.5 μm, O₃: ozone, CO: carbon monoxide. All pollutants were measured my monitoring stations, except CALINE4 NO_x that were local traffic-generated NO_x concentrations estimated using the CALINE4 dispersion model.

^c IQR stands for inter-quartile range. The inter-quartile range increase in NDVI exposure is 0.109 for 50 m buffers, 0.121 for 100 m buffer and 0.131 for 150 m buffers.

decreased risk of preterm birth associated with greenness (Dadvand et al., 2012a, 2012c; Donovan et al., 2011). However, for both birth weight and preterm birth, associations are weak and patterns by NDVI quartile are not clearly indicative of dose-response relationships. We may therefore not exclude chance as a possible explanation for our findings.

Confounding might also affect our results. We could not adjust for maternal smoking and body mass index. Smoking, but not body mass index, has been inversely associated with greenness in Canada (Villeneuve et al., 2012), and residual confounding might persist even after adjustment for socioeconomic variables, maternal age and race/ ethnicity. We had no data on noise or heat in the vicinity of homes, or on maternal stress (Fan et al., 2011). These factors might be on the pathway of relationships between greenness and pregnancy outcomes, thus not necessarily confounders to adjust for. This is also possibly the case of air pollution (Dadvand et al., 2012b). Our findings of increased term birth weight associated with NDVI are not affected by adjustment for any air pollution variable, which suggests that this association is independent from air pollution. However, our results for preterm birth and NDVI considered as a continuous variable are sensitive to adjustment for PM_{2.5} and traffic density. Sensitivity analyses suggest that the loss of a statistically significant association between NDVI and preterm birth after adjustment for PM_{2.5} might be due to a loss of statistical power or selection bias since PM_{2.5} had 10% missing data (Supplementary Material Table S4). However, potential confounding by PM_{2.5} cannot be totally excluded.

We further explored whether adjusting for PM_{2.5} and traffic density would over-adjust the NDVI effect since air pollution exposure might be on the plausible causal pathway between NDVI and preterm birth. We found odds ratios for the association between preterm birth and traffic density (but not PM_{2.5}) decreased with the increase in the levels of surrounding NDVI (Supplementary Material Table S5). Provided that exposure to traffic-related air pollution likely increases the risk of preterm birth (Wilhelm and Ritz, 2003; Wu et al., 2011), this observation suggests the reduction of air pollution exposure (here, exposure resulting from traffic density) by NDVI as a plausible pathway between NDVI and preterm birth. However, since greenness may mitigate exposure to air pollution but not totally suppress it, confounding by traffic density cannot totally be ruled out considering NDVI as a continuous variable. Still, we observed decreased preterm birth risk for the upper quartile of NDVI exposure ($p \le 0.06$), even after adjusting for PM_{2.5} or traffic density. Finally, we acknowledge that our air pollution indicators also have limitations that were discussed extensively elsewhere (Laurent et al., 2013; Wu et al., 2011) and that they cannot reflect accurately the amount of air pollution removed by the vegetal cover (Novak, 2000).

Our NDVI exposure indicators were restricted to circular buffers of limited radii around maternal homes. While access to green spaces can foster physical activities and social contacts that are health beneficial, such mechanisms are most likely related to access

Table 4

Odds ratios for preeclampsia per inter-quartile range increase in NDVI exposure (four hospitals in Southern California, 1997-2006).

	NDVI within 50 m buffers			NDVI within 10	NDVI within 100 m buffers			NDVI within 150 m buffers		
	Odds ratio per IQR ^c in NDVI exposure	95% Confidence interval	р	Odds ratio per IQR ^c in NDVI exposure	95% Confidence interval	р	Odds ratio per IQR ^c in NDVI exposure	95% Confidence interval	р	
Base model ^a Base model ^a ,	1.008	(0.967, 1.052)	0.70	0.968	(0.929, 1.009)	0.13	0.983	(0.933, 1.035)	0.52	
further adjusted for NO _x ^b	1.005	(0.965, 1.048)	0.81	0.966	(0.928, 1.006)	0.09	0.981	(0.934, 1.031)	0.45	
Base model ^a , further adjusted for PM ₁₀ ^b	1.008	(0.967, 1.052)	0.70	0.967	(0.927, 1.009)	0.13	0.982	(0.931, 1.036)	0.51	
Base model ^a , further adjusted for PM _{2.5} ^b	1.032	(0.985, 1.082)	0.18	0.984	(0.940, 1.030)	0.49	0.993	(0.927, 1.063)	0.84	
Base model ^a , further adjusted for O ₃ ^b	1.012	(0.968, 1.058)	0.61	0.970	(0.930, 1.012)	0.16	0.985	(0.935, 1.038)	0.57	
Base model ^a , further adjusted for CO ^b	1.005	(0.968, 1.045)	0.78	0.967	(0.930, 1.005)	0.08	0.981	(0.936, 1.030)	0.44	
Base model ^a , further adjusted for traffic density within 50 m	1.021	(0.965, 1.081)	0.46	0.974	(0.928, 1.023)	0.30	0.989	(0.934, 1.046)	0.69	
Base model ^a , further adjusted for traffic density within 150 m	1.014	(0.968, 1.063)	0.55	0.972	(0.929, 1.016)	0.21	0.986	(0.936, 1.040)	0.61	
Base model ^a , further adjusted for traffic density within 300 m	1.015	(0.967, 1.065)	0.56	0.974	(0.928, 1.023)	0.29	0.989	(0.934, 1.048)	0.72	
Base model ^a , further adjusted for CALINE4 NO _x ^b	1.014	(0.985, 1.044)	0.35	0.974	(0.944, 1.006)	0.11	0.991	(0.952, 1.031)	0.65	

^a Generalized estimating equations model with logit link function including NDVI, maternal age and maternal age squared, poverty and poverty squared, insurance status, race/ethnicity, parity and diabetes as dependent variables.

^b NO_x: nitrogen oxides, PM₁₀: particulate matter of less than 10 μm, PM_{2.5}: particulate matter of less than 2.5 μm, O₃: ozone, CO: carbon monoxide. All pollutants were measured my monitoring stations, except CALINE4 NO_x that were local traffic-generated NO_x concentrations estimated using the CALINE4 dispersion model.

^c IQR stands for inter-quartile range. The inter-quartile range increase in NDVI exposure is 0.109 for 50 m buffers, 0.121 for 100 m buffer and 0.131 for 150 m buffer.

to large green spaces such as parks (Dadvand et al., 2012a). Our NDVI metrics rather reflect a less polluted, more quiet and generally more appeasing residential environment (van den Berg et al., 2010). The use of 30 m resolution raster data to calculate the average NDVI within small buffers might have led to imprecise exposure estimate in case of irregular greenness patterns due to fragmented land uses, especially for the 50 m buffers. This seems unlikely to produce nonrandom errors in exposure estimate, however. Besides, NDVI carries no information about the nature and use of the vegetation (grass, trees, kitchen gardens) (Richardson et al., 2012) Despite these limitations, it has the advantage of being an objective indicator. NDVI and air pollution exposures could only be estimated for maternal homes at the time of birth. Characterizing them throughout pregnancy would be a desirable improvement for future studies. A finer characterization of vegetation type and its spatial distribution would also be useful, notably to better quantify the amount of air pollution locally removed by vegetation (Novak, 2000).

5. Conclusion

In the largest study of greenness and pregnancy outcomes ever conducted, we found modest support for increased birth weight in term born babies and a slight reduction of the risk of preterm birth associated with exposure to greenness. No association with preeclampsia was observed. These findings call for confirmation in other study settings.

Funding

The study was supported by the Health Effect Institute (HEI 4787-RFA09-4110-3 WU) and the National Institute of Environmental Health Sciences (NIEHS R21ES016379). The funding sources had no role in the study design, in the collection, analysis,

and interpretation of data, in the writing of the manuscript or in the decision to submit the manuscript for publication.

Acknowledgements

The authors thank Judith Chung (University of California, Irvine, USA) for her help in initiating the project and Scott Bartell (University of California, Irvine, USA) for providing some advice on statistical analyses.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.healthplace.2013. 09.016.

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