



Exploring links between greenspace and sudden unexpected death: A spatial analysis



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ABSTRACT

Greenspace has been increasingly recognized as having numerous health benefits. However, its effects are unknown concerning sudden unexpected death (SUD), commonly referred to as sudden cardiac death, which constitutes a large proportion of mortality in the United States. Because greenspace can promote physical activity, reduce stress and buffer air pollutants, it may have beneficial effects for people at risk of SUD, such as those with heart disease, hypertension, and diabetes mellitus. Using several spatial techniques, this study explored the relationship between SUD and greenspace. We adjudicated 396 SUD cases that occurred from March 2013 to February 2015 among reports from emergency medical services (EMS) that attended out-of-hospital deaths in Wake County (central North Carolina, USA). We measured multiple greenspace metrics in each census tract, including the percentages of forest, grassland, average tree canopy, tree canopy diversity, near-road tree canopy and greenway density. The associations between SUD incidence and these greenspace metrics were examined using Poisson regression (non-spatial) and Bayesian spatial models. The results from both models indicated that SUD incidence was inversely associated with both greenway density (adjusted risk ratio [RR] = 0.82, 95% credible/ confidence interval [CI]: 0.69–0.97) and the percentage of forest (adjusted RR = 0.90, 95% CI: 0.81–0.99). These results suggest that increases in greenway density by 1 km² and in forest by 10% were associated with a decrease in SUD risk of 18% and 10%, respectively. The inverse relationship was not observed between SUD incidence and other metrics, including grassland, average tree canopy, near-road tree canopy and tree canopy diversity. This study implies that greenspace, specifically greenways and forest, may have beneficial effects for people at risk of SUD. Further studies are needed to investigate potential causal relationships between greenspace and SUD, and potential mechanisms such as promoting physical activity and reducing stress.

1. Introduction

Sudden unexpected death (SUD), commonly referred to as sudden cardiac death, is one of the leading causes of mortality in the United States (Adabag et al., 2010; Nanavati et al., 2014; Stecker et al., 2014). It is estimated that SUD incidence is between 180,000 and 450,000 each year in the US, although this estimate varies considerably depending on data sources, definition of SUD, methods of estimation and other factors (Adabag et al., 2010; Kong et al., 2011).

Currently, risk factors for SUD are not well understood. Underlying or pre-existing health conditions, such as coronary heart disease, hypertension, diabetes mellitus, dyslipidaemia and ventricular

hypertrophy, contribute to the occurrence of SUD (Adabag et al., 2010). Family history of sudden death, and socioeconomic and psychosocial status may also be risk factors (Adabag et al., 2010; Dekker et al., 2006; Mounsey et al., 2017; Ruberman et al., 1984). Several studies also suggest that some environmental factors, such as air pollution and temperature, might trigger the occurrence of cardiac arrest or sudden death (Dales et al., 2004; Dennekamp et al., 2010; Onozuka and Hagihara, 2017). Because of the high number of SUD cases and the low survival rate of sudden cardiac arrest, prevention measures are highly desired.

Greenspace refers generally to areas covered with trees, grass or other vegetation, and includes forests, parks, gardens, and street-side

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landscaping. It is increasingly recognized that greenspace has many benefits to human health. Many studies have shown that exposure to greenspace was associated with a lower risk of obesity (Lee et al., 2017), diabetes (Astell-Burt et al., 2014; Bodicoat et al., 2014; Brown et al., 2016; Dalton et al., 2016; Ngom et al., 2016), hypertension (Brown et al., 2016), and cardiovascular disease (Bijnens et al., 2017; Lane et al., 2017; Paquet et al., 2014; Pereira et al., 2012; Tamosiunas et al., 2014; Yitshak-Sade et al., 2017). The protective benefits provided by greenspace regarding these health outcomes are attributed to its many ecosystem services, such as filtering air pollution and noise, relieving stress and depression, promoting social contact and physical activity, and reducing temperature extremes (de Jesus Crespo and Fulford, 2018; Egorov et al., 2017; Maas et al., 2009; Markevych et al., 2017; Oliveira et al., 2011; Pugh et al., 2012; Roe et al., 2013; Shanahan et al., 2016). Since these health outcomes are also related to SUD, we hypothesized that exposure to greenspace might be associated with a lower risk of sudden cardiac arrest.

The main objective of this ecological study is to explore the relationship between SUD incidence and local greenspace using spatial techniques. Using the Sudden Unexpected Death in North Carolina (SUDDEN) case registry in Wake County, North Carolina (<https://www.med.unc.edu/medicine/cardiology/sudden>), we first conducted analyses to identify spatial patterns of SUD cases and other relevant variables. Then, we applied Bayesian spatial models as well as Poisson regression models to examine the associations between SUD incidence and multiple greenspace metrics at the census tract level.

2. Methods

2.1. Study area

The study area is Wake County, central North Carolina (Fig. 1). With a subtropical climate, Wake County has moderate temperatures in the spring, fall, and winter but high temperatures in summer. With a

population of about one million, Wake County is the second-most populated county in North Carolina and one of the fastest growing counties in the US. The population is composed of 68.5% White, 21.2% Black, and 6.9% Asian based on the data from the US Census Bureau in 2016. Wake County also has a large number of residents who may be at risk for sudden cardiac arrest. According to health statistics for 2010, cardiovascular disease was the second cause of death in North Carolina, responsible for 30% of all deaths in that year (Tchwenko, 2012).

2.2. Sudden unexpected death data

The SUD cases in Wake County from March 1, 2013 to February 28, 2015 were collected through the Sudden Unexpected Death in North Carolina (SUDDEN) project, which was approved by the Institutional Review Board (IRB) at the University of North Carolina at Chapel Hill (Study #14-2036). SUD cases were screened from all deaths aged 18 to 64 attended by emergency medical services in Wake County. The identification criteria were described previously (Mounsey et al., 2017; Nanavati et al., 2014) and are briefly illustrated in Fig. S1. For each SUD case, the location of the death event was recorded by a Global Positioning System (GPS). Personal information for each case, including home address, age, gender, race and medical history, was also recorded. Based on the incident location, SUD cases were mapped in a Geographic Information System (GIS) using ArcGIS 10.3 (ESRI, CA); then cases were aggregated by census tract using 2010 boundaries obtained from the US Census Bureau. SUD incidence was calculated using total population aged 18 to 64 multiplied by 2 years as the denominator.

2.3. Demographic and socioeconomic status data

Demographic and socioeconomic status data were obtained for 187 census tracts in Wake County from the US Census Bureau's five-year American Community Survey data summary centered on 2014. The variables included total population, the percentages of populations at

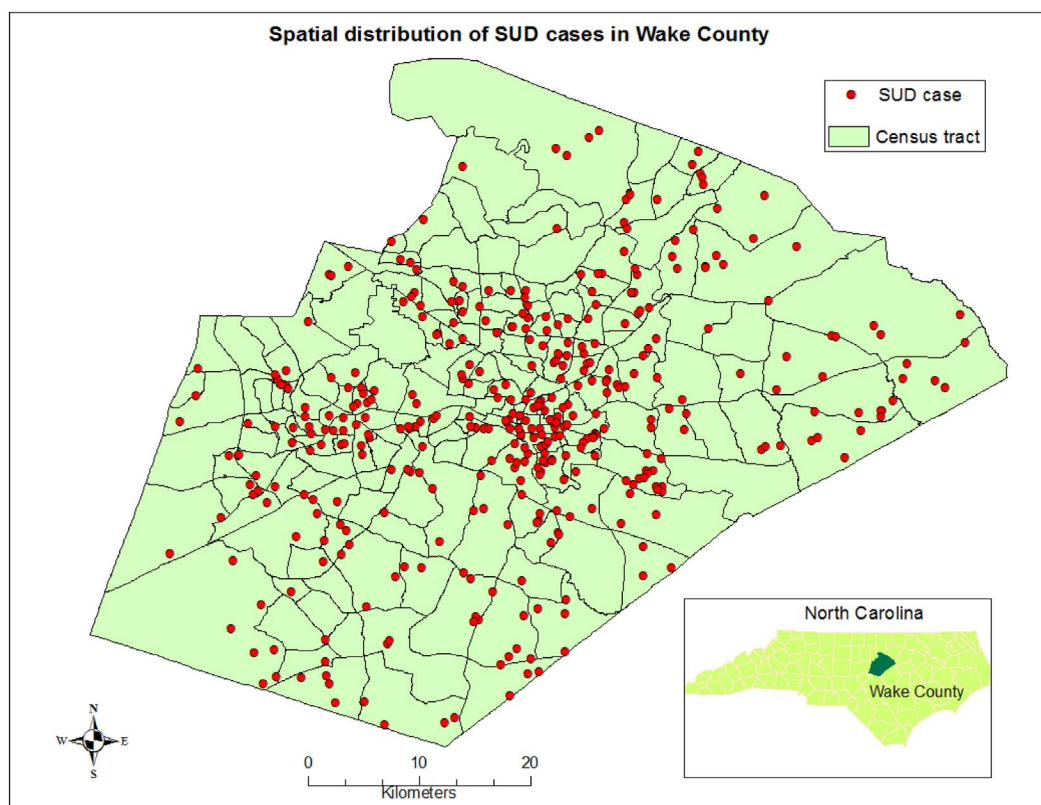


Fig. 1. The study area and the spatial distribution of SUD cases in Wake County.

different age groups from 18 to 64, male and female populations, the percentage of households in poverty, the percentage of unemployment, household median income values, the percentage of married households, the percentage of non-family households, and the percentages of white, black and Asian populations. Population density was calculated using the total population in a census tract divided by its area.

2.4. Greenspace metrics

Multiple metrics were calculated to measure greenspace in each census tract, including average land cover composition and pattern, tree canopy specifically along major roads, and greenway density. The land cover composition metrics estimate overall outdoor greenness that may buffer environmental hazards, reduce stress and promote healthful lifestyles in the local vicinity of the residence. The percentage of near-road tree canopy was selected as an exploratory metric due to the potential for tree cover along busy roadways to trap or dilute airborne vehicular pollutants downwind of travel lanes (Baldauf, 2017; Brantley et al., 2014). Greenway density was considered in this study because greenway trails may promote physical activity and reduce stress. We calculated the diversity of tree canopy to understand if the pattern of tree distribution has any influence on SUD.

Land cover components by census tract were calculated using the National Land Cover Dataset (NLCD) 2011 (Homer et al., 2015), which was created by the Multi-Resolution Land Characteristics (MRLC) consortium by classifying 2011 Landsat Thematic Mapper satellite imagery with a spatial resolution of 30 m (<https://www.mrlc.gov/nlcd2011.php>). We reclassified this dataset as described previously (Wu and Jackson, 2016) and calculated the percentages of nine major land cover classes: water, open land, developed land (e.g., buildings and pavement), barren land, forest, shrubland, grassland, agriculture and wetland (Fig. S2).

The NLCD 2011 Cartographic Canopy dataset (http://www.mrlc.gov/nlcd11_data.php) was used to calculate average tree canopy for each census tract (Fig. S3). The canopy dataset includes individual tree coverage throughout the study area, whereas the forest class in the land cover dataset reflects only larger tree patches. It was also created based on 30 m Landsat satellite imagery. In this dataset, each pixel has a value indicating tree canopy coverage between zero and 100%. Average tree canopy by census tract was calculated by summing the product of each pixel value and the number of pixels with that value, divided by the total number of pixels in the census tract.

In addition, we calculated the Shannon diversity index (H') to indicate pattern in tree canopy coverage according to the equation (Shannon and Weaver, 1998):

$$H' = - \sum_{i=1}^s p_i \ln p_i$$

where s is the number of canopy coverage values, i is the index of canopy coverage values, p_i is the proportion of individual coverage value i , and \ln is the natural logarithm. Each pixel has 101 possible values from 0 to 100.

Near-road tree canopy was calculated according to the approach described previously (Wu and Jackson, 2017). Briefly, we obtained a GIS polyline layer for major roadways (> 54 mph) from NavTEQ™ (Chicago, IL). Then we created 50 and 100 m buffers around the road centerlines and used these to clip the NLCD tree canopy dataset. The average percent tree canopy within the road buffers in each census tract was calculated as the percentage of near-road tree canopy. Road density was calculated using the total length of major roads in a census tract divided by the total area of that census tract.

Greenway data contained in a GIS polyline layer were obtained from the GIS division of Wake County Government, North Carolina. The data include greenways, trails, and multi-use trails in Wake County (Fig. S4). The data were imported into ArcGIS to calculate greenway density. This

metric captures the length of greenway per square kilometer, which was calculated using the total length of greenways (including trails) in a census tract divided by the total area of that census tract.

Considering that air quality might be a confounder in the relationship between SUD and greenspace, we calculated weighted road density, a simple index of traffic-related air pollution (Rose et al., 2009). We included major roads and lower-speed roads (speed limits ≥ 35 miles [56 km] per hour) and, using a weight ratio of 10: 1, calculated the index following a published procedure (Rose et al., 2009).

2.5. Spatial pattern analysis

To examine whether census tracts with a higher number of SUD cases were clustered, Global Moran's Index (Moran's I), a common index to indicate the spatial autocorrelation of individual variables, was calculated using ArcGIS 10.3 (Moran, 1950). For the Global Moran's I statistic, the spatial autocorrelation is weak when the index value is close to zero. A general equation for calculating Global Moran's I can be found in the literature (Moran, 1950; Waller and Gotway, 2004). We calculated Moran's I for key variables including SUD incidence, the percentages of forest, grassland and developed land, average tree canopy, near-road tree canopy, greenway density and major road density.

We also carried out Kernel Density Estimation (KDE) using ArcGIS 10.3 to find where SUD events were clustered. KDE is a statistical method to estimate the probability density of a feature (e.g., SUD cases) in an area around the events. It generates a smoothly curved surface (a raster layer) to fit over each point using a weighted distance function, such as a Gaussian kernel (Gatrell et al., 1996; Silverman, 1986). In the process of KDE, the search radius was set at 0.1^0 (~11 km); the default was used for other parameters. After the kernel density layer was created, we reclassified the density into five classes: highest, higher, intermediate, lower and lowest. The area with the highest density is the hotspot of SUD events. Then we calculated SUD cases and incidence in the census tracts with the highest density and compared them with those in the remaining census tracts.

2.6. Statistical analysis

2.6.1. Poisson regression models

Since the SUD cases are count data and not significantly over-dispersed, we selected Poisson regression models to examine the relationship between the incidence of SUD and exploratory variables. Before the models were constructed, we plotted histograms to show the distribution of each variable (Fig. S5), then explored the relationship between SUD and key variables using Pearson correlation analysis and scatter plots (Fig. S6).

We assumed that the number of SUD cases in each census tract followed a Poisson distribution, namely, $E(Y) = \text{Var}(Y) = \mu$. Where Y is the count of SUD cases, $E(Y)$ and μ are the expected number of the SUD count, and $\text{Var}(Y)$ is the variance of the SUD count. A general equation of a Poisson regression model can be written as below (Kleinbaum et al., 2013):

$$E(Y_i) = \mu_i = l_i r_i$$

$$\ln(\mu_i) = \ln(l_i) + \beta_0 + \beta_1 x_{1i} + \dots + \beta_n x_{ni}$$

where i is the index of a census tract, r is SUD incidence, l is the population at risk multiplied by time (here, time is 2 years), \ln is the natural logarithm and $\ln(l_i)$ is used as the offset term; x_1, \dots, x_n are the exploratory variables and β_1, \dots, β_n are the regression coefficients of the exploratory variables. First, we included one greenspace variable per model as the exploratory variable to obtain unadjusted associations between SUD incidence and greenspace metrics; then we examined the interactive effects of greenspace metrics and median household income on SUD incidence. Next, we adjusted the model for SES (the median household income), race (the percentage of Asian population) and

Table 1
Descriptive statistics of dependent and exploratory variables.

Variable	No. census tracts	Mean	Standard deviation	Minimum	Maximum
Incidence (per year per 1000 persons)	187	0.32	0.28	0.00	1.64
Case	187	2.12	2.01	0.00	13.00
Water (%)	187	1.36	2.59	0.00	17.64
Open land (%)	187	33.65	18.01	1.35	79.40
Developed land (%)	187	29.71	18.59	0.12	95.21
Barren land (%)	187	0.35	0.98	0.00	6.37
Forest (%)	187	23.06	17.69	0.00	95.68
Shrub land (%)	187	0.87	1.21	0.00	5.38
Grassland (%)	187	2.99	3.55	0.00	14.99
Agriculture (%)	187	6.04	8.70	0.00	37.32
Wetland (%)	187	1.99	2.74	0.00	18.24
Average tree canopy (%)	187	49.33	13.55	5.85	94.72
Near-road tree canopy in 100 m (%)	187	36.91	12.07	5.00	88.00
Near-road tree canopy in 50 m (%)	187	31.04	11.82	5.00	80.00
Major road density (km/km ²)	187	1.26	0.74	0.00	4.78
Greenway density (km/km ²)	187	1.09	0.75	0.00	4.05
H' (Diversity of tree canopy)	187	3.44	0.95	0.00	4.31
Population density (person/km ²)	187	759.58	557.48	0.09	3347
Size of census tract (km ²)	187	14.32	20.18	1.17	154.99
Household in poverty (%)	187	11.66	11.69	0.00	58.5
Married household (%)	187	51.77	19.63	0.00	100.00
Unemployment (%)	186	7.17	4.05	0.00	26.7
Median income (\$)	185	74,652	32,413	17,441	169,028
White (%)	186	72.07	18.01	8.80	100
Black (%)	186	18.00	16.54	0.00	90.6
Asian (%)	186	5.52	7.41	0.00	38.8
Male population (%)	187	48.49	5.40	0.00	66.97
Female population (%)	187	50.98	5.52	0.00	62.28

population density. These variables were chosen because their models had smaller values for the Akaike information criterion (AIC). We also adjusted the model for weighted road density to take the potential confounding effect of traffic-related air pollution into account. Pearson correlation analysis and variance inflation factors (VIF) were used to examine and avoid multicollinearity among exploratory variables. Only one of two highly-correlated variables was considered if multicollinearity was determined (e.g. $r > 0.6$ or $VIF > 5$) (Wu et al., 2015).

The associations between SUD incidence and the exploratory variables were indicated by risk ratio (RR, the ratio of SUD incidence between two exposure groups), initially corresponding to a one unit change in the exploratory variables (equal to a 1% change in greenspace values). Because a 1% change in greenspace values leads to very tight RR values (close to 1) and is not highly meaningful as an intervention, we changed the greenspace unit definition to 10% by dividing the values of these metrics by ten. A positive association was assumed if the RR was above 1.00, while a negative or inverse association was assumed if the RR was below 1.00. The significance level was selected at 0.05.

2.6.2. Bayesian spatial model

Considering the possibility for significant spatial autocorrelation, we further developed a Bayesian spatial model to examine the association between SUD incidence and greenspace metrics. The model is derived from the Poisson regression model described above. Similarly, we assumed that the count of SUD cases follows a Poisson distribution and used the same dependent variable and exploratory variables as in the first model. Differently, we included an unstructured random effect term U and a structured spatial random effect term S to account for spatial autocorrelation.

$$Y_i \sim \text{Poisson}(\mu_i)$$

$$\ln(\mu_i) = \ln(l_i) + \beta_0 + \beta_1 x_{i1} + \dots + \beta_n x_{ni} + U_i + S_i$$

where, S_i is assumed to follow an intrinsic conditional autoregressive (ICAR) distribution with mean \bar{s}_i and variance σ_s^2 . Here, \bar{s}_i is a function

of a spatial weight matrix ω . If a census tract i and another census tract j are adjacent, $\omega_{i,j} = 1$; otherwise, $\omega_{i,j} = 0$. σ_s^2 was assumed to follow an inverse Gamma distribution $\tau_s = \frac{1}{\sigma_s^2} \sim \text{Gamma}(a_s, b_s)$. U_i follows a normal distribution with mean equal to 0 and variance equal to σ_U^2 , which has the same distribution as σ_s^2 . β_0 was assigned a uniform prior, namely, $\beta_0 \sim \text{dflat}()$. The regression coefficients, $\beta_1 \dots, \beta_n$ were assumed to follow a normal distribution with mean ($\mu_\beta = 0$) and variance ($\sigma_\beta^2 = \frac{1}{\tau_\beta}$). Based on the literature (Lawson, 2013), common selected values were set for parameter a_s, b_s and τ_β , respectively, to get weakly informative priors. Similar to the Poisson regression model, we identified the best fitted model as the one with the lowest value for the Deviance Information Criterion (DIC).

The model was fitted by a Markov chain Monte Carlo (MCMC) sampling approach in OpenBUGs 14.3. The spatial weight matrix was created in ArcGIS 10.3 with the *Adjacency For WinBUGS Tool* (https://www.umesc.usgs.gov/management/dss/adjacency_tool.html) developed by the U.S. Geological Survey. We ran the MCMC chain for each model parameter for 5000 iterations and removed the first 2000 iterations as a “burn-in” period. Then, samples from every third iteration were kept for a total of 1000 samples. The trace plots and autocorrelation plots of these parameters were monitored to diagnose the convergence of the MCMC iterations.

To examine how the choices of prior parameters affect model outcomes, a sensitivity analysis was conducted following the literature (Wu et al., 2014). We used the same model described above, with percent forest as the exploratory variable and the same three control variables. Previously, we assumed that the regression coefficient followed a normal distribution and set the prior parameters $\mu_\beta = 0$ and $\tau_\beta = 0.0001$. In this sensitivity analysis, we changed the value of τ_β to 0.001, 0.01 and 0.1 and 1, respectively. The model outcomes, including the regression coefficient and RR, were compared to evaluate the influence of the choice of prior values.

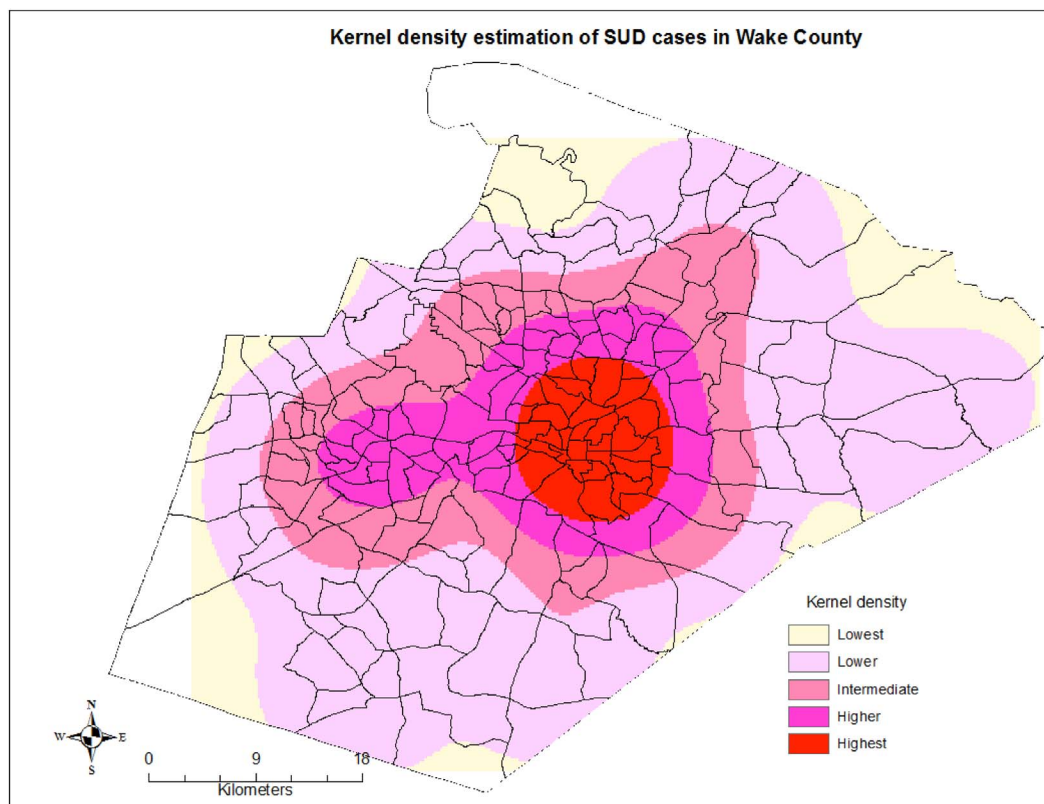


Fig. 2. Kernel density estimation of SUD cases in Wake County.

3. Results

3.1. Description of SUD data and greenspace metrics

In total, 396 SUD deaths were identified in 148 of 187 Wake County census tracts during March 2013 to February 2015. For 366 cases, the event and home addresses were the same, accounting for 92.4% of the cases. For 26 cases, the incident and home addresses were different. The average number of SUD cases per census tract was 2.12, with a maximum number of 13 cases. The average incidence of SUD in these census tracts was 0.32 case per 1000 persons per year (Table 1, Fig. S7).

In these census tracts, forest is one of the major land cover classes, accounting for 23.06% on average, and less than only open land (33.65%) and developed land (29.71%). Grassland is a very small percentage, with a mean of 2.99%. Average tree canopy coverage ranges from 5.85% to 94.72%, with a mean of 49.33%. Near-road tree canopy accounts for 36.91% on average within the 100 m road buffer, slightly higher than that within the 50 m road buffer. Mean greenway density for these census tracts is 1.09 km per km² (Table 1).

3.2. Spatial pattern analysis of SUD data and greenspace metrics

Fig. 1 showed the general location of each SUD event. Cases were more frequent in central Wake County. Spatial autocorrelation analysis using Moran's *I* indicated that SUD cases were significantly spatially clustered (Moran's *I* = 0.182, $p < 0.001$). The analysis also showed that other key variables (e.g., forest and grassland pixels, and average tree canopy values per pixel) were also significantly spatially clustered (Table S1). The SUD hotspots identified using KDE are shown in Fig. 2. The central area in red covers 31 census tracts with an average of 3.43 cases each and a mean incidence of 0.53 cases per 1000 persons per year. These values are much higher than those for the remaining census tracts (which had an average of 1.79 cases each and 0.27 cases per 1000 persons per year).

3.3. Relationship between SUD and greenspace metrics

Pearson correlation analysis showed that SUD incidence had significant and negative correlations with greenway density and percent forest, and also with average tree canopy and near-road tree canopy in both 100 m and 50 m buffers. SUD incidence did not have significant correlations with the percentage of grassland or the diversity of tree canopy (Table 2). Greenspace metrics were moderately correlated with median household income (e.g., $r = 0.349$, $p < 0.001$ for percent forest; $r = 0.194$, $p = 0.008$ for greenway density). There was no evidence of interaction between any greenspace metric and medium household income in our analysis (Table S2).

The results from Bayesian spatial models showed that SUD incidence had significant and negative associations with greenway density and percent forest, but not with other greenspace metrics. Adjusted risk ratios (RR) for SUD incidence corresponding to a 1 km/km² increase in greenway density and a 10% increase in forest were 0.82 (95% CI: 0.69–0.97) and 0.90 (95% CI: 0.81–0.99), respectively (Fig. 3). Sensitivity analysis of the priors in the Bayesian spatial models indicated that changing the prior values of the regression coefficients did not change the model results (Table S3).

Similar results were observed from Poisson regression models. Greenway density (adjusted RR = 0.82, 95% CI: 0.69–0.97) and forest (adjusted RR = 0.90, 95% CI: 0.81–0.99) still had significant negative associations with SUD incidence but other greenspace metrics did not (Fig. S8). When weighted road density was included in the models, the associations between SUD incidence and greenspace metrics did not change appreciably (Fig. S9). The results are similar when other weight ratios, such as 4:1 and 16:1 were also tested. The associations between SUD incidence and greenspace metrics were also not affected when the percentage of the population in a specific age group was included in the models (Table S4 and Table S5).

Table 2
Pearson correlation between SUD incidence and exploratory variables.

Exploratory variables	n	r	p	Exploratory variables	n	r	p
Water (%)	187	-0.072	0.327	Major road density (km/km2)	187	0.215	0.003
Open land (%)	187	-0.022	0.763	Greenway density (km/km2)	187	-0.212	0.004
Developed land (%)	187	0.099	0.177	Unemployment (%)	186	0.307	< 0.001
Barren land (%)	187	0.015	0.842	Median income (\$)	185	-0.443	< 0.001
Forest (%)	187	-0.157	0.032	Married household (%)	187	-0.184	0.012
Shrub land (%)	187	0.070	0.338	Non-family household (%)	187	0.108	0.141
Grassland (%)	187	-0.036	0.623	Population density (person/km2)	187	0.011	0.882
Agriculture (%)	187	0.098	0.181	White (%)	186	-0.238	0.001
Wetland (%)	187	0.157	0.032	Black (%)	186	0.354	< 0.001
Average tree canopy (%)	187	-0.201	0.006	Asian (%)	186	-0.253	0.001
Near-road tree canopy in 100 m (%)	187	-0.192	0.008	Male population (%)	187	0.012	0.866
Near-road tree canopy in 50 m (%)	187	-0.173	0.018	Female population (%)	187	0.098	0.182
H' (Diversity of tree canopy)	187	-0.090	0.223	Size of census tract	187	0.148	0.042

Association between SUD incidence and exploratory variables (Bayesian spatial model)

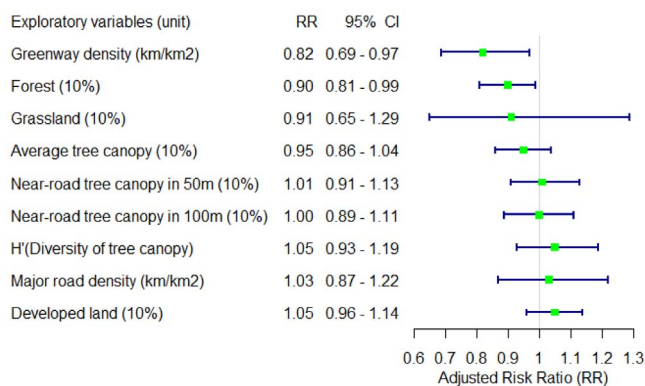


Fig. 3. The association between SUD incidence and key exploratory variables examined by Bayesian spatial models. The models were adjusted for population density, median household income and the percentage of Asian population.

3.4. Relationship between SUD and other variables

In addition to greenspace metrics, SUD incidence was significantly and negatively correlated with median household income and the percentages of married households, white population and Asian population (Table 2). However, SUD incidence had positive correlations with major-road density, unemployment rate and the percentage of black population. No significant correlations were observed between SUD incidence rate and the percentages of open land, developed land, grassland or agricultural land (Table 2). Associations between SUD incidence and major-road density and the percentages of developed land and grassland were further examined with two models. Neither Poisson regression models nor Bayesian spatial models showed that SUD incidence had significant associations with these three variables (Fig. 3 and Fig. S8).

4. Discussion

In this study, we found that SUD cases were clustered in space, and SUD incidence had significant negative associations with greenway density and percent forest. Bayesian spatial models showed that the adjusted risk ratios associated with greenway density and percent forest were 0.82 and 0.90, respectively, indicating that the increases in greenway density by 1 km/km² and in forest by 10% were associated with the decrease in SUD incidence by 18% and 10%, respectively. To our knowledge, this is the first study to examine the spatial patterns of SUD cases and explore potential associations between SUD incidence and greenspace. These findings provide new insights in SUD prevention by exposure to the natural environment, specifically neighborhood greenway trails and forest.

The greenspace metrics that we studied may affect health through a number of possible pathways, including physical activity promotion and stress reduction. Greenway trails provide attractive and safe places for walking, biking, or jogging, and create opportunities for social interaction and engagement with nature. Therefore, access to greenways can have significant beneficial effects on human health (Coutts, 2008; Shafer et al., 2000). Health benefits of forests are also well recognized. Studies showed that forest visits can reduce stress and promote psychological and physical rehabilitation (Karjalainen et al., 2010). The relationship between physical activity and sudden death is complicated (Kohl et al., 1992). On one side, vigorous physical activity such as sports can increase the risk of SUD and is regarded as a potential trigger of SUD (Kohl et al., 1992; Reddy et al., 2009). On the other side, light habitual physical activity or regular exercise might lower the risk of SUD (Kohl et al., 1992; Whang et al., 2006). Our results indicate that nearby greenway trails and forest area may promote increased physical activity and lower the risk of SUD. Emotional stress is another major risk factor for SUD (Critchley et al., 2004; Vlastelica, 2008). Greenway access and forest visits have shown to effectively reduce stress (Karjalainen et al., 2010), which may be another explanation for the observed inverse relationships.

The lack of an association between SUD incidence and average tree canopy was unexpected; it suggests that tree cover in more highly developed parts of the study area ($\geq 20\%$ impervious cover at the 30 m-pixel resolution, where forest is not classified) may not provide the ecosystem service of promoting physical activity or otherwise lead to reduced stress in the study population. One possible explanation is that tree canopy in these areas offers limited public accessibility. It is also possible that forest patches, with their larger size and less developed settings, are preferred destinations, and that they confer health-promotional benefits that trees in more developed areas do not.

Tree canopy specifically along busy roads can reduce ambient levels of traffic-related air pollution (Baldauf, 2017; Brantley et al., 2014), which is a well-known link to cardiovascular disease (Brook et al., 2004; Mills et al., 2009). Previously, we found that near-road tree canopy was inversely associated with childhood autism (Wu and Jackson, 2017). Therefore, we hypothesized that near-road canopy may also have an inverse relationship with SUD incidence through improving local air quality. However, the results from this study did not indicate any significant associations between SUD incidence and our near-road tree canopy metric at either buffer size.

Previous studies support spatial pattern as an important factor in the role of greenspace in health (Akpınar et al., 2016; Jorgensen and Gobster, 2010; Tsai et al., 2016). We examined the relationship between the diversity of tree canopy and SUD incidence but did not find that fine-scale variations in tree coverage were associated with the risk of SUD. However, the significance of the 30 m forest cover variable indicates that larger patches of forest are important compared with average tree canopy.

Rapid urbanization has been linked to many health issues (Gong et al., 2012; Moore et al., 2003). In the process of urbanization, both developed land and road density increase, leading to psychological stress (Lederbogen et al., 2011) and environmental degradation (Gong et al., 2012; Orishimo, 2012). These factors may increase the risk of SUD (Adabag et al., 2010). However, to date, little is known about the relationship between urbanization and SUD incidence. In our study, the percentages of developed land and road density were not associated with SUD incidence, suggesting that urbanization might not be a risk factor for SUD.

One major strength of our study is that we explored the links between SUD and multiple greenspace metrics, including percent forest, grassland, average and near-road tree canopy, and diversity of tree canopy. In contrast to the commonly-used normalized difference vegetation index (NDVI), the metrics used in our study may reveal the different effects and pathways exerted by different types of greenspace on human health. For example, near-road tree canopy may have benefits to human health by buffering traffic-related air pollutants and noise, while greenways can promote physical activity to improve health. However, NDVI does not discern tree cover from herbaceous cover, and thus is less helpful in determining possible mechanisms (e.g., hazard buffering versus health promoting) for health benefits of greenspace.

Another major strength of our study is that we used both a spatial model (Bayesian spatial model) and a non-spatial model (Poisson regression model) to examine associations between SUD incidence and greenspace. Though results from the two types of models are very similar, the spatial model has some advantages over the non-spatial model. First, many variables showed spatial autocorrelation and the effects of spatial dependence are considered in the spatial model. Second, the Bayesian approach was used to fit the spatial model, which takes the uncertainty of unknown parameters into account. In addition, the posterior distribution of parameters estimated with the Bayesian approach provides more information about the parameters than the Poisson regression model, which provides only a few point estimates (e.g., mean and 95% CI). Therefore, the Bayesian spatial model is preferred in this analysis. To our knowledge, it is rarely used in studies examining the relationships between greenspace and non-communicable diseases. Our study provides a good example of using such a method in this field. Furthermore, multiple SES metrics by census tract were available for our study; these include median household income, marriage status and employment rate. As a result, we were able to control for potential confounding effects of these metrics at an aggregate level.

The primary challenge of this study was obtaining accurate information about exposure to greenspace. Though we used multiple greenspace metrics, it is unknown how frequently the study subjects visited greenway trails and forest and how long they were exposed to greenspace. Furthermore, our analysis was conducted at the census tract level rather than the individual level, thus, the effect of greenspace on human health at the census tract level may be different from that at the individual level. The significant associations between SUD and a few greenspace metrics in our study do not imply any cause-effect relationship. They provide useful information for initially examining influential factors and generating hypotheses rather than deriving definitive conclusions. Though we controlled for several variables in the models, we cannot rule out other factors that might affect the links between greenspace and SUD incidence, such as family medical history. A minor issue is that the year of land cover and tree canopy datasets (2011) is different from the year that SUD cases were collected (2013–2015). Exposure to greenspace may be a long-term process, and land cover change may influence the measurement of greenspace metrics, thus influencing the model results. However, we compared major land cover classes in 2006 with those in 2011 and found that they changed slightly and are highly correlated at census tract level (Table S6). As a result, this issue is unlikely to affect our results significantly. It

should be mentioned that the greenspace metrics were calculated based on address of SUD incidence (where people died) instead of home address where the environment is more likely to affect people's health. However, both addresses were the same for most cases (92.4%) and the results of the models based on home address were similar to those based on the event address (Fig. S10). We used the event address for the primary address in the models to maintain consistency with the address used for spatial pattern assessment.

5. Conclusions

By exploring relationships between SUD and multiple greenspace metrics with robust approaches, we found that SUD incidence was inversely associated with greenway density and percent forest after controlling for confounding factors such as household income, population density and race. Major mechanisms underlying the statistically beneficial effects of greenspace on SUD need to be further investigated, particularly focusing on physical activity promotion and stress reduction.

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Disclaimer

The research described in this article has been reviewed by the National Health and Environmental Effects Research Laboratory, US EPA, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Agency, nor does the mention of trade names of commercial products constitute endorsement or recommendation for use.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2018.01.021>.

References

- Adabag, A.S., Luepker, R.V., Roger, V.L., Gersh, B.J., 2010. Sudden cardiac death: epidemiology and risk factors. *Nat. Rev. Cardiol.* 7 (4), 216–225.
- Akpinar, A., Barbosa-Leiker, C., Brooks, K.R., 2016. Does green space matter? Exploring relationships between green space type and health indicators. *Urban For. Urban Green.* 20, 407–418.
- Astell-Burt, T., Feng, X., Kolt, G.S., 2014. Is neighborhood green space associated with a lower risk of type 2 diabetes? Evidence from 267,072 Australians. *Diabetes Care* 37 (1), 197–201.
- Baldauf, R., 2017. Roadside vegetation design characteristics that can improve local, near-road air quality. *Transp. Res. Part D: Transp. Environ.* 52, 354–361.
- Bijmens, E.M., Nawrot, T.S., Loos, R.J., Gielen, M., Vlietinck, R., Derom, C., Zeegers, M.P., 2017. Blood pressure in young adulthood and residential greenness in the early-life environment of twins. *Environ. Health* 16 (1), 53.
- Bodicoat, D.H., O'Donovan, G., Dalton, A.M., Gray, L.J., Yates, T., Edwardson, C., Hill, S., Webb, D.R., Khunti, K., Davies, M.J., 2014. The association between neighbourhood

- greenspace and type 2 diabetes in a large cross-sectional study. *BMJ Open* 4 (12), e006076.
- Brantley, H.L., Hagler, G.S., Deshmukh, P.J., Baldauf, R.W., 2014. Field assessment of the effects of roadside vegetation on near-road black carbon and particulate matter. *Sci. Total Environ.* 468, 120–129.
- Brook, R.D., Franklin, B., Cascio, W., Hong, Y., Howard, G., Lipsett, M., Luepker, R., Mittleman, M., Samet, J., Smith, S.C., 2004. Air pollution and cardiovascular disease: a statement for healthcare professionals from the expert panel on population and prevention science of the American Heart Association. *Circulation* 109 (21), 2655–2671.
- Brown, S.C., Lombard, J., Wang, K., Byrne, M.M., Toro, M., Plater-Zyberk, E., Feaster, D.J., Kardys, J., Nardi, M.L., Perez-Gomez, G., 2016. Neighborhood greenness and chronic health conditions in Medicare beneficiaries. *Am. J. Prev. Med.* 51 (1), 78–89.
- Coutts, C., 2008. Greenway accessibility and physical-activity behavior. *Environ. Plann. B Plann. Des.* 35 (3), 552–563.
- Critchley, H.D., Taggart, P., Sutton, P.M., Holdright, D.R., Batchvarov, V., Hnatkova, K., Malik, M., Dolan, R.J., 2004. Mental stress and sudden cardiac death: asymmetric midbrain activity as a linking mechanism. *Brain* 128 (1), 75–85.
- Dales, R., Burnett, R.T., Smith-Doiron, M., Stieb, D.M., Brook, J.R., 2004. Air pollution and sudden infant death syndrome. *Pediatrics* 113 (6), e628–e631.
- Dalton, A.M., Jones, A.P., Sharp, S.J., Cooper, A.J., Griffin, S., Wareham, N.J., 2016. Residential neighbourhood greenspace is associated with reduced risk of incident diabetes in older people: a prospective cohort study. *BMC Public Health* 16 (1), 1171.
- de Jesus Crespo, R., Fulford, R., 2018. Eco-health linkages: assessing the role of ecosystem goods and services on human health using causal criteria analysis. *Int. J. Public Health* 63 (1), 81–92.
- Dekker, L.R., Bezzina, C.R., Henriques, J.P., Tanck, M.W., Koch, K.T., Alings, M.W., Arnold, A.E., de Boer, M.-J., Gorgels, A.P., Michels, H.R., 2006. Familial sudden death is an important risk factor for primary ventricular fibrillation. *Circulation* 114 (11), 1140–1145.
- Dennekamp, M., Akram, M., Abramson, M.J., Tonkin, A., Sim, M.R., Fridman, M., Erbas, B., 2010. Outdoor air pollution as a trigger for out-of-hospital cardiac arrests. *Epidemiology* 21 (4), 494–500.
- Egorov, A.I., Griffin, S.M., Converse, R.R., Styles, J.N., Sams, E.A., Wilson, A., Jackson, L.E., Wade, T.J., 2017. Vegetated land cover near residence is associated with reduced allostatic load and improved biomarkers of neuroendocrine, metabolic and immune functions. *Environ. Res.* 158, 508–521.
- Gatrell, A.C., Bailey, T.C., Diggle, P.J., Rowlingson, B.S., 1996. Spatial point pattern analysis and its application in geographical epidemiology. *Trans. Inst. Br. Geogr.* 256–274.
- Gong, P., Liang, S., Carlton, E.J., Jiang, Q., Wu, J., Wang, L., Remais, J.V., 2012. Urbanisation and health in China. *Lancet* 379 (9818), 843–852.
- Homer, C., Dewitz, J., Yang, L., Jin, S., Danielson, P., Xian, G., Coulston, J., Herold, N., Wickham, J., Megown, K., 2015. Completion of the 2011 National Land Cover Database for the conterminous United States—representing a decade of land cover change information. *Photogramm. Eng. Remote. Sens.* 81 (5), 345–354.
- Jorgensen, A., Gobster, P.H., 2010. Shades of green: measuring the ecology of urban green space in the context of human health and well-being. *Nat. Cult.* 5 (3), 338–363.
- Karjalainen, E., Sarjala, T., Raitio, H., 2010. Promoting human health through forests: overview and major challenges. *Environ. Health Prev. Med.* 15 (1), 1.
- Kleinbaum, D., Kupper, L., Nizam, A., Rosenberg, E., 2013. *Applied Regression Analysis and Other Multivariable Methods*. Nelson Education.
- Kohl, H., Powell, K., Gordon, N., Blair, S., Paffenbarger Jr, R., 1992. Physical activity, physical fitness, and sudden cardiac death. *Epidemiol. Rev.* 14 (1), 37–58.
- Kong, M.H., Fonarow, G.C., Peterson, E.D., Curtis, A.B., Hernandez, A.F., Sanders, G.D., Thomas, K.L., Hayes, D.L., Al-Khatib, S.M., 2011. Systematic review of the incidence of sudden cardiac death in the United States. *J. Am. Coll. Cardiol.* 57 (7), 794–801.
- Lane, K.J., Stokes, E.C., Seto, K.C., Thanikachalam, S., Thanikachalam, M., Bell, M.L., 2017. Associations between greenness, impervious surface area, and nighttime lights on biomarkers of vascular aging in Chennai, India. *Environ. Health Perspect.* 125 (8), 087003.
- Lawson, A.B., 2013. *Bayesian Disease Mapping: Hierarchical Modeling in Spatial Epidemiology*. CRC press.
- Lederbogen, F., Kirsch, P., Haddad, L., Streit, F., Tost, H., Schuch, P., Wüst, S., Pruessner, J.C., Rietschel, M., Deuschle, M., 2011. City living and urban upbringing affect neural social stress processing in humans. *Nature* 474 (7352), 498–501.
- Lee, J.J., Hwang, S.J., Mutalik, K., Corey, D., Joyce, R., Block, J.P., Fox, C.S., Powell-Wiley, T., 2017. Association of built environment characteristics with adiposity and glycemic measures. *Obes. Sci. Pract.* 3 (3), 333–341.
- Maas, J., Van Dillen, S.M., Verheij, R.A., Groenewegen, P.P., 2009. Social contacts as a possible mechanism behind the relation between green space and health. *Health Place* 15 (2), 586–595.
- Markevych, I., Schoierer, J., Hartig, T., Chudnovsky, A., Hystad, P., Dzhambov, A.M., de Vries, S., Triguero-Mas, M., Brauer, M., Nieuwenhuijsen, M.J., Lupp, G., Richardson, E.A., Astell-Burt, T., Dimitrova, D., Feng, X., Sadeh, M., Standl, M., Heinrich, J., Fuertes, E., 2017. Exploring pathways linking greenspace to health: theoretical and methodological guidance. *Environ. Res.* 158, 301–317.
- Mills, N.L., Donaldson, K., Hadoke, P.W., Boon, N.A., MacNee, W., Cassee, F.R., Sandström, T., Blomberg, A., Newby, D.E., 2009. Adverse cardiovascular effects of air pollution. *Nat. Rev. Cardiol.* 6 (1), 36.
- Moore, M., Gould, P., Keary, B.S., 2003. Global urbanization and impact on health. *Int. J. Hyg. Environ. Health* 206 (4–5), 269–278.
- Moran, P.A., 1950. Notes on continuous stochastic phenomena. *Biometrika* 37 (1/2), 17–23.
- Mounsey, L.A., Lin, F.-C., Pursell, I., Joodi, G., Lewis, M.E., Nwosu, A., Hodonsky, C., Simpson, R.J., Mounsey, J.P., 2017. Relation of household income to incidence of sudden unexpected death in Wake County, North Carolina. *Am. J. Cardiol.* 119 (7), 1030–1035.
- Nanavati, P.P., Mounsey, J.P., Pursell, I.W., Simpson, R.J., Lewis, M.E., Mehta, N.D., Williams, J.G., Bachman, M.W., Myers, J.B., Chung, E.H., 2014. Sudden Unexpected Death in North Carolina (SUDDEN): methodology review and screening results. *Open Heart* 1 (1), e000150.
- Ngom, R., Gosselin, P., Blais, C., Rochette, L., 2016. Type and proximity of green spaces are important for preventing cardiovascular morbidity and diabetes—a cross-sectional study for Quebec, Canada. *Int. J. Environ. Res. Public Health* 13 (4), 423.
- Oliveira, S., Andrade, H., Vaz, T., 2011. The cooling effect of green spaces as a contribution to the mitigation of urban heat: a case study in Lisbon. *Build. Environ.* 46 (11), 2186–2194.
- Onozuka, D., Hagihara, A., 2017. Out-of-hospital cardiac arrest risk attributable to temperature in Japan. *Sci. Rep.* 7, 39538.
- Orishimo, I., 2012. *Urbanization and Environmental Quality*. Springer Science & Business Media.
- Paquet, C., Coffee, N.T., Haren, M.T., Howard, N.J., Adams, R.J., Taylor, A.W., Daniel, M., 2014. Food environment, walkability, and public open spaces are associated with incident development of cardio-metabolic risk factors in a biomedical cohort. *Health Place* 28, 173–176.
- Pereira, G., Foster, S., Martin, K., Christian, H., Boruff, B.J., Knuiman, M., Giles-Corti, B., 2012. The association between neighborhood greenness and cardiovascular disease: an observational study. *BMC Public Health* 12 (1), 466.
- Pugh, T.A., MacKenzie, A.R., Whyatt, J.D., Hewitt, C.N., 2012. Effectiveness of green infrastructure for improvement of air quality in urban street canyons. *Environ. Sci. Technol.* 46 (14), 7692–7699.
- Reddy, P.R., Reinier, K., Singh, T., Mariani, R., Gunson, K., Jui, J., Chugh, S.S., 2009. Physical activity as a trigger of sudden cardiac arrest: the Oregon Sudden Unexpected Death Study. *Int. J. Cardiol.* 131 (3), 345–349.
- Roe, J.J., Thompson, C.W., Aspinall, P.A., Brewer, M.J., Duff, E.I., Miller, D., Mitchell, R., Clow, A., 2013. Green space and stress: evidence from cortisol measures in deprived urban communities. *Int. J. Environ. Res. Public Health* 10 (9), 4086–4103.
- Rose, N., Cowie, C., Gillett, R., Marks, G.B., 2009. Weighted road density: a simple way of assigning traffic-related air pollution exposure. *Atmos. Environ.* 43 (32), 5009–5014.
- Ruberman, W., Weinblatt, E., Goldberg, J.D., Chaudhary, B.S., 1984. Psychosocial influences on mortality after myocardial infarction. *N. Engl. J. Med.* 311 (9), 552–559.
- Shafer, C.S., Lee, B.K., Turner, S., 2000. A tale of three greenway trails: user perceptions related to quality of life. *Landsc. Urban Plan.* 49 (3), 163–178.
- Shanahan, D.F., Bush, R., Gaston, K.J., Lin, B.B., Dean, J., Barber, E., Fuller, R.A., 2016. Health benefits from nature experiences depend on dose. *Sci. Rep.* 6, 28551.
- Shannon, C.E., Weaver, W., 1998. *The Mathematical Theory of Communication*. University of Illinois Press.
- Silverman, B.W., 1986. *Density Estimation for Statistics and Data Analysis*. CRC press.
- Stecker, E.C., Reinier, K., Marijon, E., Narayanan, K., Teodorescu, C., Uy-Evanado, A., Gunson, K., Jui, J., Chugh, S.S., 2014. Public health burden of sudden cardiac death in the United States. *Circ. Arrhythm. Electrophysiol.* 7 (2), 212–217 (CIRCEP. 113.001034).
- Tamosiunas, A., Grazuleviciene, R., Luksiene, D., Dedele, A., Reklaitiene, R., Baceviciene, M., Vencloviene, J., Bernotiene, G., Radisauskas, R., Malinauskiene, V., 2014. Accessibility and use of urban green spaces, and cardiovascular health: findings from a Kaunas cohort study. *Environ. Health* 13 (1), 20.
- Tchwenko, S., 2012. Burden of Cardiovascular Disease in North Carolina – September, 2012. N.C. Department of Health and Human Services.
- Tsai, W.-L., Floyd, M.F., Leung, Y.-F., McHale, M.R., Reich, B.J., 2016. Urban vegetative cover fragmentation in the US: associations with physical activity and BMI. *Am. J. Prev. Med.* 50 (4), 509–517.
- Vlastelica, M., 2008. Emotional stress as a trigger in sudden cardiac death. *Psychiatr. Danub.* 20 (3), 411–414.
- Waller, L.A., Gotway, C.A., 2004. *Applied Spatial Statistics for Public Health Data*. John Wiley & Sons.
- Whang, W., Manson, J.E., Hu, F.B., Chae, C.U., Rexrode, K.M., Willett, W.C., Stampfer, M.J., Albert, C.M., 2006. Physical exertion, exercise, and sudden cardiac death in women. *JAMA* 295 (12), 1399–1403.
- Wu, J., Jackson, L., 2016. Association of land use and its change with beach closure in the United States, 2004–2013. *Sci. Total Environ.* 571, 67–76.
- Wu, J., Jackson, L., 2017. Inverse relationship between urban green space and childhood autism in California elementary school districts. *Environ. Int.* 107, 140–146.
- Wu, J., Gronewold, A.D., Rodriguez, R.A., Stewart, J.R., Sobsey, M.D., 2014. Integrating quantitative PCR and Bayesian statistics in quantifying human adenoviruses in small volumes of source water. *Sci. Total Environ.* 470–471, 255–262.
- Wu, J., Tschakert, P., Klutse, E., Ferrar, D., Ricciardi, V., Hausermann, H., Oppong, J., Smithwick, E.A., 2015. Buruli ulcer disease and its association with land cover in Southwestern Ghana. *PLoS Negl. Trop. Dis.* 9 (6), e0003840.
- Yitshak-Sade, M., Kloog, I., Novack, V., 2017. Do air pollution and neighborhood greenness exposures improve the predicted cardiovascular risk? *Environ. Int.* 107, 147–153.