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Is green space associated with opioid-related mortality? An ecological study at the U.S. county level

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ABSTRACT

Opioid consumption, both legal and illicit, has risen precipitously in the U.S. over the past few decades, as has the number of deaths due to the use and misuse of opioids. Exposure to green spaces may help to alleviate the problematic levels of opioid use. Such exposure has been tied to health benefits relevant to opioid use. To explore the potential influence of green space on opioid-related health outcomes, we analyzed the association between tree canopy cover and mortality attributable to opioid use and abuse using 2008–2018 death rate data on a county level ($n = 3087$) across the contiguous U. S. We fitted spatial general additive model while controlling for socioeconomic factors, healthcare access measures, opioid prescription rates, and particulate air pollution. Contrary to expectations, canopy cover was positively associated with opioid mortality. A sensitivity analysis with forest land cover showed similar results while a sensitivity analysis with total greenness (NDVI) was nonsignificant. Stratified models by urbanicity level suggested suburban and rural counties drove the positive associations observed in the nationwide models. The findings for forest and canopy cover are unexpected, given the myriad health benefits of green spaces, yet might be explained by heavily forested areas (i.e., Appalachia) being home to injury-prone natural resource extraction employment sectors. The steady decline of these industries has created poor socioeconomic conditions that exacerbate the already elevated risk of opioid use and misuse. Alternatively, the magnitude of the protective effects of greenspace on pain reduction are insufficient to counter opioid demand. Further research is warranted, especially in studies with individual-level data. Entities with responsibility or interest in reducing the incidence of deaths from opioids are cautioned that green spaces might not be a viable option for reducing opioid mortality.

1. Introduction

Mortality caused by opioids, substances based on opium with addictive properties, has risen substantially over the past two decades (Rudd et al., 2015), accounting for roughly 450,000 deaths in the United States (U.S.) (Wilson, 2020). A rise in opioid prescription rates has occurred simultaneously (Guy Jr et al., 2017). The misuse of opioids has become so widespread and damaging that it has spurred an "opioid epidemic" (Murthy, 2016). Policymakers and public health officials have pursued an array of solutions, including revised prescribing guidelines issued by the Centers for Disease Control and Prevention (CDC) (Dowell et al., 2016). Exposure to natural settings such as green spaces could act as part of the solution to the unnecessary deaths caused by opioid use and misuse.

Living amidst or having regular contact with green spaces (e.g., forests, parks, and other places rich with plant life) has been linked to numerous beneficial health outcomes (James et al., 2015; Twohig-Bennett, Jones, 2018; Yang et al., 2021) and therefore might help to ameliorate the opioid crisis. Green space exposure may activate four pathways related to reducing opioid use, which may lead to lower occurrence of opioid-related death.

First, green space exposurecan benefit physical health. Multiple studies have shown an increase in self-perceived general health among individuals living in greener areas (Maas et al., 2006; Astell-Burt & Feng, 2019). Substantial reductions in several types of morbidity, including cardiovascular, musculoskeletal, respiratory, and neurological

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conditionshave also been reported (Maas et al., 2009; Liu et al., 2022; Rojas-Rueda et al., 2019). For example, one cohort study in Ontario, Canada, found reduced odds of six mortality types, including respiratory and cardiovascular disease (Villeneuve et al., 2012).

Second, nature exposure has also been linked to improved mental health status, both measured and self-reported. Higher self-reported mental health scores have been observed among those living in greener areas compared to those living in less green areas (Alcock et al., 2014; Astell-Burt & Feng, 2019; Helbich et al., 2018; Van den Berg et al. 2016). Lower incidence of anxiety disorders and depression have also been found in areas with more green space (Maas et al., 2009). The presence of general greenness and parks lessens stress in individuals via enhanced social support (Fan et al., 2011).

Third, several studies have shown that exposure to natural settings may increase pain tolerance. Simultaneous exposure to views and sounds of nature provide distraction from pain and relaxation, which reduces reported pain in general hospital patients (Kline, 2009) and patients undergoing bone marrow procedures (Lechtzin et al., 2010). Subjects shown scenes of greenery have been found to have a higher pain detection threshold than those shown blank screens (Tse et al., 2002). Green space exposure likely affects pain tolerance by acting through several key mechanisms, including exposure to beneficial airborne organic compounds and bolstering immune and neurological function via negative air ions (Stanhope et al., 2020) and by distracting the subject from painful stimuli (Tanja-Dijkstra et al., 2018; White et al., 2018).

Fourth, exposure to green spaces may help reduce the occurrence and severity of substance abuse by improving the ability to manage addictive tendencies. Patients in surgical recovery with views of natural settings had shorter postoperative hospital stays and required fewer analgesic pharmaceuticals than those with a non-natural view (Ulrich, 1984). Knee and hip surgery patients living in greener settings took fewer opioids following surgery (Donovan et al., 2019). Greater access to and residential views of green space were associated with decreased intensity and frequency of addictive cravings (Martin et al., 2019). Individuals living in greener environments have demonstrated improved decision-making ability regarding their health, including general health and addiction decisions (Berry et al., 2020), smoking (Martin et al., 2020; Wu, Chiou, 2019), and dietary choices (Kao et al., 2019).

Numerous conditions, both physical and mental, have been identified as predictors of opioid use and abuse (Katz et al., 2013; Mojtabai, 2018). Individuals with higher sensitivity to pain were more likely to use and misuse opioids (Wachholtz et al., 2019; Zahari et al., 2016). Patients with opioid dependence displayed significantly worse self-control and impulsiveness than control subjects (Peters & Soyka, 2019). In turn, prescription and usage rates of opioids determine the number of deaths attributable to opioids (Dart et al., 2015). Opioid-related death rates closely follow the rise in the use of both prescription and illicit opioids from 2010 to 2015 in the U.S. (Rudd et al., 2016).

A final reason to suspect a relationship between green spaces and opioid mortality is the strong and persistent association between green spaces and other mortality endpoints. The pooled risk of all-cause mortality was 4% lower per 0.1 increase in the amount of green space in a meta-analysis of nine cohort studies (Rojas-Rueda et al., 2019). In the lowest vs. highest green space category, a 4% reduction in cardiovascular disease mortality risk and an 8% reduction in all-cause mortality has been observed (Gascon et al., 2016). A 31% and 16% reduction in the odds of all-cause mortality and cardiovascular disease mortality, respectively, were reported for the highest compared to the lowest green space group in another study (Twohig-Bennett and Jones, 2018). In a study of Canadian adults, the risk of all-cause mortality was 8% lower for a 0.1 increase in greenness (Crouse et al., 2017). A significant negative association was found between greenness distance and all-cause/cardiovascular disease mortality in Florida (Coutts et al., 2010). The magnitude of the association between greenness and mortality across myriad of studies is large enough to potentially extend to other types of mortality, such as opioid overdoses.

Thus far, no studies have examined the relationship between nature exposure and opioid-related mortality. A large amount of research has been conducted on the relationship between green spaces and many different types of mortality, as discussed above, but we know of no studies that have examined opioid mortality in the context of green space exposure. The current study aims to fill that gap - and respond to requests for research on greenspace exposure and the opioid crisis (Berry et al., 2021) - by assessing associations between tree canopy cover, forest land cover, and total vegetative greenness with opioid mortality outcomes on a county-level for the contiguous U.S. We hypothesize that the amount of green space is inversely associated with the number of opioid-related deaths.

2. Methods

2.1. Study Design

We used an ecological, cross-sectional study design on a county level. In the U.S., counties are administrative and political units larger than towns and cities but smaller than states. The U.S. consists of 3141 counties averaging about 105,000 people and 1200 square miles (U.S. Census, 2019).Counties are the smallest unit for which opioid-related mortality data exist. The number of counties for which opioid mortality data were available to match with our study period was 2677. The 464 counties had missing, unreliable, or otherwise incomplete opioid mortality data.

2.2. Data

Dependent Variable: Our dependent variable was annual opioid-related death count aggregated across 2008–2018. There are eleven mortality International Classification of Disease (ICD) codes relevant to opioid mortality from two code series: T40 and X40–44. The former contains deaths by poisonings (overdoses and underdoses) from natural and synthetic opioids, and the latter includes accidental poisonings by opioid substances. These eight specific mortality endpoints are representative of opioid-related behaviors. The ICD codes included are described in detail in Supplementary Table S1. Opioid mortality data were retrieved from the Center for Disease Control and Prevention's (CDC) WONDER database (CDC, 2020a). The WONDER database is constructed with data reported to the CDC by the vital statistics divisions of county health departments and has been used earlier (Hampson, 2016; Zhang et al., 2018).

Green Space: The primary variable of interest is percent of county land that is tree canopy cover, population-weighted and buffered (1 kilometer) by census tract, abbreviated to Canopy in the Results. Population weighting gives higher weight to human population centers to reflect the amount of actual exposure (Heo & Bell, 2019). Expanding the area by adding a 1 km buffer around each tract captured a larger potential green area exposure, as individuals are rarely confined to their tract (Maas et al., 2006; Richardson et al., 2012; Su et al., 2019). Tree canopy data came from the National Land Cover Database (NLCD) 2011 (Coulston et al., 2012). The NLCD has been deemed highly accurate in its designation of land covers by independent evaluation (Wickham et al., 2017) and has been used previously (Nowak et al., 2014; Richardson et al., 2012; Tsai et al., 2018).

2.3. Other Covariates

We adjusted for a number of important socioeconomic factors that have been included in previous studies on opioid mortality (Grigoras et al., 2018; Katz et al., 2013), including the median age of county residents (abbreviated as Age in the Results), percentage of county residents that are female (Female), percentage of county residents that identify as Caucasian/White and non-Hispanic (White), percentage of county residents with at least a bachelor's degree (Education), percentage of county residents living under the poverty line (Poverty), and median household income of county residents (Income) (United States Census Bureau, 2019).

Our models were also adjusted for the share of the county's workforce that was employed in manual labor positions (Manual): agriculture, fishing and hunting, forestry, and mining. The data for this variable were from the 2007–2011 four-year American Community Survey, provided by the Integrated Public Use Microdata Series (IPUMS) program (Ruggles et al., 2015).

An area's level of urbanization has been identified as a key determinant of opioid use, misuse, and mortality in several studies (Keyes et al., 2014; Kurani et al., 2020; Luu et al., 2019). Given this fact, we included the urban-rural classification scheme (Urban-rural) developed by the Centers for Disease Control and Prevention (CDC) (Ingram, 2014). This scheme ranges from 1 (most urban) to 6 (most rural). The CDC developed this scheme to accurately capture the health profile and healthcare access infrastructure of America's counties for the purpose of health and healthcare research.

Healthcare access, such as the number of physicians and hospitals per resident, have been associated with opioid prescription rates and opioid mortality at the county level (Grigoras et al., 2018). To control for potential confounding, we included healthcare access for the county; the number of primary care physicians (Doctors), hospitals (Hospitals), and hospital beds (Beds) per 10,000 county residents extracted from the Area Health Resource Files provided by the United State Department of Health and Human Services (HRSA, 2018).

Because opioid mortality rates are highly correlated with opioid prescription rates (Dart et al., 2015; Rudd et al., 2016), we control for the number of opioid prescriptions prescribed annually per 100 county residents (Rx). Opioid prescription rate data were obtained from the IQVIA Xponent System 2006–2018 data, provided by the CDC.

Air pollution is a key determinant of premature mortality (Lelieveld et al., 2015), especially in the Medicare population (Di et al., 2017). Improved air quality is also one of the mechanisms by which green spaces are thought to affect human health or mediate other pathways (Heo & Bell, 2019; Kuo, 2015) as plants can remove pollutants from the air (Selmi et al., 2016). Therefore, we included the average annual concentration of fine particulate matter with diameters that were < 2.5 micrometers (in micrograms per cubic meter of air) ($PM_{2.5}$) obtained from the CDC WONDER database (CDC, 2020b).

2.4. Statistical Analysis

We calculated descriptive statistics to summarize the data. Next, to explore bivariate relationships between the variables, we computed bivariate Pearson correlations. Multicollinearity among the covariates was assessed with variance inflation factor (VIF) scores. A VIF score threshold of 5.0 was selected in compliance with Johnston et al. (2018).

For the main analysis, we employed general additive models (GAM) (Wood, 2017) based on restricted maximum likelihood to assess the relationship between opioid-related death and green space. For our count data, the Poisson distribution was well suited, which assumed mean-variance equivalence. Due to significant overdispersion, violating a fundamental model assumption, we re-fitted the model as a negative binomial regression. Rather than including only the number of deaths, mortality rates were modeled via the inclusion of an offset term with the log of the county population. To mitigate the fact that adjacent counties are likely correlated with each other (Helbich et al., 2018), we included a Markov Random Field (MRF) to capture arising spatial correlations based on an adjacent neighborhood structure. We tested for residual independence by means of the Moran's I statistics. Pseudo p-values were received from 999 Monte Carlo simulations against the null hypothesis of spatial independence.

Our model building process comprised three models with increasing adjustment levels; Model 1 adjusted only for tree canopy cover and included a MRF smoother, Model 2 added socioeconomic variables, and Model 3 was fully adjusted with all variables. All statistical analyses were performed in the R software program, version 3.6.3 (R Core Team, 2020).

2.5. Stratified Analyses

We performed stratified analyses to determine associations between tree canopy cover and opioid mortality in six levels of urbanicity. Previous research on greenness and health outcomes that has conducted sub-analyses based on urbanicity has reported results that vary, often substantially, by level of urbanization (Becker, Browning, 2021; Maas et al., 2006; Mitchell & Popham, 2007; for review, see Browning et al., 2022), as do the determinants of opioid mortality (Wilkes et al., 2021). To perform analyses within each strata, the dataset was divided into six samples according to CDC urban-rural scheme designation and GAM models were run on each of the strata. The Markov Random field spatial component was omitted in these analyses because of the separations between spatial units, which precluded the accurate and consistent construction of neighborhood weight matrices.

2.6. Sensitivity Analyses

We conducted three sensitivity analyses to confirm the robustness of our results from the fully adjusted model. First, we tested an additional greenness measure obtained from NLCD; forested land cover (Forest), which is defined by the NLCD as a 30 m cell that is at least 51% covered in trees (Model 3a). Although both canopy cover and forest land cover data measure trees, they do so with different methodologies; tree canopy cover is calculated using physical tree canopy inventories and aerial photography alongside remotely sensed data, whereas forest land cover is estimated entirely from remote sensing data (Coulston et al., 2012; Homer et al., 2015). Second, we substituted the Normalized Difference Vegetation Index (NDVI) for canopy cover (Model 3b). NDVI is a long-standing measure of vegetation density (Hartley et al., 2020; Rojas-Rueda et al., 2019; Zhan et al., 2020). NDVI data came from the Moderate Resolution Imaging Spectroradiometer (MODIS) satellite platform, provided by the Google Earth Engine (Gorelick et al., 2017). Third, in Model 3c, we suspected some geographic variation in the relationship between green spaces and opioid mortality. To explore this, we added an interaction term between tree canopy cover and ecological regions ("ecoregions") as defined by the Level 1 Ecoregions developed by the Environmental Protection Agency (EPA) (Omernik & Griffith, 2014). The interaction term was tested for significance through a likelihood ratio test. If significant, data were split to calculate ecoregions-specific estimates.

3. Results

3.1. Descriptive Statistics and Bivariate Correlations

Descriptive statistics for all variables are found in Table 1. Average opioid-related deaths across the years 2008–2018 in a county ranged from 0 to 6201 with a mean of 103.5 and standard deviation (SD) of 306.5.

Fig. 1 displays the complete bivariate correlation coefficients between all variables. The correlation between death count and tree canopy cover was -0.05 ($p < 0.05$). High death counts were concentrated in the central Appalachian region (Kentucky, Tennessee, North Carolina, Virginia, and West Virginia), New England (Connecticut, Rhode Island, New Hampshire, Vermont, and Maine), Florida, and the Southwest (Fig. 2).

Fig. 3 displays tree canopy percentage by county. The areas of the country with the highest tree canopy coverage were Appalachia, the Southeast, Northeast, upper Midwest, and Pacific Northwest (Oregon and Washington). The minimum percent canopy cover in a county was

Table 1
Descriptive statistics of study variables.

	Min.	Max.	Range	Median	Mean	SD
Deaths (per 100,000 residents)	0.0	6201.0	6201.0	22.0	103.5	5.9
Canopy (%)	0.0	84.1	84.1	21.0	27.0	0.4
Age (years)	22.9	64.1	41.2	40.7	40.6	0.1
Female (%)	27.7	57.4	29.8	50.5	50.1	0.0
White (%)	10.0	98.9	88.9	86.9	80.3	0.3
Black (%)	0.0	85.6	85.6	2.3	8.9	0.3
Native (%)	0.0	83.5	83.5	0.5	1.9	0.1
Asian (%)	0.0	33.3	33.3	0.6	1.3	0.0
Hispanic (%)	0.2	96.5	96.3	3.6	8.7	0.3
Education (%)	5.6	74.0	68.5	18.3	20.5	0.2
Income (1000 USD)	20.7	122.9	102.2	45.1	46.9	0.235
Doctors (per 10,000 residents)	0.0	175.8	175.8	6.7	9.2	0.2
Hospitals (per 10,000 residents)	0.0	9.2	9.2	0.3	0.6	0.0
Hospital Beds (per 10,000 residents)	0.0	758.5	758.5	21.2	31.9	44.6
Urban-rural (scale 1–6)	1.0	6.0	5.0	5.0	4.6	0.0
$PM_{2.5}$ (μg/m^3)	7.2	14.9	7.7	11.9	11.6	1.5
Rx (per 10,000 residents)	1.1	583.8	582.7	85.9	91.9	47.0
Poverty (%)	0.0	46.7	46.7	9.3	10.6	0.1
Manual (%)	0.0	52.4	52.4	4.2	7.0	0.2

0 and the maximum was 84.1% with a mean of 27% and SD of 23.28%.

3.2. *Main analyses*

There was no multicollinearity among the covariates; no variable exceeded a VIF value of 5.0. Table 2 shows the results of the GAM regressions. The beta coefficient of the Canopy variable was negative ($\beta = -0.012$) and statistically significant ($p = 0.000$) in Model 1. Model 2 with socioeconomic covariates added showed a slightly positive ($\beta = 0.01$) and significant ($p = 0.041$) coefficient for Canopy. In Model 3, Canopy was positively ($\beta = 0.01$) and significantly ($p = 0.001$) related to opioid mortality. All covariates' coefficients were also statistically significant except for Income and $PM_{2.5}$. The final model explained 62.8% of the deviance and had an adjusted R^2 of 0.58. Regression residuals of Model 3 were well-behaved in terms of normality (Fig. S2 in the supplementary materials). This was also confirmed in the insignificant Moran's I statistic ($p = 0.600$).

3.3. *Stratified Analyses across Urbanization Levels*

Model results varied by degree of urbanization (Table 3). The coefficient estimate of tree canopy cover was not statistically significant in level 1 (large central metro), 3 (medium metro), 4 (small metro), or 5 (micropolitan). The coefficient was statistically significant in level 2 (large fringe metro) and 6 (non-core rural), with a positive sign in both cases that was similar in magnitude to that of the model ran on the entire nation.

3.4. *Sensitivity Analysis*

Forest was also positively and statistically significantly related to opioid mortality in fully adjusted models ($\beta = 0.01, p = 0.000$) (Table 2, Model 3a). In contrast, NDVI was not associated with opioid mortality ($p = 0.945$) (Model 3b). We found no evidence that the association between tree canopy cover and ecoregions varied spatially (Model 3c, Supplementary Table S2). The likelihood ratio test between Model 3 and Model 3c was nonsignificant ($p = 0.34$).

4. Discussion

4.1. *Interpretation of Results*

We sought to discern if an association exists between the amount of green space in a U.S. county and the number of deaths attributable to

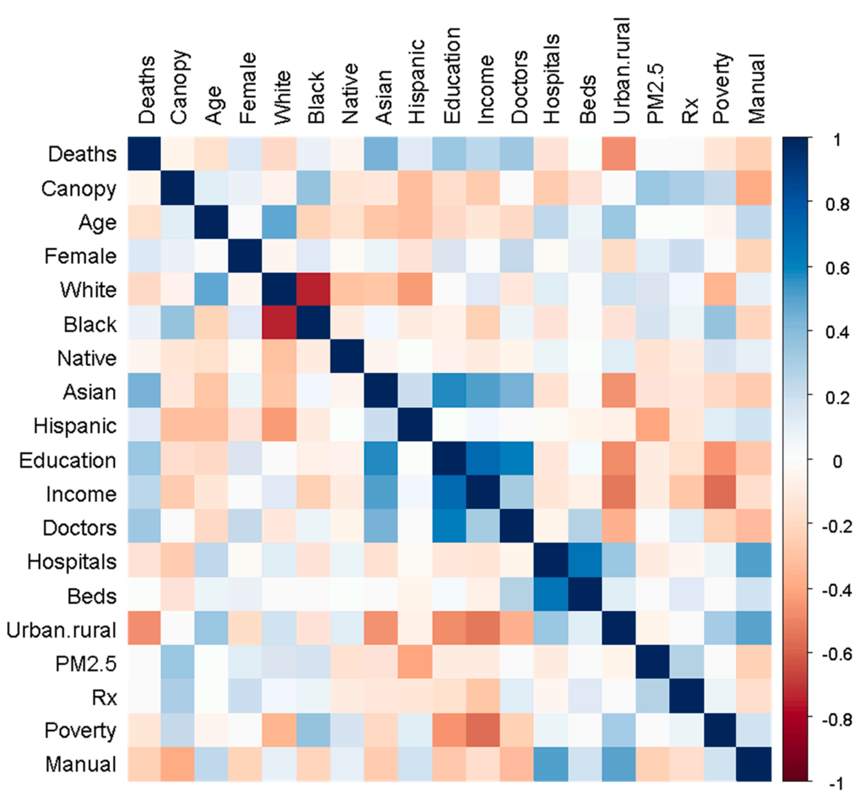

Fig. 1. Bivariate correlation matrix graph. Blue cells indicate a positive correlation, red cells a negative correlation.

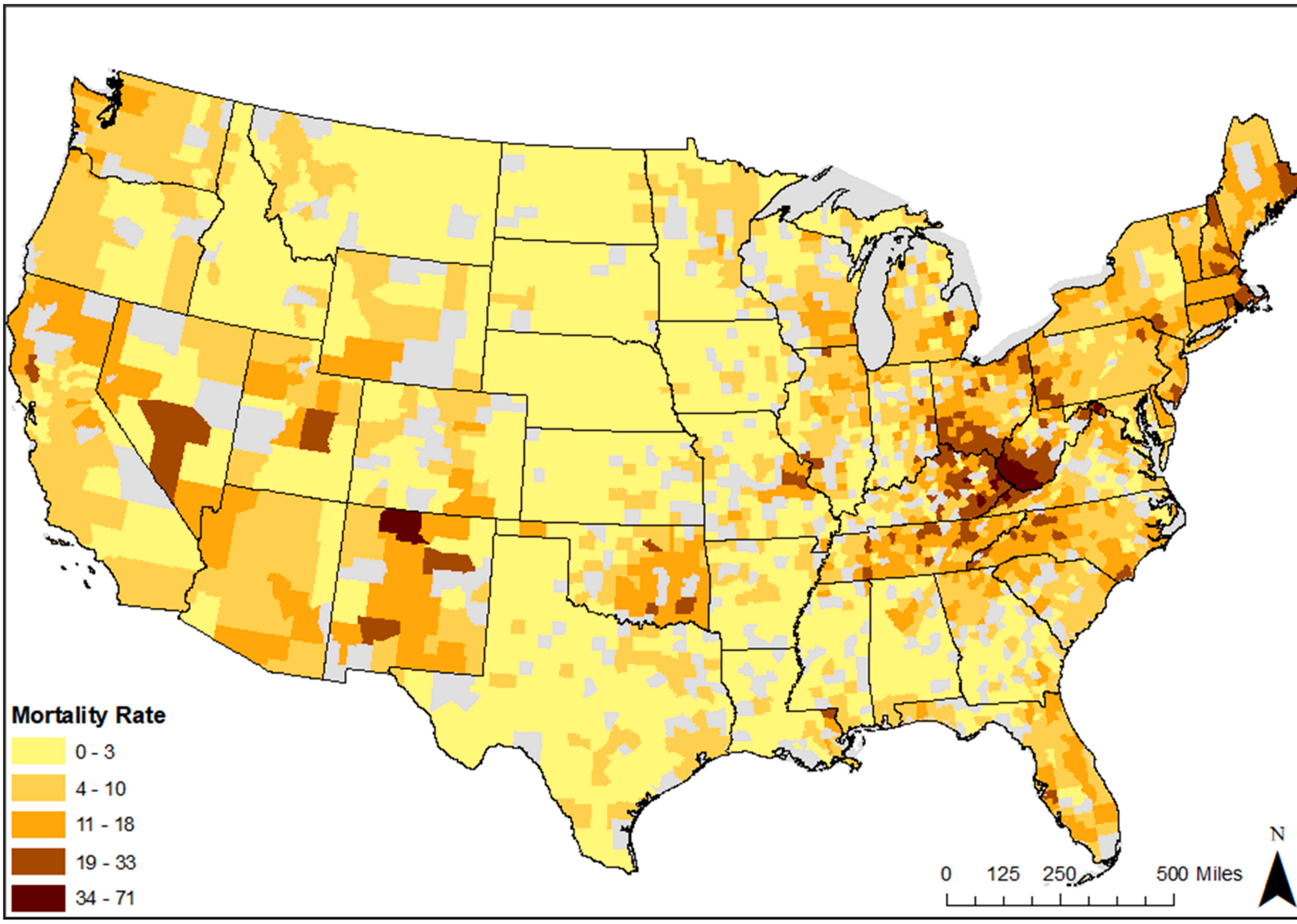

Fig. 2. County-level opioid-related mortality rate per 100,000 residents by quintile. Counties with missing data are denoted in grey.

opioid use and misuse. Contrary to our hypothesis,we found significant positive associations between opioid-related mortality rates and two measures of green space (tree canopy cover and forested land cover). These findings are unexpected and do not align with the majority of other studies that have tied green space exposure to lower all-cause mortality rates (for review, see Rojas-Rueda et al., 2019; but for conflicting evidence, see Coutts et al., 2017; Richardson et al., 2021). Neither do these findings align with a growing number of studies, including randomized control trials, assessing effects of brief exposures to nature and demand/use of painkillers (i.e., Donovan et al., 2019; Kline, 2009; Prabhu et al., 2020a, Prabhu et al., 2020b; Ulrich, 1984; Yeung et al., 2021).

Berry et al. (2020) recently put forward strong rationale for greenspace buffering against opioid use disorder as a consequence of pain reduction, mental and physical health, acute reductions in delay discounting, social connections, and reduced substance cravings. We hypothesized an inverse association between greenspace and opioid-related mortality for the same reasons as for opioid use disorder, in addition to the strong evidence for greenspace protecting against premature death. Our study, though, was the first to empirically test the link between greenspace and opioid-related endpoints.

The first potential explanation for our unexpected findings is that trees and opioid prescriptions are common in the same areas. Trees and opioid deaths also appear in the same areas, which is distinctly noticeable in Figs. 1 and 2. As prominent examples of these coincidental occurrences, Appalachia and New England are heavily forested and have among the highest number of opioid deaths in the country. Large portions of Appalachia, most notably Kentucky, Tennessee, North Carolina, and West Virginia, have very high rates of opioid use and mortality due to a confluence of factors unique to the region, including high levels of poverty and unemployment, low health insurance coverage, and a high percentage of the population currently or formerly employed in manual labor, especially natural resource extraction sectors (i.e., lumber and mining) (Moody et al., 2017). These factors are likely caused in part by the high volume of timber and coal and little to no presence of other prominent economic sectors such as high-tech and other white-collar industries (Lobao et al., 2016). Appalachia also has a high burden of environmental hazards relative to the rest of the U.S. (Krometis et al., 2017), which contribute to higher incidences of morbidity and mortality.

The results of the stratified urbanization analysessuggest that rural areas (and to a lesser extant, small metro areas) were driving the nationwide results. These two urbanicity categories accounted for over half (1427 of 2677) of all counties in the dataset. That the positive association between canopy and opioid mortality results mostly from rural counties is not entirely surprising, since rural counties, especially those in Appalachia, have lower quality healthcare infrastructure, services, and access than do more urbanized and developed counties (Anderson et al., 2015) and worse health-related behavior (Matthews et al., 2017). Rural areas in Appalachia have also relied heavily on ecological degradation of forested lands for economic livelihoods through coal mining, forestry, and other forms of resource extraction (Small et al., 2021; Wishart, 2014). Such employment opportunities have declined during the opioid crisis, yet these dangerous and labor-intensive jobs instigated the high demand for painkillers, while the declining economic conditions encouraged their ongoing use and abuse (Krometis et al.,

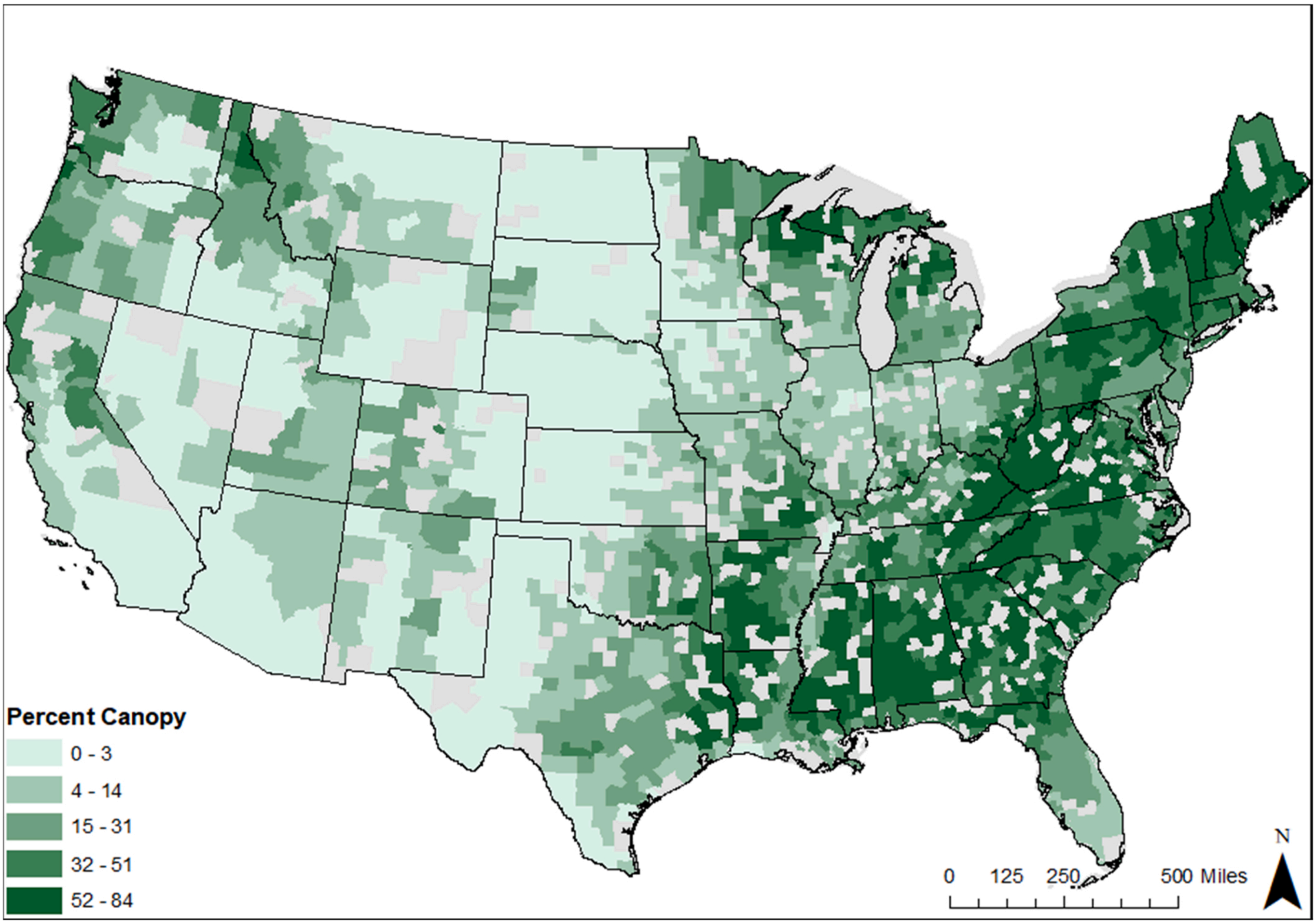

Fig. 3. County-level percent of land cover that is tree canopy by quintile. Counties with missing data are denoted in grey.

Table 2
Fully adjusted geographic additive models (GAM) examining associations between tree canopy cover and opioid mortality in counties (N = 2677) across the continental U.S.

	Model 1 (unadjusted)		Model 2 (adjusted for SES covariates)		Model 3 (fully adjusted)		Forest sensitivity analysis (Model 3a)		NDVI sensitivity analysis (Model 3b)	
Variable	Beta	*p*-value	Beta	*p*-value	Beta	*p*-value	Beta	*p*-value	Beta	*p*-value
Canopy	-0.012	0	0.01	0.041	0.01	0.001	0.01	0	-0.04	0.945
Age			-0.07	0	-0.05	0	-0.06	0	-0.05	0.000
Female			0.08	0	0.05	0.001	0.05	0.001	0.05	0.003
White			0.01	0.002	0.01	0.004	0.01	0.011	0.01	0.001
Income			0	0.023	0	0.578	0	0.687	0.00	0.458
Education			-0.02	0.001	-0.02	0	-0.02	0	-0.02	0.001
Poverty			-0.07	0	-0.05	0	-0.05	0	-0.04	0.000
Manual			-0.09	0	-0.07	0	-0.07	0	-0.07	0.000
UrbanRural			-0.13	0	-0.1	0	-0.1	0	-0.09	0.001
Doctors					0.01	0.005	0.01	0.004	0.01	0.012
Hospitals					-0.93	0	-0.95	0	-0.90	0.000
Beds					0	0.003	0	0.002	0.00	0.007
Rx					0.01	0	0.01	0	0.01	0.000
$PM_{2.5}$					0.14	0.057	0.13	0.066	0.13	0.082
MRF smoother	NA	0	NA	0	NA	0	NA	0	NA	0.000
Adjusted R^2	0.865		0.233		0.577		0.603		0.623	
Deviance explained	51.6%		60.4%		62.8%		62.8%		62.7%	
Moran's *I*	0.05	0.001	0.006	0.3	-0.003	0.6	0	0.5	-0.001	0.5

2017; Monnat et al., 2019). We posit these conditions were partly the consequence of the existence of these heavily forested areas (and associated rich natural resources) in these rural U.S. counties. In conjunction with the lack of alternative forms of livelihood (i.e., white or blue collar), the employment opportunities afforded by green spaces in these areas may have explained why more canopy cover predicted more opioid deaths.

A second possible reason for our unespected findings is that the beneficial effects of exposure to green spaces may not be strong enough to reduce the need or desire for opioids or the misuse of those

Table 3
Fully adjusted geographic additive models (GAM) stratified by urbanicity examining associations between tree canopy cover and opioid mortality in counties across the continental U.S.

	Level 1: Large central metro		Level 2: Large fringe metro		Level 3: Medium metro		Level 4: Small metro		Level 5: Micropolitan		Level 6: Non-core rural [a]	
	Beta	*p-value*	Beta	*p-value*	Beta	*p-value*	Beta	*p-value*	Beta	*p-value*	Beta	*p-value*
Canopy	0.01	0.162	0.01	0.007	0.00	0.742	0.01	0.085	0.01	0.166	0.02	0.000
Age	0.02	0.268	-0.05	0.000	0.02	0.135	0.00	0.809	0.02	0.352	-0.03	0.000
Female	-0.12	0.073	0.06	0.102	0.06	0.176	0.00	0.958	-0.03	0.531	0.06	0.000
White	0.01	0.014	0.02	0.000	0.01	0.146	0.00	0.652	0.00	0.932	0.02	0.000
Income	0.00	0.650	0.00	0.617	0.00	0.605	0.00	0.878	0.00	0.322	0.00	0.007
Education	-0.03	0.002	-0.02	0.025	-0.01	0.269	0.01	0.562	-0.01	0.292	-0.01	0.420
Poverty	0.04	0.161	-0.01	0.437	-0.02	0.277	-0.02	0.362	-0.02	0.429	-0.03	0.000
Manual	-0.12	0.245	-0.10	0.000	-0.04	0.032	0.00	0.830	-0.04	0.008	-0.03	0.000
Doctors	0.01	0.093	0.01	0.140	0.02	0.011	0.00	0.459	0.01	0.571	0.05	0.000
Hospitals	-0.39	0.743	-0.84	0.009	-1.41	0.000	-1.59	0.000	-0.66	0.018	-0.88	0.000
Beds	0.01	0.033	0.01	0.000	0.00	0.379	0.00	0.815	0.00	0.342	0.00	0.096
Rx	0.00	0.730	0.00	0.009	0.01	0.000	0.01	0.000	0.01	0.000	0.01	0.000
PM	0.11	0.003	0.02	0.476	0.04	0.283	0.10	0.060	0.08	0.140	0.07	0.000
Adjusted R^2	0.716		0.711		0.685		0.451		0.166		0.038	
Deviance explained	69.2%		29.4%		21.9%		19.1%		12.0%		37.7%	
n	67		333		337		320		526		1094	

[a] The dispersion parameter theta in the negative binomial regression type of the GAM was manually set to a value (6) that enabled the model to properly fit the data in CDC Level 6.

substances. Emami et al. (2018) found only a 5% difference in pain intensity between nature and non-nature groups in an experiment with cancer patients. Patients reported an 18% reduction in the occurrence of moderate or severe pain while recovering from bone marrow biopsies and treatments in a natural setting (Lechtzin et al., 2010). Subjects recorded an average 20% reduction in pain threshold and pain tolerance when viewing a video of nature compared to those not viewing such videos (Tse et al., 2002). While these studies do find improvements in pain tolerance in natural versus control settings in the short-term, lasting improvements may be weaker and insufficient to translate to measurably lower opioid use and mortality rates. The mechanisms through which green space exposure influences health, such as boosting mood (Ulrich, 1983; Ulrich et al., 1991), increasing physical activity (Hartig et al., 2014; Sugiyama et al., 2014), distracting from pain (Tanja-Dijkstra et al., 2018; White et al., 2018), and improving cognitive function (Clatworthy, 2013; Kaplan & Kaplan, 2011), may simply not be potent enough to counteract the desire or need for opioids.

The third potential explanation for our unexpected findings is that a generalized measure of trees was used. A high density of trees, which mainly exists in forest areas, may be less effective for promoting mental health than other types of green infrastructure. A recent meta-analysis found that the positive effects on anxiety, anger, and negative affect were greatest for low density forests (stand density < 500/ha), but such benefits became smaller or insignificant as tree density increased (Eunsoo Kim et al., 2021). Forests with low openness and ease of movement were also found to be less effective in promoting positive emotions (Staats et al., 1997), and could even induce stress and attention fatigue (Gatersleben et al., 2013). Although trees often dominate the composition of green spaces and appear commonly in the greenness and health literature (Ulmer et al., 2016), they are not the only component of restorative natural landscapes. Bushes, shrubs, grasses, crops, flowering plants, and other smaller plants also exist and have on their own been tied to human health outcomes (Alcock et al., 2015; Becker et al., 2019; Tsai et al., 2018). Thus, it is entirely possible that one or more of these other types of vegetation could exert a positive influence on opioid-related mortality.

A final explanation for green spaces being related to increased opioid mortality is the possible existence of a genuinely detrimental effect of green spaces on mortality. A small number of studies have found either no association or a positive association between the amount of green space in an area and mortality rates. For example, no association was detected between all-cause mortality and green space in a study of Florida counties (Coutts et al., 2010). Furthermore, no association was found in U.S. cities between green spaces and heart disease, lung cancer, and diabetes mortality; only all-cause mortality was higher in cities with more green space (Richardson et al., 2012). While such findings are in the minority of studies on green spaces and mortality, they do suggest that green space exposure does not always relate to lower mortality rates.

4.2. Strengths and Limitations

This study holds multiple strengths. County-level analysis affords large study areas wherein hundreds of millions of Americans live. A wealth of data is available for a wide number of social, economic, healthcare, and environmental phenomena at the county level, which allowed us to control for crucial confounding factors. Counties are also often uniform in shape and size depending on what state they reside in and are linked contiguously to, affording ease of comparison and the ability to reliably control for spatial autocorrelation.

Our study also has limitations. The ecological study design based on aggregated county data prevents conclusions to be drawn about smaller units (e.g., neighborhoods) or individuals. As inherent in every ecological analysis, our reported associations are possibly deceptive due to the presence of aggregation and zoning effects (i.e., modifiable areal unit problem) (Fotheringham & Wong, 1991). The cross-sectional nature of our study design might entail examining an anomalous year where one or more factors was an outlier compared to longer-term trends. The observed associations might also have been confounded by personal factors that we were unable to measure. One such personal factor is occupation; people with jobs in the physical labor sectors of the economy are much more likely to begin and continue using opioids than those in white-collar occupations (Moody et al., 2017). However, we were unable to consider specific types of manual labor because county-level data only included total manual labor statistics. Other variables that could be relevant or were found to be important in other studies on opioid morbidity and mortality exist. For example, type of health insurance (Schoenfeld et al. 2019), transportation and commercial infrastructure (Chichester et al., 2020), hospital visit information (Wilkes et al., 2021), and employment in specific industries (Monnat et al., 2019) could have also confounded our results. However, we were unable to control for such factors due to our study design and timeframe. Although we centered the years of data for the dependent variable around the 2011 NLCD to best match our datasets, there was a discrepancy between the dependent (2008–2018) and independent (2011) variables; thus, we cannot exclude spatiotemporal contextual uncertainties originating from temporality ill-aligned environmental exposure assessments (Helbich, 2019). We also cannot exclude predispositions toward greenness that may play a role in understanding relationships exposure and risk of opioid use and misuse. Last, tree canopy cover data from the NLCD is not without inaccuracy and discrepancies, especially when comparing urban and rural tree canopy densities (Nowak & Greenfield, 2012).

4.3. Research and Policy Implications

The creation and expansion of large forested areas may not be a viable option for reducing the frequency of opioid use, misuse, and overdose. However, our ecological study design is not able to speak to whether living amid or having regular exposure to forested areas plays a role in opioid use and mortality. Further research, such as studies on the mechanisms that tie green spaces to mortality; the use of time-series data; exploration of racial and economic disparities; and studies with individual-level data should be pursued to better understand how nature is related to opioid-related outcomes. The fact that poverty and healthcare access (doctors, hospitals, hospital beds, and pharmaceutical prescriptions) were significant in nationwide models indicates that economic and health infrastructure are crucial determinants of opioid-related outcomes and could also be of interest to public health researchers as well as policymakers and others tasked with slowing or reversing those events.

5. Conclusion

The extent and severity of the opioid epidemic has compelled health professionals and researchers to find ways to mitigate the need for and use of opioid substances. Because exposure to green spaces has been tied to numerous beneficial health outcomes relevant to opioid use, exposure might be expected to reduce the prevalence of opioid use and ultimately deaths. This study does not confirm this expectation. We found a statistically significant and slightly positive association between the tree canopy cover and opioid mortality. No significant associations were observed for total vegetative cover and opioid mortatliy, however. Our study is the first to examine these relationships, and our findings were limited by greenspace expsoure estimates at the county level. Further research on this topic should be pursued using more powerful study designs and more granular data.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ufug.2022.127529.

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