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The natural environment, plant diversity, and adult asthma: A retrospective observational study using the CDC's 500 Cities Project Data

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ABSTRACT

A wealth of evidence links microbial exposure to better human immune function. However, few studies have examined whether exposure to plant diversity is protective of immune diseases, despite the fact that plant leaves support $\sim 10^{26}$ bacterial cells. Using the Centers for Disease Control and Prevention's 500 cities project data, we found that a 1-SD increase in exposure to taxonomic plant diversity is associated with a 5.3 (95% CI: 4.2–6.4; $p < 0.001$) percentage-point decline in Census-tract level adult-asthma rate. In contrast, A 1-SD increase in overall greenness exposure (measured using the normalized difference vegetation index) was associated with a 3.8 (95% CI: 2.9–4.8; $p < 0.001$) percentage-point increase in adult-asthma rate. Interactions between air pollution and both overall greenness and plant diversity were positive, suggesting that air pollution may potentiate the allergic effects of plant pollen. Results show that the relationship between the natural environment and asthma may be more complex than previously thought, and the combination of air pollution and plant pollen may be a particular risk factor for asthma in adults.

1. Introduction

The impact of global biodiversity loss on ecological (Dunne et al., 2002), agricultural (Butler et al., 2007), and economic (Balmford et al., 2008) systems is well documented. However, biodiversity loss may have other less intuitive impacts. In particular, loss of plant diversity, and associated microbial communities, may have a negative impact on human immune development, which may, in turn, be contributing to a global increase in immune diseases, especially in high-income countries (Haahtela et al., 2013). However, few studies have examined the link between biodiversity and specific adverse health outcomes. We address this gap in the literature by testing the hypothesis that exposure to plant diversity is protective of adult asthma using the Centers for Disease Control and Prevention's (CDC) 500 Cities Project Data (Centers for Disease Control and Prevention, 2018).

1.1. Literature review

The protective effect of microbial exposure on immune diseases is well established and has entered the popular lexicon via the hygiene hypothesis, which posits that early-life exposure to microbes promotes immune maturation and thereby reduces the risk of immune disease (Yazdanbakhsh et al., 2002). The hygiene hypothesis was developed by David Strachan (1989), and was based on the observation that children from larger families were less likely to develop hay fever. Since this pioneering work, a broad range of proxies for microbial exposure have been shown to be protective of allergic disease including day-care attendance (Ma et al., 2002), breastfeeding (Jackson and Nazar, 2006), birth order (Goldberg et al., 2007), and growing up on a farm (Douwes et al., 2007). In addition, proxies for microbial exposure have been found to be protective of other immune diseases including childhood acute lymphoblastic leukemia (Greaves, 2018), Type-1 diabetes (Cardwell et al., 2005), and multiple sclerosis (Fleming and Cook, 2006).

Despite the wealth of evidence linking microbial exposure to better immune function (Hanski et al., 2012), few, if any, studies have examined whether exposure to plant diversity is protective of immune diseases. One exception is a New Zealand study, which found that children who are exposed to more diverse land-cover are less likely to develop asthma (Donovan et al., 2018).

Several studies have examined the relationship between exposure to the natural environment (not specifically plant diversity) and childhood asthma. A recent review (Hartley et al., 2020) identified seven studies of

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greenness and asthma, of which only one (Donovan et al., 2018) found a direct association between greenness and a reduced incidence of childhood asthma. However, several of the other studies found that greenness was protective for specific strata of the sample. For example, one study found that greenness was protective of asthma among children who were exposed to environmental tobacco smoke (Eldeirawi et al., 2019), and another found a protective effect among children who were exposed to high traffic volume (Feng and Astell-Burt, 2017). None of the six studies that failed to find a main effect of greenness on childhood asthma accounted for the composition of the greenness exposure. Five of the six measured greenness using the Normalized Difference Vegetation Index (NDVI), which is a greenness index bounded by −1 and 1, and the sixth used exposure to publicly-accessible greenspace.

Another recent review examined the relationship between early-life exposure to the natural environment and allergic respiratory diseases (Ferrante et al., 2020). The authors included 14 studies in their review and concluded that the overall evidence is suggestive of an association between early-life exposure and the probability of developing allergic respiratory disease; however, differences in study design, exposure metrics, and study populations make it difficult to draw stronger conclusions.

Beyond immune diseases, such as asthma, a handful of studies have examined the relationship between exposure to biodiversity and self-reported wellbeing, generally finding a positive association (Dallimer et al., 2012).

The lack of research on the association between exposure to plants and immune diseases is notable, given that the total leaf area of the world's plants is 1,017,260,200 km^2 (twice the world's land area), and plant leaves support $\sim 10^{26}$ bacterial cells (Vorholt, 2012).

2. Methods

2.1. Outcomes

Our outcome was the rate of adult asthma at the Census-tract level for the 500 largest cities in the US. The source was the 500 Cities Project Data, which is a partnership between the CDC and the Robert Wood Johnson Foundation (Table 1). The 500 cities project data contains Census-tract level data on health outcomes (asthma, for example), unhealthy behaviors (smoking, for example), and health-prevention measures (annual medical checkups, for example) for the 500 largest cities in the US. The 500 Cities data don't distinguish between adult-onset asthma and asthma that began in childhood and continued into adulthood.

Table 1
Data sources for outcomes, exposures, and covariates.

Variables	Source
Asthma rates, health-risk factors, and health-promotion activities	CDC (2018). 500 Cities: Census Tract-level Data (GIS Friendly Format), 2017 release. Centers for Disease Control and Prevention.
Socio-economics, race, and ethnicity	US Census (2018). Census 2013–2017 American Community Survey 5-year Summary File. U.S. Department of Commerce, U.S. Census Bureau
Air quality	EPA (2018). Air Quality Index (AQI) by county for 2018. US Environmental Protection Agency
Climate zones	PRISM (2019). USDA Plant Hardiness Zone GIS Datasets. PRISM Climate Group, Oregon State University.
Plant diversity	GBIF.org (2019). Plant occurrence data, Global Biodiversity Information Facility
Land cover	NLCD (2016). National Land Cover Database, Land Cover Conterminous United States. Multi-Resolution Land Characteristics (MRLC) consortium
Normalized Difference Vegetation Index (NDVI)	USGS (2018). USGS EROS Archive - Vegetation Monitoring - eMODIS Remote Sensing Phenology: Maximum NDVI for 2018. USGS EROS
Road density	USGS (2019). USGS National Transportation Dataset. U.S. Geological Survey, National Geospatial Technical Operations Center

2.2. Exposures

We created two categories of exposure metrics: 1) exposure to plant diversity; 2) exposure to overall greenness. We used plant-occurrence data from the Global Biodiversity Information Facility (GBIF) to calculate plant-diversity metrics. GBIF contains over 2 billion geo-coded plant records globally, of which 13,082,093 are in the US (data downloaded 25th September 2019). Of these records, 5,806,248 had valid latitude/longitude coordinates. Despite being the world's most comprehensive source of biodiversity data, GBIF sampling intensity was not sufficient to provide a statistically sound estimate of plant diversity at the Census-tract level. Indeed, of the 72,538 Census tracts in the contiguous US (2017 tract boundaries), 16,860 have no GBIF records. Similarly, of the 28,505 Census tracts in the 500 cities project data, 11,663 have no GBIF records. In addition, GBIF data come from multiple sources, so they are not a random sample of plants in the US. Therefore, we first counted the number of unique plant species in national land-cover-climate classes and then used these national totals to calculate tract-level metrics (Fig. 1). In the presence of non-random sampling, this point-to-grid approach is most accurate, when points are aggregated to large units such as national land-cover-climate classes (Schmitt et al., 2017). We used composite land-cover-climate classes, rather than simple land-cover classes, because they would better reflect potential species diversity at the local level. Specifically, land-use-climate classes are a composite of National Land Cover data (20 land-cover types) and USDA plant hardiness zones (13 10-Farenheit zones). Of the 260 possible land-use-climate classes, only 132 were non-empty, as not all NLCD

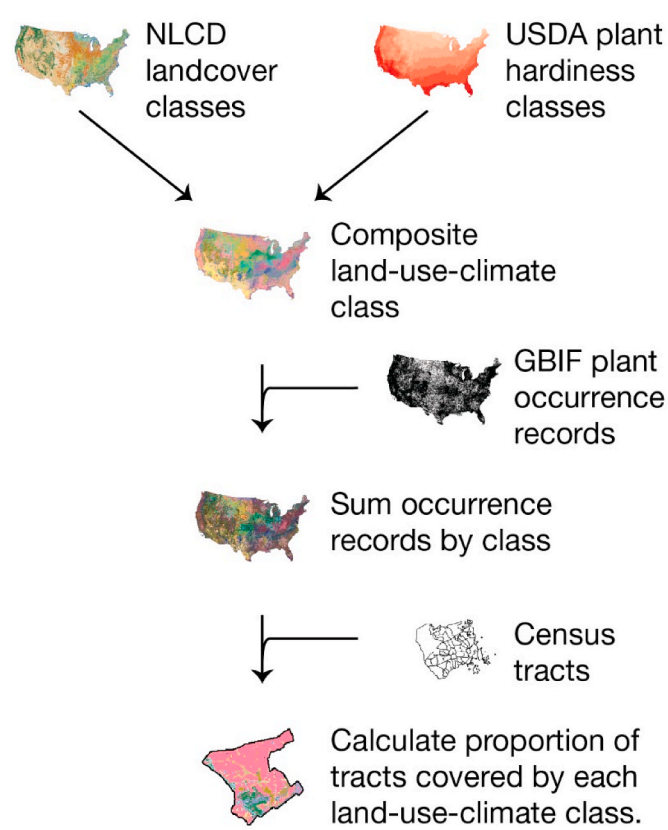

Fig. 1. Flowchart showing how Census-tract level plant-diversity metrics were calculated. Figure credit: Miles Scheuering.

land-cover types were present in each climate zone.

We calculated tract-level metrics by multiplying the number of species in each land-cover-climate class by the proportion of a tract covered by that class and then summing across all land-cover-climate classes. For example, if 40% of a tract was covered by land-cover-climate class type 1 (100 unique species nationally), and the remaining 60% of the tract was covered by land-cover-climate class type 2 (200 species nationally), then tract-level species richness would be $(0.4*100)+(0.6*200) = 160$.

In addition to simple species richness, we calculated indices of rarefied species richness and taxonomic distance using the *R* package Vegan (Oksanen, 2019).

We calculated rarefied species richness, because simple species richness can be misleading, if, as is the case with GBIF data, sampling intensity isn't constant across sampling units. Land-use-climate classes may appear more diverse simply because of higher sampling intensity. Rarefaction corrects for this issue by normalizing to a common sampling intensity across observational units.

Simple species richness does not account for the degree of taxonomic difference between two species. For example, two species from the same genus are given the same weight as two species that come from different genera. To account for the degree of difference between species, we calculated a taxonomic-distance index in which plants of different species but the same genus were given a score of one, plants in different genera but the same family were given a score of two, plants in different families but the same order were given a score of three, and plants in different orders were given a score of four. See Oksanen (2019) for details of how all indices were calculated.

To measure exposure to overall greenness, we used the Normalized Difference Vegetation Index (NDVI), which is a greenness index bounded by −1 and 1, which is typically derived from satellite imagery. Specifically, we used maximum NDVI for 2018 derived from the USGS EROS Archive. Tract-level values were the average of the 250 m NDVI pixels within each tract boundary. There were some pixels that were either undetectable (100 in original data) or water (255 in data). These were set to null, and data were then rescaled to 1–100 before averaging.

For ease of interpretation, we standardized all biodiversity and greenness metrics by subtracting the mean and dividing by the standard deviation.

Census tracts in the US sometimes cross jurisdictional boundaries of cities and towns. If a Census tract was divided between two cities that both appeared in the 500 cities data project, then we assigned outcome data to both tracts. If a neighboring city was not part of the sample, then outcome data was assigned solely to fractional tract that was part of the 500 cities data project. We only included fractional tracts, if over 50% of the tract's population fell within a city included in the sample.

2.3. Covariates

We controlled for a range of covariates that previous research has found to be associated with asthma rates including race (Centers for Disease Control Prevention, 2004), socioeconomic status (Miller, 2000), air pollution and proximity to roads (Guarnieri and Balmes, 2014). For data sources see Table 1.

2.4. Statistical analysis

Our data were structured hierarchically: tracts are clustered within cities, and cities are clustered within states. Policies at both the city and state level could affect asthma rates; therefore, we estimated a mixed linear model of tract-level adult asthma rates including random effects at the city and state level. Model selection was done using backwards selection with progressively lower p-value thresholds (final threshold: $p < 0.05$). We systematically reintroduced insignificant variables—with particular focus on variables associated with asthma in previous studies—and retained them, if they induced a greater than 10% change in coefficients of interest.

To guard against including highly collinear combinations of variables in our models, we estimated simple linear versions of all regression models (without city- or state-level random effects). This allowed us to calculate variance inflation factors (we investigated any variable with a VIF>5).

Finally, to investigate spurious correlation, we used out-of-sample validation (Steyerberg and Harrell, 2016) to compare the performance of our final regression model to two reduced-form models: 1) No variables describing greenness (NDVI) or plant diversity; 2) No variables describing plant diversity (but including greenness). The rationale for out-of-sample validation is that spurious associations with good explanatory power in-sample tend to perform poorly out-of-sample. In contrast, causal associations that perform well in-sample will also have good predictive power out-of-sample. We trained both models on 90% of the sample (drawn randomly from the full sample) and predicted asthma rates using the remaining 10%. The sample was randomized, and this process was repeated 1000 times. After each iteration of the full or reduced-form models, we recorded the mean squared error (MSE) of the asthma-rate predictions.

3. Results

The full 500 Cities data project contains 500 cities and 28,505 Census tracts. However, our analytic sample was restricted to the 498 cities in the contiguous US, as not all data sources were available for Alaska and Hawaii. Dropping these two states reduced the number of Census tracts in the sample by 296. The sample was reduced by a further 1842 tracts dues to missing outcome and covariate data. Table 2 provides descriptive statistics for the analytical sample.

We found that taxonomic diversity had greater explanatory power (measured using the Akaike Information Criterion) than simple richness or rarefied richness. Therefore, we used taxonomic diversity in all models.

Asthma rates were higher in tracts with a higher proportion of African Americans and lower in tracts with more Asians and Hispanics (percentage white was excluded due to collinearity) (Table 3). Variables indicating lower socioeconomic status (percent of households headed by a female, percent of households below the federal poverty line, unemployment rate, and percent of residents without health insurance) were positively associated with adult asthma rate. In contrast, variables

Table 2
Tract-level descriptive statistics for outcomes, exposure, and covariates for analytic sample (498 cities, 26,367 tracts).

Variable	Mean	SD
White (%)	60.2	27
Hispanic (%)	24.4	25
Asian (%)	7.2	11.1
African American (%)	20.5	26.8
American Indian (%)	0.65	1.5
Population	4494	2314
Health Insurance (%)	87.9	8.3
Population under 18 (%)	22.4	7.7
Female head of household (%)	15.9	10.1
Population >25 graduated high school (%)	84.3	12.8
Population >25 bachelor's degree	32.0	21.1
Unemployment >16 (%)	8.0	5.8
Median household income ($)	58,726	31,458
Adult asthma rate (%)	9.7	1.9
Adult smoking rate (%)	18.2	6.1
Adult obesity (BMI ≥ 30) rate (%)	30.2	8.2
Adults who sleep <7 h a night (%)	36.7	5.9
Adults had routine medical checkup in last year (%)	69.4	6.4
Maximum NDVI (2018)	0.54	0.18
Species richness	1943	241
Rarefied species richness	255	12
Taxonomic diversity	118	9.8

Table 3
Association between Census-tract level adult asthma rates and exposure to taxonomic plant diversity for the 498 largest cities in the contiguous US, controlling for race, ethnicity, socioeconomic status, behavioral risk factors, health prevention, air pollution, and overall greenness (n = 26,367).

Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
African American (%)	0.496	0.432	0.560	<0.001
American Indian (%)	0.0873	−0.316	0.491	0.553
Asian (%)	−3.200	−3.290	−3.109	<0.001
Hispanic (%)	−1.754	−1.806	−1.702	<0.001
Female head of household (%)	1.022	0.939	1.105	<0.001
High-school graduates (%)	−0.0222	−0.0231	−0.0213	<0.001
Bachelor's degree (%)	−0.00402	−0.00458	−0.00346	<0.001
Population below poverty line (%)	0.0274	0.0268	0.0280	<0.001
Unemployment rate >16 (%)	0.00906	0.00784	0.0103	<0.001
No health insurance (%)	0.00707	0.00607	0.00808	<0.001
Routine medical checkup in last year (%)	0.00786	0.00540	0.0103	<0.001
Obesity (BMI ≥ 30) rate (%)	0.0334	0.0300	0.0369	<0.001
Sleep <7 h a night (%)	0.111	0.106	0.117	<0.001
Maximum PM2.5 concentration (stand.)	0.392	0.304	0.481	<0.001
Taxonomic diversity (stand.)	−0.0528	−0.0638	−0.0418	<0.001
Maximum NDVI (stand.)	0.0383	0.0290	0.0475	<0.001
Taxonomic-diversity*PM2.5	0.0383	0.0290	0.0475	<0.001
NDVI*PM2.5	0.0289	0.0190	0.0387	<0.001

associated with higher socioeconomic status (percent of the population 25 years and older who graduated high school, and percent of the total population with a bachelor's degree) were negatively associated with adult asthma rate. Tracts with a higher proportion of adults who had a routine checkup in the last year had higher rates of asthma. Clearly, medical checkups do not cause asthma. Rather, routine checkups provide an opportunity to diagnose health conditions including asthma. Tracts with higher rates of adult obesity (BMI≥30), or higher rates of adults sleeping less than seven hours a night, had higher rates of adult asthma. Finally, poorer air quality was associated higher rates of adult asthma.

Two variables describing exposure to the natural environment were significantly associated with adult asthma rates. NDVI (greenness) was positively associated with adult asthma rate, whereas taxonomic diversity was negatively associated with adult asthma. In addition, interactions between NDVI and air pollution, and between taxonomic diversity and air pollution, were positive. This indicates that in areas with poor air quality, increased greenness and taxonomic diversity are associated with an additional increase in adult asthma rates.

As NDVI, taxonomic diversity, and maximum annual PM2.5 enter the model alone and in interaction terms, individual coefficients do not represent the full aggregate effect of these three variables. Therefore, we used the delta method to calculate combined effects and associated confidence intervals (Table 4).

Table 4
Coefficients for air pollution, taxonomic plant diversity, and NDVI accounting for main effect and interaction terms.

Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
Maximum PM2.5 concentration (stand.)	0.392	0.304	0.480	<0.001
Taxonomic diversity (stand.)	−0.0527	−0.0637	−0.0417	<0.001
Maximum NDVI (stand.)	0.0383	0.0291	0.0476	<0.001

Out-of-sample validation showed that the full model (MSE = 0.0281) performed better than a reduced-form model without either plant diversity or NDVI (MSE = 0.0368). A one-sided *t*-test showed that this difference in performance was statistically significant ($p < 0.001$). Fig. 2 shows the simulation results for the 1000 iterations of these two models. The full model also performed better than a reduced form model without plant diversity but including NDVI (MSE = 0.0299), and a one-sided *t*-test showed that this difference was statistically significant ($p = 0.013$). Note that NDVI and taxonomic diversity are uncorrelated (correlation coefficient = 0.091).

4. Discussion

In this large national study, we found significant associations between Census-tract level adult asthma rates and exposure to both taxonomic plant diversity and overall greenness. Exposure to taxonomic diversity was associated with reduced rates of adult asthma, whereas greenness was associated with increased rates. The magnitude of the protective effect of plant diversity was not trivial: a 1-Standard Deviation (SD) increase in exposure to taxonomic plant diversity was associated with a 5.3 (95% CI: 4.2–6.4; $p < 0.001$) percentage-point decline in adult-asthma rate. A 1-SD increase in NDVI, in contrast, was associated with a 3.8 (95% CI: 2.9–4.8; <0.001) percentage-point increase in adult-asthma rate. Interactions between plant diversity and NDVI and maximum annual PM2.5 levels were both positive, which suggests that in high-pollution areas, NDVI is a greater risk for asthma, and the protective effect of plant diversity is attenuated. This finding is consistent with previous research showing that air pollution can potentiate the allergic effects of plant pollen (Janssen et al., 2003).

The extant research on greenness and asthma is inconclusive and has primarily focused on childhood asthma (Hartley et al., 2020). Most studies either found no relationship between greenness exposure and childhood asthma, or found that greenness was only protective if a child was exposed to environmental risk factors such as tobacco smoke or traffic-related air pollution. In contrast, we found that exposure to greenness was a risk factor for adult asthma. Our findings are not a function of using different exposure metrics as all but one of the seven studies included in the recent review of greenness and childhood asthma (Hartley et al., 2020) also used NDVI. It is possible, therefore, that our findings reflect differences in the causal pathways linking exposure to the natural environment and childhood versus adult-onset asthma (not all adult asthma in our analysis is adult onset; some may have begun in childhood). Although less is known about adult-onset asthma, it is known to have a higher prevalence among females (Gibson et al., 2010), be less associated with allergies (Shaaban et al., 2008), have a lower remission rate (De Marco et al., 2002), and have a weaker genetic component (de Nijs et al., 2013) than childhood asthma. Given these differences, it is plausible that greenness is a risk factor for adult-onset asthma but not childhood asthma. However, as this is an observational study with an ecological design, it may be appropriate to view our study as hypothesis forming rather than hypothesis testing.

Our finding that exposure to plant diversity is protective of adult asthma is consistent with the hygiene hypothesis and with a previous study in children that found that exposure to more diverse land-cover types was protective of asthma (Donovan et al., 2018). In addition, our finding that NDVI was a risk factor for adult asthma suggests that plant diversity is not merely a proxy for greenness exposure. Future green-health research may wish to consider not just the intensity of exposure to the natural environment but also the composition of that exposure.

The protective effect of plant diversity is also consistent with past research showing that common childhood infections (although not more serious infections such as pertussis and measles) are protective of adult-onset asthma (Burgess et al., 2012). If exposure to common microbial infection is protective, then it is plausible that exposure to the non-pathological microbial communities known to be associated with

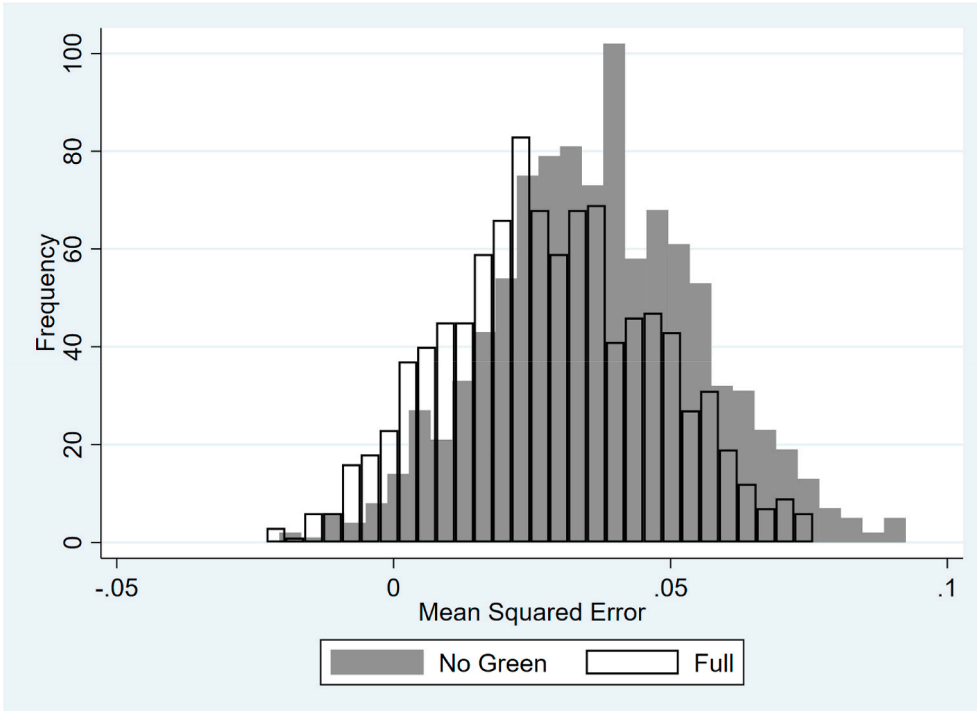

Fig. 2. Out-of-sample validation results comparing full model (Table 3) to a reduced-form model without NDVI or taxonomic diversity (1000 repetitions, 90% of sample used to train models and 10% used to predict).

plants (Kowalchuk et al., 2002) is also protective of adult-onset asthma. This protective effect is likely mediated through the microbiome, as multiple studies have found that increased diversity of the human microbiome is associated with a reduced risk of asthma (Fujimura and Lynch, 2015). Support for this mechanism is provided by a Scandinavian study (Hanski et al., 2012), which found that people living in more biodiverse areas have more diverse skin bacteria and lower rates of atopic sensitization. Similarly, a recent small study found that the diversity of participants' skin and nasal microbiota increased after exposure to diverse urban greenspace (Selway et al., 2020). Animal studies have also found a link between exposure to more diverse vegetation and diversity of the microbiome. For example, Phillips et al. (2018), found significant differences in the diversity of the gut microbiota of urban and rural white-crowned sparrows, which the authors attribute to higher plant diversity in urban areas.

We found that taxonomic plant diversity explained more of the variation in adult asthma than equivalent metrics based on species richness or rarefied species richness. This finding also suggests that plant microbial communities may play a role in the protective effect of plant diversity, as research has shown that more taxonomically diverse plant communities support more diverse microbial communities (Kowalchuk et al., 2002).

The significant interactions between air pollution and both NDVI and plant diversity suggests that planting vegetation in areas with high levels of air pollution should be undertaken cautiously. For example, several studies have shown trees along busy roads can absorb harmful air pollutants (Vailshery et al., 2013). However, the combination of trees and traffic-related air pollution may also result in allergic sensitization (Janssen et al., 2003). We are not suggesting that trees and other vegetation should never be planted in high-pollution areas. Rather, future research could valuably focus on identifying plants that, when combined with air pollutants, pose the greatest risk of allergic sensitization.

Past studies have shown that exposure to the natural environment is associated with other drivers of adverse health outcomes including race, education, and income (Jesdale et al., 2013). This raises the possibility that our results are driven by an omitted variable that is causally associated with both adult asthma rate and the natural environment (spurious correlation). However, out-of-sample validation shows that the inclusion of both plant diversity and greenness improved the predictive power of models, which suggests that our results are not due to spurious correlation.

Our study does have several limitations. This is an observational study, so we were unable to establish a causal relationship between greenness, plant diversity, and asthma. The study's ecological design means that results may be subject to ecological bias. In addition, plant-diversity metrics were based on species abundance in national land-cover-climate classes, and it is unlikely that every species present in these national classes is present in every Census tract that is covered by that class. Furthermore, not all data sources are from the same year. Finally, we were not able to distinguish between adult-onset asthma and asthma that began in childhood.

Despite these limitations, our study has several strengths. We used a large national sample consisting of the 498 largest cities in the contiguous US, so there were few sample-selection issues. Unlike other green-health studies, we considered both the intensity of exposure to the natural environment (NDVI) as well as the composition of that exposure (taxonomic diversity). Furthermore, this is one of the few studies to focus on asthma in adults rather than children. Finally, our use of out-of-sample validation means that the reported associations are not due to spurious correlation.

5. Conclusions

Our results suggest that the causal pathways linking exposure to the natural environment and asthma may be different in adults than children. In addition, our finding that exposure to more diverse plants is protective of asthma suggests that the composition of exposure to nature may be as important as the intensity of exposure.

Data availability

All data and code are freely available from the corresponding author.

Author contributions

GHD developed the research idea, conducted the statistical analysis, and wrote the majority of the paper. SML conducted the geo-spatial analysis and wrote sections of the methods. DG calculated the plant-diversity metrics.

Declaration of competing interest

This study received no outside funding and none of the authors have any competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.healthplace.2020.102494.

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