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Using high-resolution residential greenspace measures in an urban environment to assess risks of allergy outcomes in children

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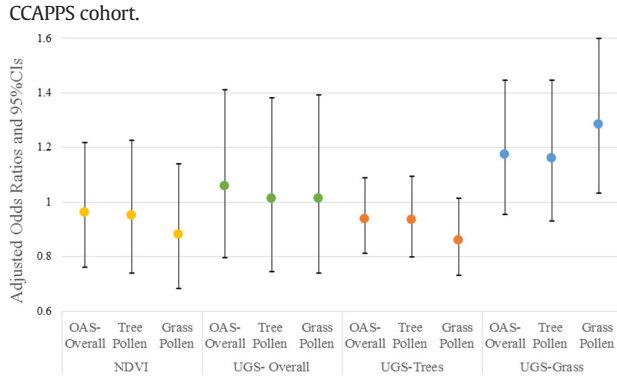
HIGHLIGHTS

- Residential greenspace exposure with two GS metrics assessed for childhood allergy
- Land-use derived GS and NDVI data used for specificity comparisons for GS type
- Land-use derived Grass cover per 10% change increased grass pollen allergy risk.
- Assessing GS exposure type may improve elucidation of allergy benefits and risks.

GRAPHICAL ABSTRACT

Comparison of Residential Greenspace Metrics (400 m) and Outdoor Aeroallergen Sensitization at 7 years, CCAPPS cohort.



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ABSTRACT

Despite reported health benefits of urban greenspace (gs), the epidemiological evidence is less clear for allergic disease. To address a limitation of previous research, we examined the associations of medium- and high-resolution residential gs measures and tree and/or grass canopies with allergic outcomes for children enrolled in the longitudinal cincinnati childhood allergy and air pollution study (ccaaps). We estimated residential gs based on 400 m radial buffers around participant addresses ($n = 478$) using the normalized differential vegetation index (ndvi) and land cover-derived urban greenspace (ugs) (tree and grass coverage, combined and separate) at 30 m and 1.5–2.5 m resolution, respectively. Associations between outdoor aeroallergen sensitization and allergic rhinitis at age 7 and residential gs measures at different exposure windows were examined using multivariable logistic regression models. A 10% increase in ugs-derived grass coverage was associated with an increased risk of sensitization to grass pollens (adjusted odds ratio [aor]: 1.27; 95% confidence interval = 1.02–1.58). For each 10% increase in ugs-derived tree canopy coverage, nonstatistically significant decreased

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odds were found for grass pollen sensitization, tree pollen sensitization, and sensitization to either (aor range = 0.87–0.94). Results similar in magnitude to ugs-tree canopy coverage were detected for ndvi and allergic sensitizations. High-resolution (down to 1.5 m) gs measures of grass- and tree-covered areas showed associations in opposite directions for different allergy outcomes. These data suggest that measures strongly correlated with tree canopy (e.g., ndvi) may be insufficient to detect health effects associated with proximity to different types of vegetation or help elucidate mechanisms related to specific gs exposure pathways.

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1. Introduction

Childhood allergic sensitization is a risk factor for allergic rhinitis and asthma later in life (Codispoti et al., 2010). The prevalence of allergies in childhood has not only increased considerably over time, but there is research that suggests that children can become sensitized to outdoor allergens at an early age (Wong et al., 2012). Further, the critical time periods for exposures and sensitization to outdoor allergens are unknown. Many studies report associations between environmental exposures during infancy or early childhood and allergic sensitization (Codispoti et al., 2010; Bowatte et al., 2015; Biagini Myers et al., 2010; Ruokolainen et al., 2015). Exposures later in childhood also may contribute to allergic sensitization, given the variability in allergy development and the changing nature of contact with the surrounding environment across the life course, though findings are mixed (United States Environmental Protection Agency, 2008; Gehring et al., 2010; Gruzieva et al., 2012; Bowatte et al., 2015; Jung et al., 2015).

Residential proximity to urban greenspace (GS) is associated with both multiple health benefits and potential disadvantages in children and adults (Hartig et al., 2014; Nieuwenhuijsen et al., 2014; Dadvand et al., 2014; Braubach et al., 2017). The health benefits include decreased mortality, increased birth weight, and improved sleep, cognitive functioning, physical activity, social connectivity, and neighborhood safety (Vienneau et al., 2017; Twohig-Bennett and Jones, 2018; Astell-Burt et al., 2013; Dadvand et al., 2012; Donovan et al., 2011; Hystad et al., 2014; James et al., 2016; Kondo et al., 2015; McMorris et al., 2015). The evidence is less clear regarding impacts of GS on allergic disease (Hanski et al., 2012; Lovasi et al., 2013; Lovasi et al., 2008; Fuertes et al., 2014; Markevych et al., 2017; Ruokolainen et al., 2015; Fuertes et al., 2016; Frumkin et al., 2017; Tischer et al., 2017). Some studies report increased risk of childhood allergic disease for areas with more residential GS (Lovasi et al., 2013; Dadvand et al., 2014; Fuertes et al., 2014). Others report that the relationship between greenness and allergic response varies across different land uses and regions (Ruokolainen et al., 2015; Fuertes et al., 2016). Quality estimation of GS composition and exposure is a persistent limitation in studies of GS and allergic disease (Fuertes et al., 2016).

Normalized Differential Vegetation Index (NDVI) has served as a primary measure of GS in epidemiology studies (Markevych et al., 2017). NDVI estimates the density of green vegetation by calculating the ratio of red to infrared reflectance exhibited by leafy vegetation from satellite imagery. In the absence of other nationwide GS measures, many epidemiologic studies utilize NDVI to assess GS, typically developing measures within varying radial distances from a residence (Dadvand et al., 2014; Donovan et al., 2011; Fuertes et al., 2016; Hystad et al., 2014). Although NDVI estimates vegetation cover and density, it does not differentiate specific types of vegetation or qualities of GS that may influence human-environment interactions and help elucidate specific exposure pathways and mechanisms (Dadvand et al., 2014; Fuertes et al., 2016; Fuertes et al., 2014). Recently, Light Detection and Ranging (LiDAR) imagery combined with aerial photographs has been applied as a GS measure, and, relative to NDVI, can provide both higher resolution imagery at a regional scale and distinguish among different types of GS. Li et al. (2015) reported high correlations between NDVI and LiDAR-derived tree canopy, but not between NDVI and LiDAR-derived grass. Although previous studies have used NDVI-derived data to estimate pollen counts (Skøth et al., 2013), others have questioned the value of NDVI data (Li et al., 2015; Fuertes et al., 2016; Markevych et al., 2017) for estimating exposures relevant to allergic disease. To our knowledge comparative analysis of aerial GS imagery with the ability to distinguish GS type has not been conducted with health outcomes. Such an analysis could be particularly informative for evaluating allergic disease outcomes given that distribution patterns of GS and tree and grass pollen concentrations and dispersal can differ across landscapes (Skøth et al., 2013; Fuertes et al., 2014; Cariñanos et al., 2002).

Given the mixed epidemiological evidence to date and the uncertain mechanistic pathways involved in the development of allergic responses, the objectives of this study were to compare residential GS based on two aerial measures of GS (NDVI vs. LiDAR-derived imagery of overall and specific types of urban vegetation) in relation to childhood allergic disease in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS).

2. Methods

2.1. Study population

2.1.1. Cohort description

The CCAAPS study design, recruitment strategy and clinical evaluation are described elsewhere (Codispoti et al., 2015; LeMasters et al., 2006; Ryan et al., 2005). Briefly, participants were recruited from 2001 to 2003 birth records in Southwest Ohio (Butler, Clermont, Hamilton, and Warren Counties) and Northern Kentucky (Boone, Campbell, and Kenton Counties). Inclusion criteria required participants to have a birth record address located either <400 m or further than 1500 m from a major road (Reponen et al., 2003; Ryan et al., 2007). Additionally, at least one parent was required to be sensitized to at least one of 15 regionally relevant aeroallergens in a skin prick test (LeMasters et al., 2006). The study was approved by the University of Cincinnati institutional review board #2013–4038, and written informed consent was obtained from participants before administering any study procedures.

2.1.2. Health outcomes at age 7

Children enrolled in CCAAPS completed clinical evaluations for allergic sensitization and allergic rhinitis (AR) at 1, 2, 3, 4, and 7 years of age (Codispoti et al., 2010). Evaluations included skin prick tests for 15 regional aeroallergens (LeMasters et al., 2006). For our analysis, participants with a positive skin prick test to at least one outdoor aeroallergen by 7 years of age were categorized as having outdoor aeroallergen sensitization (OAS). A positive test was determined as a difference in wheal circumference of 3 mm or greater between the allergen and a negative control 15 min after administration with a bifurcated needle. We assessed three OAS outcomes: 1] OAS specific to grass pollen (sensitivity to timothy grass (*Phleum pratense*), short ragweed (*Ambrosia* sp.), or meadow fescue (*Festuca pratensis*)); 2] OAS specific to tree pollen (sensitivity to maple mix (*Acer sp.)*, eastern red cedar (*Juniperus virginiana*), white oak (*Quercus alba*), or American elm (*Ulmus americana*)); and 3] overall OAS (grass or tree pollen).

During each clinical evaluation, parents or guardians provided medical and residential information for questionnaires adapted from the International Study of Asthma and Allergies in Childhood (Asher et al., 1995). AR was defined as having allergic sensitization (to any of the

15 aeroallergens tested) and a positive parental/guardian response to the question: "in the past 12 months, has your child ever had a problem with sneezing, or a runny, or a blocked nose when he/she DID NOT have a cold/flu?" (Codispoti et al., 2015).

2.2. Exposure assessments

Residential GS was estimated using both NDVI and land cover-derived urban greenspace (UGS) measures for participants' self-reported addresses at age 7. All addresses were geocoded using EZ-Locate software from Tele Atlas (Ryan et al., 2005). NDVI provides a continuous measure of vegetation density derived from Landsat satellite imagery calculated as the ratio of the difference between the near-infrared region and red reflectance and the sum of the near-infrared region and red reflectance. Using cloud-free in-leaf imagery collected June 19, 2010, NDVI raster data sets were created from spectral bands 4 (near infrared) 3 (red) using Landsat Scene Path at 30 m resolution. NDVI values for each 30 m grid cell range from −1 to +1, with values closer to +1 indicating a higher density of vegetation (Weier and Herring, 2000).

2.2.1. Land cover-derived urban greenspace

We also used high-resolution land cover data from the United States Department of Agriculture (USDA) Forest Service's Urban Tree Canopy assessment to estimate GS exposure by vegetation type. Land cover data for Hamilton County, OH were obtained from the Cincinnati Area Geographic Information System using geographic object-based image analysis (AMEC Environment and Infrastructure I, 2011). To derive these data, the USDA Forest Service re-sampled 2010 6-inch countywide imagery (in-leaf) from 3- and 4-band aerial imagery (1.5 m resolution) for Hamilton County as well as county-level data on parcels, transportation, and buildings. Land cover data for Boone, Campbell, and Kenton Counties resulted from a collaboration between the Northern Kentucky Urban and Community Forestry Council, SavATree Consulting Group, and the University of Vermont's Spatial Analysis Laboratory (Galvin et al., 2015). Seven classes of land cover were developed (2.5 m resolution) from 2011 and 2012 LiDAR imagery: tree canopy, grass (including weeds and shrub), agriculture, water, roads, other impervious surfaces, and bare soil. Fig. 1 shows a side by side comparison of land-use derived metrics and NDVI around a randomly selected location in the study area.

(Fig. 1 here. File is separate.)

2.2.2. Greenspace estimates

To measure GS within a walkable distance around participants' residences, we compared estimates derived from NDVI and land cover-derived UGS at 400 m radial buffers around participants' primary home addresses (Hystad et al., 2014). NDVI was calculated as the mean of all NDVI raster cell values within the buffer and reported for an interquartile range increase. UGS-overall was calculated as the percentage of tree canopy and grass/shrub coverage and reported for each 10% increase (IQR: 10.4%); we also assessed tree canopy (UGS-tree, IQR: 21.7%) and grass/shrub coverage separately (UGS-grass, IQR: 11.8%) and reported results for a 10% increase to compare metrics. Buffers with boundaries extending beyond the four counties were excluded ($n = 3$).

As a supplemental analysis, we estimated residential GS for 100 m and 800 m buffers around participant addresses to approximate nearby GS and ambient GS, respectively (Dadvand et al., 2014; Hystad et al., 2014).

2.3. Analysis

We used multivariable logistic regression to evaluate the relationship between GS metrics and OAS and AR outcomes detected by age 7. Unadjusted and adjusted results for NDVI are reported in terms of an interquartile range increase in mean NDVI. UGS results are reported per 10% increase in coverage. We calculated Pearson correlation coefficients to examine the relationships between the GS exposure measures. We examined spatial autocorrelation of the GS and traffic related air pollution (TRAP) measures using Global Moran's I (Ryan et al., 2007). All

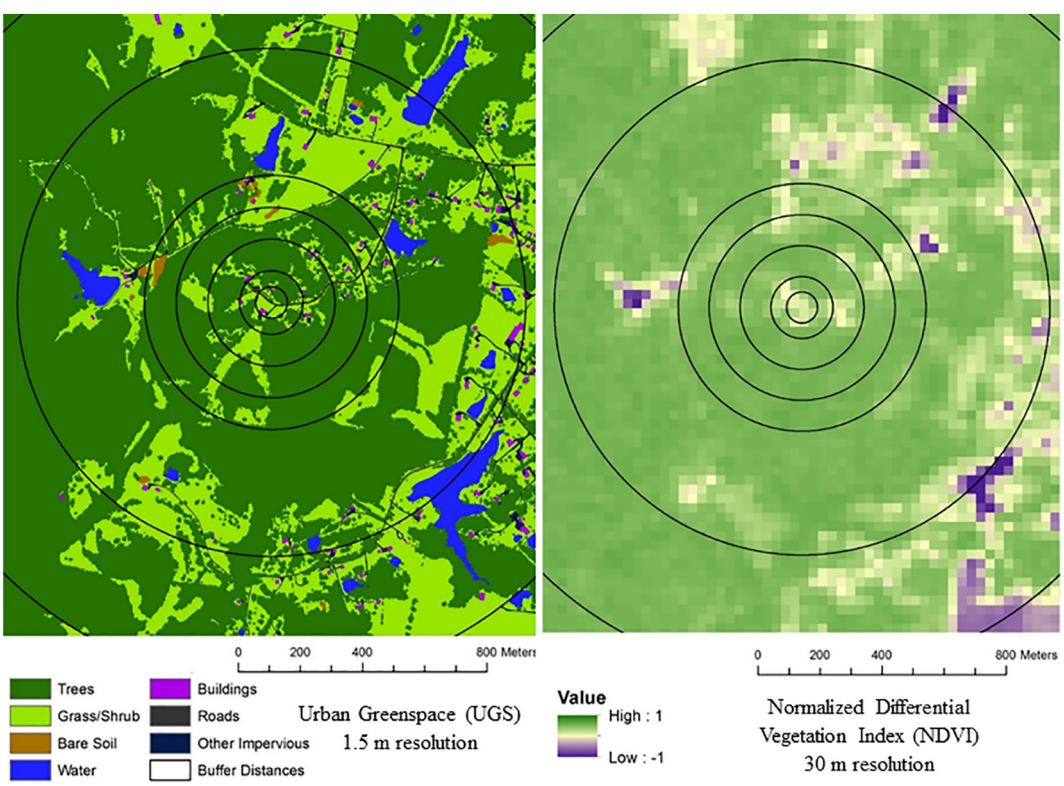

Fig. 1. Comparison of residential GS metrics: NDVI (30 m resolution) and UGS (1.5 m resolution) for a randomly selected location in the study area (Hamilton County).

spatial analysis was performed with ArcGIS Desktop: Release 10.3.3 (ArcGIS, 2012). All statistical analysis was performed with SAS® software, version 9.4 (SAS, 2012).

Covariates were selected a priori for inclusion in multivariable regression models based on established risk factors for allergic sensitization and AR (Codispoti et al., 2015; Dadvand et al., 2014). These included race, sex, environmental tobacco smoke (ETS) exposure, mother's education at 7 years of age, cumulative TRAP exposure at 7 years of age, and an index of neighborhood-level socioeconomic status (SES) (Table 1). For the primary analysis, ETS was defined as the total number of self-reported cigarettes smoked per day by each adult in the child's household at age 7. As part of a sensitivity analysis of a smaller subset of the population, we also adjusted for hair cotinine measures at age 2 years in separate models to examine the potential impact of confounding. TRAP exposure estimates were estimated using a previously developed and validated land-use regression model for elemental carbon attributable to traffic sources (Ryan et al., 2007). The SES index included seven variables: median household income; percentage of households with income ≤$50,000; percentage of households with interest, dividends, or net rental income; median value of owner-occupied homes; percentage of workforce in management, professional, or related occupations; percentage of population with at least high school diploma or equivalent, and percentage of population with at least a bachelor's degree (Hajat et al., 2013). SES variables were obtained from the American Community Survey (ACS) 5-year estimates (2006–2010) at the census tract level. All ACS-derived covariates were aggregated to a 1600 m buffer around participant addresses using ratio apportionment in ArcGIS. This accounted for high margins of error in the census-tract level estimates and approximated participants' neighborhood-level SES (Spielman et al., 2014).

Table 1
Study characteristics of outdoor allergic sensitization and allergic rhinitis in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) cohort, four-county area.

	N[a]	OAS ($n = 478$)		AR ($n = 474$)	
		Cases	Noncases	Cases	Noncases
Totals	478	172	306	209	265
Covariates		Mean (standard deviation) or frequency (%)			
African American	478	49 (28.5)	81 (26.5)	56 (26.7)	72 (27.2)
Male	478	99 (57.6)	156 (51.0)	117 (56.0)	136 (51.3)
ETS exposure[b]	473	3.1 (9.2)	3.9 (9.9)	4.7 (11.6)	2.8 (7.8)
TRAP exposure[c]	478	0.38 (0.1)	0.39 (0.1)	0.38 (0.1)	0.39 (0.1)
Annual income	471				
°<$30,000		37 (21.5)	74 (24.2)	44 (21.1)	67 (25.2)
°$30,000–$70,000		39 (22.7)	92 (30.1)	67 (32.1)	63 (23.8)
°>$70,000		89 (51.7)	140 (45.8)	96 (45.9)	130 (49.1)
Maternal education	478				
°<High school		6 (3.5)	7 (2.3)	4 (1.9)	9 (3.4)
°High school diploma		21 (12.2)	48 (15.7)	31 (14.8)	38 (10.4)
°Some college		39 (22.7)	75 (24.5)	52 (24.9)	61 (23.0)
°College		72 (41.9)	135 (44.1)	84 (40.2)	120 (45.3)
°Graduate		34 (19.8)	41 (13.4)	38 (18.2)	37 (14.0)
Neighborhood SES[d] (1600-m buffer)	478	6.8 (4.2)	6.4 (4.4)	6.5 (4.0)	6.7 (4.4)
Greenspace metrics					
NDVI (mean) 400-m buffer	473	0.57 (0.1)	0.57 (0.1)	0.57 (0.1)	0.57 (0.1)
UGS (%) overall, 400-m buffer	470	81.9 (8.8)	82.2 (8.0)	82.0 (8.0)	82.1 (8.5)
UGS (%) trees, 400-m buffer	470	37.6 (14.8)	39.4 (14.2)	38.7 (14.0)	38.8 (14.9)
UGS (%) grass, 400-m buffer	470	30.6 (10.7)	29.6 (9.9)	29.8 (9.2)	30.0 (11.0)

AR = allergic rhinitis; CI = confidence interval; GS = greenspace; NDVI = Normalized Differential Vegetation Index (30 m resolution); OAS = outdoor aeroallergen sensitization; OR = odds ratio; UGS = urban greenspace (1.5–2.5 m resolution).

[a] Values <478 represent missing data (e.g., income data missing for 7 participants).

[b] Environmental Tobacco Smoke exposure, measured as the total number of self-reported cigarettes smoked per day by each adult in the child's household at age 7.

[c] Traffic-Related Air Pollution Exposure, yearly estimates from land-use regression mg/m^3.

[d] Socio-economic status (Hajat et al., 2013).

(Table 1 here. File is separate.)

For comparison with the main analysis of residential GS and allergy outcomes at age 7, supplemental analyses evaluated OAS and AR diagnosed in earlier childhood (i.e., participants with at least one positive skin prick test prior to age 4) using NDVI and census estimates from the year 2000. Multispectral airborne imagery collected on June 6, 2000, was used to calculate NDVI, which was matched to addresses reported at 6 months of age; corresponding UGS data were not available. Analyses of the earlier-onset outcomes adjusted for individual- and neighborhood-level covariates reported at 6 months of age.

3. Results

3.1. Cohort description

Of the 617 CCAAPS participants who completed the age 7 clinical evaluation, 478 (76%) resided in the four-county area with available NDVI and UGS data at 400 m for age 7 addresses. Compared to the full cohort, the four-county area had a slightly higher percentage of African American participants (27% vs. 22%), and slightly lower income (23% vs. 19% in lowest income category), though no differences were observed in OAS or AR prevalence (data not shown). Few patterns were detected between cases and noncases, although boys were more likely to be diagnosed with both OAR and AR (Table 1).

3.2. Correlation and autocorrelation analysis

We observed strong Pearson correlation coefficients (r_P) between NDVI and UGS-overall ($r_P = 0.93$) within the study area (data not shown). Strong correlations also were noted between NDVI and UGS-tree ($r_P = 0.82$), but not UGS-grass ($r_P = 0.18$). For GS and TRAP estimates, there was evidence of spatial autocorrelation within the study area buffers (Global Moran's *I*, inverse-distance-weighted, 1 km threshold distance): NDVI ($I = 0.73$, $p < 0.001$); UTC ($I = 0.58$, $p < 0.05$); TRAP ($I = 1.07$, $p < 0.001$).

3.3. Health analyses

3.3.1. Outdoor aeroallergen sensitization

Although results were largely null for all three OAS outcomes per each 10% increase in overall UGS coverage (Table S2; Fig. 2), we consistently observed adjusted odds ratios (aORs) <1 for UGS-tree (aOR range = 0.87–0.94). These were similar in magnitude to those observed for an interquartile increase in NDVI. In contrast, UGS-grass was consistently associated with higher aORs (range = 1.16–1.27) for all OAS-grass pollen, OAS-tree pollen, and overall OAS, although results did not achieve statistical significance for most outcomes. The strongest association was observed for grass coverage and OAS-grass pollen (aOR = 1.27; 95% confidence interval [CI] 1.02, 1.58).

3.3.2. Allergic rhinitis

We detected largely null results for AR and all GS measures. Although not statistically significant, aORs consistent in magnitude were detected for AR per 10% increase in UGS-overall (aOR = 0.90; 95% CI: 0.69, 1.19) as well as UGS-grass (aOR = 0.92; 95% CI: 0.75, 1.12).

3.4. Supplemental analyses

The supplemental analysis shows that UGS-grass was consistently associated with higher aORs for both 100 m and 800 m for OAS-grass pollen, OAS-tree pollen, and overall OAS (Table S1). Although results for early onset allergic sensitization were largely null, we found more protective associations for early onset allergic rhinitis based on NDVI (year 2000) exposures for 400 m (aOR = 0.79; 95% CI = 0.54, 1.15) and 800 m (aOR = 0.63; 95% CI = 0.44, 0.92) buffers representing an earlier life stage (6 months) (Table S3).

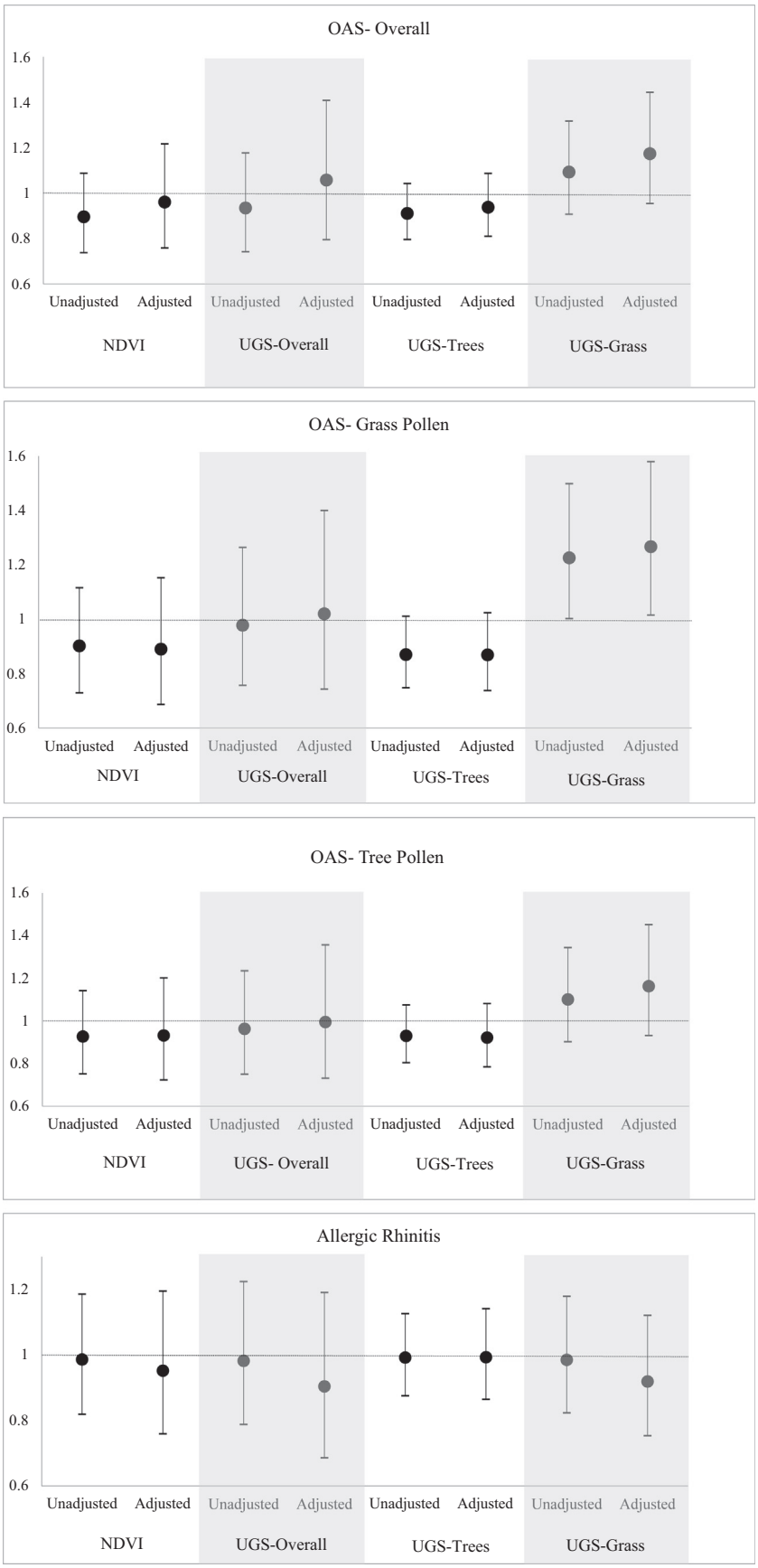

Fig. 2. Residential GS metrics (400 m) and allergy outcomes at age 7: adjusted odds ratios and 95% CIs. Models are adjusted for the following covariates: race, sex, environmental tobacco smoke exposure, exposure to traffic-related air pollution, mother's education (7 years), and neighborhood SES (7 years).

Based on our sensitivity analysis of a smaller population subset with hair cotinine measures at age 2 years, we saw consistently larger aORs (including several that were statistically significant) for cotinine-adjusted models for OAS, OAS-tree pollen and OAS-grass pollen based on the UGS-grass coverage metric irrespective of buffer size examined (Table S2). Similarly, we saw larger aORs for the overall UGS measure for the 100 and 400 m buffers (Table S2). The inverse associations for AR were also stronger based on the 400 m (aOR = 0.81, 95% CI: 0.58, 1.12) and 800 m (aOR = 0.79; 95% CI = 0.63, 0.98) buffers for both NDVI and the overall UTC measure. Most of the other associations were largely null and/or were comparable to what was seen in the larger population that included adjustment of ETS based at age 7 (Table S2).

4. Discussion

To our knowledge, this is the first study to evaluate relationships between different estimates of residential GS assessed through aerial imagery and allergy outcomes. We observed different patterns in effect estimates between grass- and tree-covered areas and OAS outcomes. Notably, a 10% increase in UGS-grass was associated with between 20 and 27% increased odds of all allergic sensitization outcomes, while NDVI and UGS-tree estimates were both consistently associated with between 8 and 11% reduced odds of allergy, although only one result achieved statistical significance. These results suggest that UGS-overall alone may be an insensitive measure without differentiating grass- from tree-covered areas. Our results are also consistent with the heterogeneous findings of previous studies, and further add to those authors' conclusions that NDVI-derived exposure measures may not adequately capture GS qualities most relevant to allergic outcomes (Li et al., 2015; Fuertes et al., 2016; Markevych et al., 2017).

Several hypotheses have emerged to explain how residential GS could affect allergic disease. One hypothesis posits that increased biodiversity in GS contributes to the human microbiome, improving immune system function against possible allergens (Fuertes et al., 2014; Hanski et al., 2012; Ruokolainen et al., 2015). Evidence for this hypothesis is mixed, though recent studies report protective associations with proximity-based residential GS in both rural and temperate-climate areas (Fuertes et al., 2016; Tischer et al., 2017). Alternatively, nearby GS likely increases exposures to local pollen concentrations in residential urban areas; some studies report increased allergic sensitization with increased pollen levels, potentially trapped by urban tree canopies (DellaValle et al., 2012; Lovasi et al., 2013). Finally, the nature of GS engagement could affect allergic sensitization through increased allergen exposure during outdoor activities (Dadvand et al., 2014; Frumkin et al., 2017; Hartig et al., 2014; Keddem et al., 2015; Markevych et al., 2017; Nieuwenhuijsen et al., 2014).

Our disparate findings between tree and grass coverage could result from different aeroallergen distributions between open, grass-covered areas and tree-covered areas, or potential differences in species composition, among other factors. Studies show pollen distribution and concentrations are affected by land use with two land use-based GS studies reporting decreased OAS with increased GS levels (Gonzalo-Garijo et al., 2006; Hanski et al., 2012; Ruokolainen et al., 2015). This also is consistent with findings that relationships between allergy and GS differed by regions and cohorts (Fuertes et al., 2016; Fuertes et al., 2014; Tischer et al., 2017).

The associations we detected for tree canopy and NDVI, which are highly correlated measures, are consistent with Hanski et al. (2012). They reported higher levels of skin microbiota on adolescents with increased residential tree canopy, which was associated with reduced allergic sensitization. It is plausible that differences in biodiversity and impacts on the microbiome, including native versus invasive species and related allergies, could explain reported differences. Our study was not able to examine skin microbiota but this should be examined in future studies (Fuertes et al., 2016; Lovasi et al., 2013; Tischer et al., 2017).

The null associations we observed for AR are consistent with previous studies (Dadvand et al., 2014; Fuertes et al., 2016; Tischer et al., 2017). Previous analysis of our cohort reported associations between both tree pollen and egg/dairy sensitization and AR at age 4 (Codispoti et al., 2010). Other factors such as breastfeeding and tobacco exposure also have been associated with higher prevalence of AR, but not skin prick test sensitization (Codispoti et al., 2010; Shargorodsky et al., 2015). Overall, our data suggest that AR may result from additional environmental and social factors and that aeroallergen sensitization measures may be more readily linked to estimates of GS. Further, it is possible that the inclusion of indoor aeroallergens in the clinical definition of AR may have limited the sensitivity of the outcome to the exposures assessed.

Similar to previous GS studies based on indirect measures, our exposure assessment approach was a study limitation. We did not consider seasonal GS variations and could not assess GS characteristics such as quality and use patterns, including maintenance patterns such as mowing which may affect the availability and distribution of grass pollen in the region. In the Ohio River valley, the Cincinnati region has a number of large tributaries and valleys, resulting in a mix of upland forest, steep hillsides, and floodplains (Berland et al., 2015; Lerch et al., 1982; Bryant, 1987). The region has a large number of native and non-native tree species, and while the allergy panel accounted for several of the most common regional tree and grass species (oak, maple, elm, cedar, timothy, fescue, ragweed), other species found in the region such as beech, sweetgum, and ash, as well as other herbaceous plants were not included (Bryant, 1987). Further, we did not evaluate pollen counts, overall or by species, in relation to GS or other factors such as elevation, wind direction, potential impedance of air circulation by tree canopy or other geographic barriers, and temperature that could affect pollen concentrations and exposures and limit the ability to examine potential mechanistic pathways (Cariñanos et al., 2002). Although it wasn't a limitation for the UGS measures, we averaged positive and negative values (i.e., the latter which would result from impervious surfaces or a body of water within the buffer) in the NDVI analysis. No participant addresses were within 400 m of the Ohio River, the largest water body in the region, and no buffers had a negative mean NDVI value. While this is not anticipated to be a major source of uncertainty given the limited number of waterbodies in this study area, this approach would likely attenuate the mean scores and the effect estimates based on these values (Markevych et al., 2017). Collectively, these limitations increase the potential for exposure measurement error, which can decrease study sensitivity and could preclude the detection of associations small in magnitude that may exist.

Home addresses might not capture residential mobility between birth and age 7 and potential GS exposures at other locations where children spent time. Our analysis of different exposure windows did not show significant differences between NDVI estimates for addresses at 6 months and 7 years of age. In addition, the intraclass correlation coefficient between overall mean GS exposure and that of the last known address only at age 7 is 0.74 for this cohort (Brokamp et al., 2016). These data suggest that the impact of residential mobility may be limited relative to other sources of measurement error.

A residential GS study raised some concern regarding selection bias, as participants may choose to live in areas with elevated GS (Villeneuve et al., 2012). Overall, the loss to follow-up in our study was 24% from birth up to age 7, but we saw no evidence of differential attrition. For example, another analysis showed that CCAAPS participants typically moved to areas with increased GS (Brokamp et al., 2016), but no differences were detected by the endpoint examined (i.e., asthma incidence) compared to those who did not move. We also saw no evidence of selection bias due to the use of the four-county population, since despite minimal differences seen for some race and income categories, this selection was not related to the prevalence of the different GS measures

(data not shown). Although the sample size was fairly large, the CCAAPS selection criteria including parental sensitivity to allergens may limit the generalizability of our results. Given that our study may be underpowered to detect such small associations, we cannot completely rule out chance findings in our results.

The evidence of spatial autocorrelation for our GS and TRAP measures, potentially impacts the precision of our models. Spatial autocorrelation is a challenge in epidemiological studies evaluating GS (Maantay, 2007). Although this should not bias our effect estimates, failing to account for spatial autocorrelation may underestimate our reported standard errors. Although previous studies suggest this is not a major concern, future research could consider spatial autoregressive models to further increase study sensitivity (Berland et al., 2015; Dormann et al., 2007).

A strength of our study is that we examined both clinically-assessed OAS, including tree- and grass-specific sensitization, and AR through a validated questionnaire and a clinical measure. This included earlier and later onset sensitization and rhinitis evaluations to examine GS at an earlier exposure window. Further, the rich individual health and location information for the high-risk cohort allowed us to evaluate individual- and neighborhood-level confounders at both ages examined; among these covariates, neighborhood SES was the strongest and most consistent confounder in our models. Response rates for individual SES variables were quite high in this cohort; this is an important study strength. Nonetheless, as with other GS studies, residual confounding may be present if key confounders (e.g. measure of mold/dampness in the house) were mismeasured or not included in our models.

A primary strength of our study was the comparison of two measures of aerial GS imagery and consideration of different types of vegetative cover across different buffer sizes. Another strength of our study is our examination of NDVI exposures for birth addresses and associations with earlier and later-onset allergies. As such, we feel that the strength of this cohort and analysis of allergic disease and GS adds significantly to the current evidence base.

5. Conclusions

In the absence of definitive data on species composition and accessibility, residential proximity to grassy areas appears to be associated with higher odds of atopic sensitization to different outdoor aeroallergens in a high-risk regional cohort. Our findings should be considered within a context that indicates wide-ranging benefits of urban greenspaces. Given our contrasting findings for allergy outcomes in grass- versus tree-covered areas, examining grass and tree pollen concentrations across different land use categories and tracking GS composition over time are important for future studies of urban greenspace and allergy, as is detailed information on participant's outdoor activities. These data should also increase the sensitivity of future studies to better examine potential mechanisms that may be involved.

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Competing interests

The authors report no competing interests financial or otherwise.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.03.009.

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Table S1

Adjusted odds ratios for greenspace (GS) measures based 100 m-, 400 m- and 800-m buffers and allergy outcomes – Main analysis of 473 participants.

GS Metric	Buffer (m)	OAS OR (95% CI)	OAS-Tree Pollen OR (95% CI)	OAS-Grass Pollen OR (95% CI)	AR OR (95% CI)
NDVI	100	1.00 (0.79, 1.28)	0.95 (0.73, 1.23)	0.92 (0.70, 1.20)	0.93 (0.74, 1.17)
	400	0.96 (0.76, 1.22)	0.93 (0.72, 1.20)	0.89 (0.69, 1.15)	0.95 (0.76, 1.20)
	800	0.84 (0.66, 1.07)	0.84 (0.65, 1.10)	0.79 (0.60, 1.04)	0.92 (0.72, 1.16)
UGS- Overall	100	1.08 (0.93, 1.27)	1.04 (0.88, 1.24)	1.03 (0.87, 1.23)	0.93 (0.80, 1.07)
	400	1.06 (0.80, 1.41)	1.00 (0.73, 1.36)	1.02 (0.74, 1.40)	0.90 (0.69, 1.19)
	800	0.92 (0.76, 1.12)	0.91 (0.74, 1.12)	0.89 (0.73, 1.10)	0.87 (0.73, 1.05)
UGS-Tree	100	1.00 (0.88, 1.15)	0.96 (0.83, 1.11)	0.92 (0.79, 1.07)	1.00 (0.88, 1.14)
	400	0.94 (0.81, 1.09)	0.92 (0.79, 1.08)	0.87 (0.74, 1.02)	0.99 (0.86, 1.14)
	800	0.86 (0.73, 1.01)	0.86 (0.72, 1.02)	**0.81 (0.67, 0.96)**	0.99 (0.85, 1.15)
UGS-Grass	100	1.10 (0.93, 1.32)	1.13 (0.94, 1.37)	1.20 (0.99, 1.45)	0.90 (0.77, 1.07)
	400	1.17 (0.95, 1.44)	1.16 (0.93, 1.45)	**1.27 (1.02, 1.58)**	0.92 (0.75, 1.12)
	800	1.21 (0.97, 1.50)	1.18 (0.93, 1.49)	**1.27 (1.01, 1.60)**	0.84 (0.68, 1.04)

AR = allergic rhinitis; CI = confidence interval; GS = greenspace; NDVI = Normalized Differential Vegetation Index (30m resolution); OAS = outdoor aeroallergen sensitization; OR = odds ratio; UGS = urban greenspace (1.5-2.5m resolution).

Adjusted models include the following covariates: race, sex, environmental tobacco smoke exposure (defined as total cigarette load at 7 years), exposure to traffic-related air pollution (7 yrs.), mother's education (7 yrs.), and neighborhood SES (7 yrs.)

Effect estimates are calculating the odds of exposure among cases relative to non-cases

Bold text denotes statistical significance at α = 0.05.

Table S2

Adjusted odds ratios for greenspace (GS) measures based 100 m-, 400 m- and 800-m buffers and allergy outcomes- Cotinine-adjusted sub-analysis of 324 participants.

GS Metric	Buffer (m)	OAS OR (95% CI)	OAS-Tree Pollen OR (95% CI)	OAS-Grass Pollen OR (95% CI)	AR OR (95% CI)
NDVI	100	1.08 (0.81, 1.44)	0.99 (0.73, 1.35)	0.97 (0.71, 1.33)	0.92 (0.70, 1.21)
	400	1.05 (0.79, 1.40)	0.97 (0.71, 1.32)	0.96 (0.70, 1.32)	0.82 (0.62, 1.08)
	800	0.92 (0.68, 1.23)	0.87 (0.63, 1.19)	0.83 (0.60, 1.15)	0.77 (0.58, 1.03)
UGS	100	1.17 (0.97, 1.41)	1.11 (0.91, 1.35)	1.10 (0.90, 1.35)	0.91 (0.77, 1.09)
	400	1.24 (0.88, 1.74)	1.10 (0.77, 1.58)	1.19 (0.82, 1.73)	0.81 (0.58, 1.12)
	800	1.03 (0.82, 1.29)	0.98 (0.77, 1.25)	0.98 (0.76, 1.25)	**0.79 (0.63, 0.98)**
UGS-Tree	100	0.98 (0.85, 1.13)	0.95 (0.81, 1.11)	0.88 (0.75, 1.04)	1.00 (0.87, 1.14)
	400	0.96 (0.81, 1.14)	0.89 (0.74, 1.07)	0.89 (0.73, 1.08)	0.89 (0.76, 1.05)
	800	0.88 (0.73, 1.06)	0.83 (0.68, 1.03)	**0.80 (0.65, 0.99)**	0.88 (0.74, 1.05)
UGS-Grass	100	**1.22 (1.01, 1.47)**	**1.22 (1.00, 1.49)**	**1.34 (1.10, 1.65)**	0.91 (0.76, 1.09)
	400	**1.25 (1.00, 1.57)**	**1.30 (1.02, 1.65)**	**1.34 (1.05, 1.70)**	1.00 (0.80, 1.23)
	800	**1.29 (1.02, 1.64)**	**1.29 (1.00, 1.66)**	**1.37 (1.06, 1.76)**	0.920.73, 1.16)

AR = allergic rhinitis; CI = confidence interval; GS = greenspace; NDVI = Normalized Differential Vegetation Index (30m resolution); OAS = outdoor aeroallergen sensitization; OR = odds ratio; UGS = urban greenspace (1.5-2.5m resolution).

Adjusted models include the following covariates: race, sex, environmental tobacco smoke exposure (defined as age 2 hair cotinine concentrations (ng/mg) exposure to traffic-related air pollution (7 yrs.), mother's education (7 yrs.), and neighborhood SES (7 yrs.)

Effect estimates are calculating the odds of exposure among cases relative to non-cases

Bold text denotes statistical significance at α = 0.05.

Table S3

Adjusted odds ratios for primary and early onset allergy outcomes and Normalized Differential Vegetation Index (NDVI collected in 2000), for 100 m-, 400 m-, and 800 m-buffers around participants' residences. -Main analysis of 473 participants.

Buffer Size (m)	EOAS**	OAS-Grass Pollen*	OAS*	OAS-Tree Pollen*	EAR**	AR*
			aOR (95% CI)			
100	1.21 (0.75, 1.95)	0.81 (0.56, 1.16)	0.83 (0.59, 1.15)	0.79 (0.55, 1.12)	0.93 (0.68, 1.27)	1.08 (0.80, 1.46)
400	0.97 (0.56, 1.69)	0.96 (0.63, 1.48)	1.03 (0.70, 1.51)	0.91 (0.60, 1.39)	0.79 (0.54, 1.15)	0.86 (0.60, 1.24)
800	0.78 (0.45, 1.35)	0.92 (0.61, 1.41)	0.96 (0.66, 1.40)	0.83 (0.55, 1.25)	**0.63 (0.44, 0.92)**	0.78 (0.55, 1.11)

AR = allergic rhinitis; CI = confidence interval; EAR = Early-onset allergic rhinitis; EOAS = early outdoor aeroallergen sensitization; NDVI = Normalized Differential Vegetation Index (2000, 30m resolution); OAS = outdoor aeroallergen sensitization; aOR = adjusted odds ratio.

* Adjusted models include the following covariates: race, sex, environmental tobacco smoke exposure (defined as total cigarette load at 7 years), exposure to traffic-related air pollution (7 yrs.), mother's education (7 yrs.), and neighborhood SES (7 yrs.)

** Adjusted models include the following covariates: race, sex, environmental tobacco smoke exposure (defined as total cigarette load at 6 mos.), exposure to traffic-related air pollution (6 mos.), mother's education (6 mos.), and neighborhood SES (6 mos.)Effect estimates are calculating the odds of exposure among cases relative to non-cases

Bold text denotes statistical significance at α = 0.05.

Table S4

Adjusted odds ratios for primary and early onset allergy outcomes and Normalized Differential Vegetation Index (NDVI collected in 2000), for 100 m-, 400 m-, and 800 m-buffers around participants' residences- Cotinine-adjusted sub-analysis of 324 participants.

Buffer Size (m)	EOAS**	OAS-Grass Pollen*	OAS*	OAS-Tree Pollen*	EAR**	AR*
			aOR (95% CI)			
100	1.24 (0.75, 2.05)	0.76 (0.52, 1.11)	0.83 (0.59, 1.18)	0.84 (0.58, 1.22)	0.90 (0.65, 1.25)	1.02 (0.74, 1.41)
400	0.90 (0.50, 1.63)	0.80 (0.52, 1.24)	0.94 (0.63, 1.41)	0.89 (0.57, 1.39)	0.80 (0.54, 1.18)	0.81 (0.55, 1.19)
800	0.71 (0.40, 1.27)	0.82 (0.53, 1.27)	0.89 (0.60, 1.32)	0.81 (0.52, 1.24)	0.71 (0.48, 1.03)	0.77 (0.52, 1.12)

AR = allergic rhinitis; CI = confidence interval; EAR = Early-onset allergic rhinitis; EOAS = early outdoor aeroallergen sensitization; NDVI = Normalized Differential Vegetation Index (2000, 30m resolution); OAS = outdoor aeroallergen sensitization; aOR = adjusted odds ratio.

* Adjusted models include the following covariates: race, sex, environmental tobacco smoke exposure (defined as age 2 hair cotinine concentrations (ng/mg), exposure to traffic-related air pollution (7 yrs.), mother's education (7 yrs.) and neighborhood SES (7 yrs.)

** Adjusted models include the following covariates: race, sex, environmental tobacco smoke exposure,[1] exposure to traffic-related air pollution (6 mos.), mother's education (6 mos.), and neighborhood SES (6 mos.)

Effect estimates are calculating the odds of exposure among cases relative to non-cases