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Green Space and Mortality Following Ischemic Stroke

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Abstract

Background—Residential proximity to green space has been associated with physical and mental health benefits, but whether green space is associated with post-stroke survival has not been studied.

Methods—Patients ≥21 years of age admitted to the Beth Israel Deaconess Medical Center (BIDMC) between 1999 and 2008 with acute ischemic stroke were identified. Demographics, presenting symptoms, medical history and imaging results were abstracted from medical records at the time of hospitalization for stroke onset. Addresses were linked to average Normalized Difference Vegetation Index, distance to roadways with more than 10,000 cars/day, and US census block group. Deaths were identified through June 2012 using the Social Security Death Index.

Results—There were 929 deaths among 1,645 patients with complete data (median follow up: 5 years). In multivariable Cox models adjusted for indicators of medical history, demographic and socioeconomic factors, the hazard ratio for patients living in locations in the highest quartile of green space compared to the lowest quartile was 0.78 (95% Confidence Interval: 0.63 to 0.97) (p-trend=0.009). This association remained statistically significant after adjustment for residential proximity to a high traffic road.

Conclusions—Residential proximity to green space is associated with higher survival rates after ischemic stroke in multivariable adjusted models. Further work is necessary to elucidate the underlying mechanisms for this association, and to better understand the exposure-response

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relationships and susceptibility factors that may contribute to higher mortality in low green space areas.

Keywords

Mortality; green space

Introduction

Over half of the world's population live in urban areas, and the majority of population growth over the next four decades is expected to occur in cities (United Nations, 2012). Most but not all studies have reported that access to green space in urban areas is associated with improved overall well-being, including benefits related to both physical and mental health (Bowler et al., 2010; Lee and Maheswaran, 2011; Logan and Selhub, 2012; van den Berg et al., 2010). The mechanisms underlying these associations are not clear, but green space may be associated with lower exposure to ambient air pollution, extreme heat, and noise (Gidlöf-Gunnarsson and Öhrström, 2007; Lafortezza et al., 2009; Nowak et al., 2006; Su et al., 2009). Proximity to green space may also offer more opportunities for physical activity and social interactions (Bowler et al., 2010; Coombes et al., 2010; Giles-Corti and Donovan, 2002). Furthermore, access to green space has been associated with lower perceived stress levels and physiologic indicators of stress, as well as cognitive restoration (Hartig et al., 2011; Park et al., 2010; Van Den Berg et al., 2007; Ward Thompson et al., 2013) and lower levels of stress are associated with improved prognosis and quality of life in patients with established cardiovascular disease (Arnold et al., 2012). However, studies of the association between residential proximity to green space and health outcomes have been inconsistent. Discrepancies may be attributable to differences in socioeconomic position and biological susceptibility in the populations studied (Maas et al., 2009a; Mitchell and Popham, 2008).

Stroke remains a leading cause of serious long-term disability and an estimated 6.8 million Americans ≥20 years of age have had a stroke (Go et al., 2013; Towfighi and Saver, 2011). Neighborhood-level characteristics and socioeconomic factors have been reported to predict stroke prognosis and mortality across different populations (Addo et al., 2012). There is evidence that environmental factors, including air pollution and living in locations close to high traffic roads, are associated with mortality following stroke and other cardiovascular events (Maheswaran et al., 2010; Rosenbloom et al., 2012; Wilker et al., 2013). Evidence also suggests that social isolation (Boden-Albala et al., 2005) and depression (House et al., 2001) are associated with poorer prognosis following stroke. However, whether residential green space is associated with post-stroke mortality has not been studied.

We hypothesized that residential proximity to green space would be associated with lower all-cause mortality following ischemic stroke in a population of stroke survivors living in the greater Boston area. We also hypothesized that the association between residential green space and all-cause mortality may differ by factors related to biological susceptibility, socioeconomic position and residential proximity to high traffic roadways.

Methods

Participants

We identified 1,763 patients ≥21 years of age admitted to the Beth Israel Deaconess Medical Center (BIDMC) between April 1, 1999 and October 31, 2008, with neurologist-confirmed acute ischemic stroke. The BIDMC is a 650-bed teaching hospital of Harvard Medical School designated as a primary stroke service hospital. We excluded patients with in-hospital strokes or transient ischemic attacks and we restricted analysis to patients living in the greater Boston metropolitan area (defined as living within 40 kilometers of the hospital). This study was approved by the Committee on Clinical Investigations at BIDMC.

Information on demographics, presenting symptoms, medical history and imaging results was abstracted from medical records at the time of hospitalization for stroke. Presumed stroke pathophysiology was characterized as: (1) large-artery atherosclerosis, (2) small-vessel occlusion, (3) cardioembolism, (4) other determined cause or (5) undetermined cause, using the approach developed for the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) (Adams et al., 1999).

Exposure and Covariate Assessment

Addresses were geocoded using ArcGIS 9.2 (ESRI, Redlands, CA). Residential green space was determined by Normalized Difference Vegetation Index (NDVI) estimates from satellite images using the National Aeronautics and Space Administration (NASA) Moderate Resolution Imaging Spectroradiometer (MODIS). The NDVI measure is designed to evaluate global distribution of vegetation types, as well as their biophysical and structural properties and spatial/temporal variations (Townshend and Justice, 1995). The index is based on the reflection of visible and near-infrared light by vegetation and is calculated by the difference between near-infrared and visible radiation divided by the sum of near-infrared and visible radiation. The vegetation coverage is likely to be more dense when there is more reflected light in the near infra-red range (Weier and Herring, 2000). Values of NDVI range from -1 to 1, with higher values indicating more green space. Global NDVI data are provided every 16 days and represent a composite of the previous 16 days with a 250-meter spatial resolution as a gridded product in the Sinusoidal projection (Solano et al., 2010).

The ArcGIS GridExtract add-in module was used to assign NDVI grid-cell estimates to each residential address. We used NDVI estimates from the month of July since this month represents the period of most substantial vegetation growth in the greater Boston area and therefore typically reflects the maximum possible green space in each grid cell (Breckle, 2002). We calculated the average NDVI levels for all July estimates between 2000 (when the data first became available from NASA) and 2012 (the end of mortality follow-up period). In each year, there were two July NDVI measures for each cell, providing a total of 26 measures from 2000-2012. Estimates were available for all grid cells in all years and there were no missing data.

All averages below 0.4 (n=117) were visually inspected to determine whether the NDVI level was low because it represented a densely urban area with minimal vegetation or whether it represented a grid cell that was predominantly within a body of water. Addresses in regions directly surrounded by water were excluded from analysis since these locations may have different characteristics from low green space areas not directly adjacent to bodies of water, and because residing near a body of water has been associated with positive health benefits distinct from those of green space (White et al., 2013).

Each geocoded address was linked to the corresponding 2000 US census block group and assigned block group level median household income and percentage of adults age ≥25 years without high school diplomas. Distance to the nearest high traffic roadway, defined as a roadway with >10,000 vehicles/day, was computed in ArcGIS based on average daily traffic counts provided by the Massachusetts Department of Transportation (2013).

Outcome Assessment

Deaths were determined by Social Security Death Index (SSDI). Participants were censored at the time of death or on June 26, 2012. Follow up time was calculated as the date of symptom onset to censor date.

Statistical Analysis

Cox proportional hazard models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for the association between residential green space and all-cause mortality. Quartiles were selected for the primary analysis to evaluate potential nonlinearity and to minimize the influence of outliers in the NDVI distribution. Proportionality of hazards was evaluated by testing interactions with the log of time. We examined the association between all-cause mortality and quartiles of green space, and we conducted a test for trend by evaluating the statistical significance of a linear term using the median green space for each quartile. In the first model, we adjusted for age and sex. In a second model, we further adjusted for race (black, white/unknown), Hispanic ethnicity (yes or no), smoking status (current, former, or never), history of stroke, coronary artery disease, atrial fibrillation, heart failure, diabetes, dyslipidemia, and hypertension, percent of adults in the block group aged ≥25 years without a high school diploma (tertiles) and median household income (quartiles). In a third model, we additionally included a term for the natural logarithm of distance to a major roadway as a continuous variable, which has previously been associated with post-stroke mortality in this population (Wilker et al., 2013).

To examine whether the association between green space and post-stroke mortality varied according to major roadway proximity, a cross-product term between quartiles of NDVI and the natural logarithm of residential proximity to a major roadway was included in the model. We also used cross-product terms to test whether the associations with green space differed by factors related to biological susceptibility (age>75, diabetes, sex) and socioeconomic indicators of vulnerability (median household income in the lowest quartile and percent of adults aged ≥25 years without a high school diploma in the highest tertile) individually in separate models.

We conducted several sensitivity analyses to evaluate the robustness of our findings. In secondary analyses, we treated NDVI as a linear continuous term and scaled the hazard ratios to an interquartile range difference in NDVI (0.22). To explore the best fit of the model of green space and mortality, we also considered models with natural splines that had two, three, and four degrees of freedom in addition to primary analyses with quartiles and secondary analyses treating NDVI as a continuous linear term and evaluated whether models using splines fit the data better using likelihood ratio tests. Instead of using categorical variables, we considered nonlinear associations with socioeconomic factors using natural splines with three degrees of freedom to adjust for median household income and percent of adults aged ≥25 years without a high school diploma. We also modeled age using natural splines with two degrees of freedom rather than as a linear continuous variable. We allowed baseline mortality rates to vary by age in separate models. In addition, because people who survive to a particularly old age may reflect a different subgroup of the population, we conducted an analysis excluding the 3 participants >100 years of age. Finally, since stroke severity may be related to access to green space, models were adjusted for length of hospital stay (continuous and then as >4 vs ≤4 days) as an indicator of stroke severity.

Analyses were conducted using SAS Version 9.3 (Cary, NC) and R (RSTUDIO V 0.97, R Version 3.01, Survival Package). Plots were created in Stata (Version 12, College Station, Texas). All p-values are two sided and a p<0.05 was considered statistically significant.

Results

Of the 1763 patients initially assessed, there were 1,705 eligible who lived within 40 km of the Medical Center with recorded date and time of stroke. Complete covariate data and green space measures were obtained for 1,675 participants (98%). We excluded 30 participants with residential addresses located in NDVI grid cells made up mostly of water (2% of participants with NDVI measures), leaving a total of 1,645 participants. There were 929 deaths over up to 13.2 years of follow up, with a median follow up of 5 years. Population characteristics by quartiles of residential green space are presented in Table 1. Participants living in the lowest quartile of green space tended to be slightly younger, more likely to be black or Hispanic, lived in areas with higher percentages of individuals ≥25 years without a high school diploma and had lower median incomes. History of stroke and hypertension were highest in this group as well. The green space measures in our data ranged from 0.12 to 0.89, with a median value of 0.65 and an interquartile range of 0.22. The Spearman correlation between green space and residential proximity to a high traffic road was 0.26. A map of NDVI for the study area in July 2000 is provided in Figure 1.

Multivariable adjusted hazard ratios are presented in Table 2. In models adjusted for age and sex, the hazard ratio for living in the highest quartile of green space compared to the lowest quartile was 0.77 (95%CI: 0.64, 0.92, p-trend=0.001). After further adjustment for indicators of past medical history, demographic and socioeconomic factors, this association was attenuated slightly (HR=0.78, 95%CI: 0.63, 0.97, p-trend=0.009). After further adjustment for the natural logarithm of residential proximity to a high traffic roadway, the hazard ratio for patients living in the highest quartile of green space was 0.80 (95%CI: 0.65, 0.99) p-trend=0.02). Predicted survival curves for Model 2 results are presented in Figure 2. Consistent with results in Table 2, the steepest curve was observed for living in the lowest quartile of NDVI. Living in the second quartile was also associated with lower survival rates, but there was no discernible difference in the survival curves for the third and fourth quartiles.

In our sensitivity analyses, similar results were observed when we fit the models using continuous NDVI and scaled to an interquartile range difference of 0.22. However, associations had wide confidence intervals and did not achieve nominal statistical significance. We did not find that models with natural splines for green space improved model fit based on likelihood ratio tests. There was no evidence that the association between quartile of green space and mortality differed by natural logarithm of distance to high-traffic roadway (p-interaction=0.74). We did not detect any evidence of statistical interaction by age, diabetes status, or percent of adults age ≥25 years without a high school diploma (lowest tertile) and median household income (lowest quartile). Results were not materially different when we included natural splines for median income, percent of adults age ≥25 years without a high school diploma, or age; allowed baseline mortality rate to vary by age; excluded patients >100 years of age at the time of their stroke; or adjusted for length of stay in hospital as a continuous or categorical predictor of post-stroke mortality.

Discussion

In this study of all-cause mortality following ischemic stroke onset, living in an area with more green space was associated with a lower mortality rate even after adjusting for demographic and clinical characteristics. Compared to living in the lowest quartile of green space, the hazard ratio for living in the second quartile was 0.90 (95%CI: 0.75, 1.08) and for living in the third quartile it was 0.78 (95%CI: 0.64, 0.95). The hazard ratio was not any lower for the 4th quartile (HR=0.78, 95%CI: 0.63, 0.97)These findings were robust to further adjustment for residential proximity to a major roadway, and did not differ substantially across categories of a number of biological and socioeconomic factors. Continuous linear associations evaluated in secondary models did not achieve nominal statistical significance, although they suggested a lower mortality rate ratio with higher green space. There was no clear evidence of a nonlinear association, but we cannot rule out the possibility that power was not sufficient to detect nonlinearity.

Recent studies have reported that green space is positively associated with a number of health benefits. One study reported that the percentage of green space within a one or three kilometers of residence was associated with the perception of better overall health (Maas et al., 2006), and access to green space has been associated with improved health status, including lower body weight (Astell-Burt et al., 2013a; Pereira et al., 2013) lower risk of cardiovascular disease (Pereira et al., 2012), and diabetes (Astell-Burt et al., 2013b). Due to the complex relationship between socioeconomic factors, physical activity and green space (Lee and Maheswaran, 2011), it is challenging to determine the mechanisms underlying this association. For example, access to green space has been associated with higher levels of physical activity, but after adjustment for socioeconomic factors, both positive (Coombes et al., 2010; Richardson et al., 2013) and null findings (Hillsdon et al., 2006; Maas et al., 2008) have been reported. Green space has been associated with reduced emissions in Toronto (Su et al., 2009) and there may be small direct benefits of proximity to trees in in contributing to lower exposures to gaseous pollutants (Nowak et al., 2006). Green space may also provide cooling and shade from extreme heat (Lafortezza et al., 2009) and protection from noise disturbance (Gidlöf-Gunnarsson and Öhrström, 2007), perhaps by providing greater distance from roadside sources of noise. There may also be more direct benefits to promote social contacts and improve mental health (Maas et al., 2009a). More specifically, studies have reported lower levels of physiologic responses to stress (Hartig et al., 2003; Park et al., 2010) as well as benefits regarding immune function (Li, 2010). These may be relevant pathways that help explain the association between higher levels of green space and lower mortality rate following stroke, particularly since lower levels of psychosocial stressors and better access to social networks have been associated with improved prognosis (Boden-Albala et al., 2005; House et al., 2001).

Our findings contribute to the growing literature on green space and all-cause mortality. No previous studies have evaluated the association between green space and mortality in a prospective cohort of stroke survivors, but our results are consistent with research on the health benefit of living in an area with high levels of green space. In a recent study of 575,000 adults age 35 years or older living in Ontario, Canada, an interquartile range (IQR=0.24) difference in 500 m buffer of green space was associated with a small, but statistically significant lower rate of non-accidental mortality (HR=0.94 (95% CI: 0.93, 0.95)) (Villeneuve et al., 2012). This association remained even after adjusting for estimated residential levels of nitrogen dioxide (NO_2) or residential proximity to major roads. In a study of elderly residents living in the greater Tokyo metropolitan area, space for leisurely walks or parks and tree lined streets near their residence was associated with greater probability of five year survival (Takano et al., 2002), and a study in the United Kingdom also reported that residence in the most green quintile was associated with lower rates of all-cause mortality (Incidence Rate Ratio (IRR)=0.94 (95%CI: 0.93, 0.96) (Mitchell and Popham, 2008). A unique feature of our study is that it makes use of individual-level information including clinical risk factors for post-stroke mortality collected at the time of hospitalization, which may improve both the precision of the results and potentially provide better control of confounding than area-level aggregate measures.

In our study, there was no evidence that socioeconomic factors modified the association between green space and survival, whereas several prior studies on green space and mortality have reported associations that differed across strata of factors related to socioeconomic position and biological susceptibility. Mitchell and Popham reported that associations between income deprivation and mortality differed across categories of exposure to green space for all-cause mortality ($p<0.0001$); compared to individuals in the lowest quartile of income deprivation, the all-cause mortality rate was 1.93 (95% CI: 1.86, 2.01) times higher (IRR) for individuals in the highest quartile of income deprivation in the least green areas, while it was 1.43 (95%CI: 1.34, 1.53) in the most green areas (Mitchell and Popham, 2008). Other studies have reported that the association between lack of green space and loneliness was higher for people with low educational attainment and low income and lower levels of education (Maas et al., 2009a) and that the association between green space and prevalence of disease clusters was stronger for people in lower socioeconomic positions, who the authors hypothesized may be more likely to spend time near their residence and thus may be subject to less exposure misclassification (Maas et al., 2009b).

Different associations between green space and health have also been observed by sex and age. For example, a study in the United Kingdom reported that higher levels of green space were associated with lower rates of cardiovascular and respiratory disease in men, but not in women (Richardson and Mitchell, 2010). The authors hypothesized that this could be due to differences in green space usage. One study reported that the negative (ie: protective) association between green space and mortality was stronger in younger study participants than older participants (Villeneuve et al., 2012). Although others have found these differences in the association across subgroups, we did not observe evidence of statistical interaction by these characteristics. This may be due in part to the older age of our study participants or somewhat limited variability of the socioeconomic status of study participants.

We estimated proximity to green space according to the residential address at the time of stroke onset using NDVI. While this index provides an objective quantification of green space, it is sensitive to meteorological conditions, and does not distinguish between the types of vegetation, or whether a particular grid cell is partially developed, containing fragments of green space (Richardson et al., 2012) and therefore they do not necessarily indicate proximity to large green spaces such as parks, which may be particularly relevant if physical activity is an important mechanism for the salutogenic properties of green space (Mitchell et al., 2011). Other studies observing associations between NDVI and health outcomes have in some cases used larger buffer zones and have suggested that these may be more representative of access to parks (Dadvand et al., 2012; van den Berg et al., 2010) and promotion of walking and physical activity (Astell-Burt et al., 2013a), though this may not be the primary mechanism associated with positive health outcomes in older individuals (Ord et al., 2013; Richardson et al., 2013). As other authors have noted, a smaller buffer zone may reflect a less polluted, greener residential area, with roadside trees and small lawns (Laurent et al., 2013; Mitchell et al., 2011).

There are some limitations to this study. First, in our study, we do not have information on the severity of stroke, therefore ,we cannot determine how factors related to mobility and daily activities were affected, the types of rehabilitation that were offered, and whether residential green space at address at the time of stroke predict utilization in the period after the stroke activity. However, we note that this is unlikely to be a confounder of the association between green space and mortality. It could potential be a mediator on the pathway of this association, in which case adjusting would not be appropriate. Also, we do not have data on how much time patients spent away from home or duration of residence at the address, either prior to the stroke nor during follow-up. However, a previous study has shown that Americans spend an average of 68% of their time at home (Klepeis et al., 2001). Third we cannot rule out the possibility of residual confounding by socioeconomic factors, which could play a role in confounding, modifying or mediating the association between green space and mortality. Specifically, patients of higher socioeconomic position may have more opportunities to access and utilize green space and may choose to live near or spend time closer to green spaces. However, adjusting for individual and area-level indicators of demographic and socioeconomic status did not materially alter the results and we observed no evidence of statistical interaction by markers of socioeconomic status. Fourth, we did not take into account access to bodies of water which could also have beneficial effects. A recent study found that living near the coast was associated with better general health and mental well-being (White et al., 2013), and that the association with green space remained statistically significant after adjustment for residential proximity to the coast. While we excluded individuals who resided directly on the coast, we cannot rule out the possibility that some people living in the greater Boston area may be sufficiently close to the coast to experience health benefits. Finally, our results may not be generalizable to other populations, especially those with different land-use and geographic features.

Conclusions

In this cohort of ischemic stroke survivors in greater Boston, we observed that compared to living in an area in the highest quartile of green space, living in the lowest quartile of green space was associated with a higher mortality rate. If causal, these findings suggest that green space may be an independent predictor of survival following stroke, and may have relevant prognostic implications for future patients in response to increases in urbanicity and climate change. Further work is necessary to improve our understanding of the exposure—response relationship and factors that may contribute to greater susceptibility to mortality in low green space areas in urban areas.

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- We modeled the association between green space and post-stroke mortality.
- Models were adjusted for medical history, demographic and socioeconomic factors.
- Green space was associated with higher survival rates after ischemic stroke.
- Associations remained after adjustment for proximity to a high traffic road.

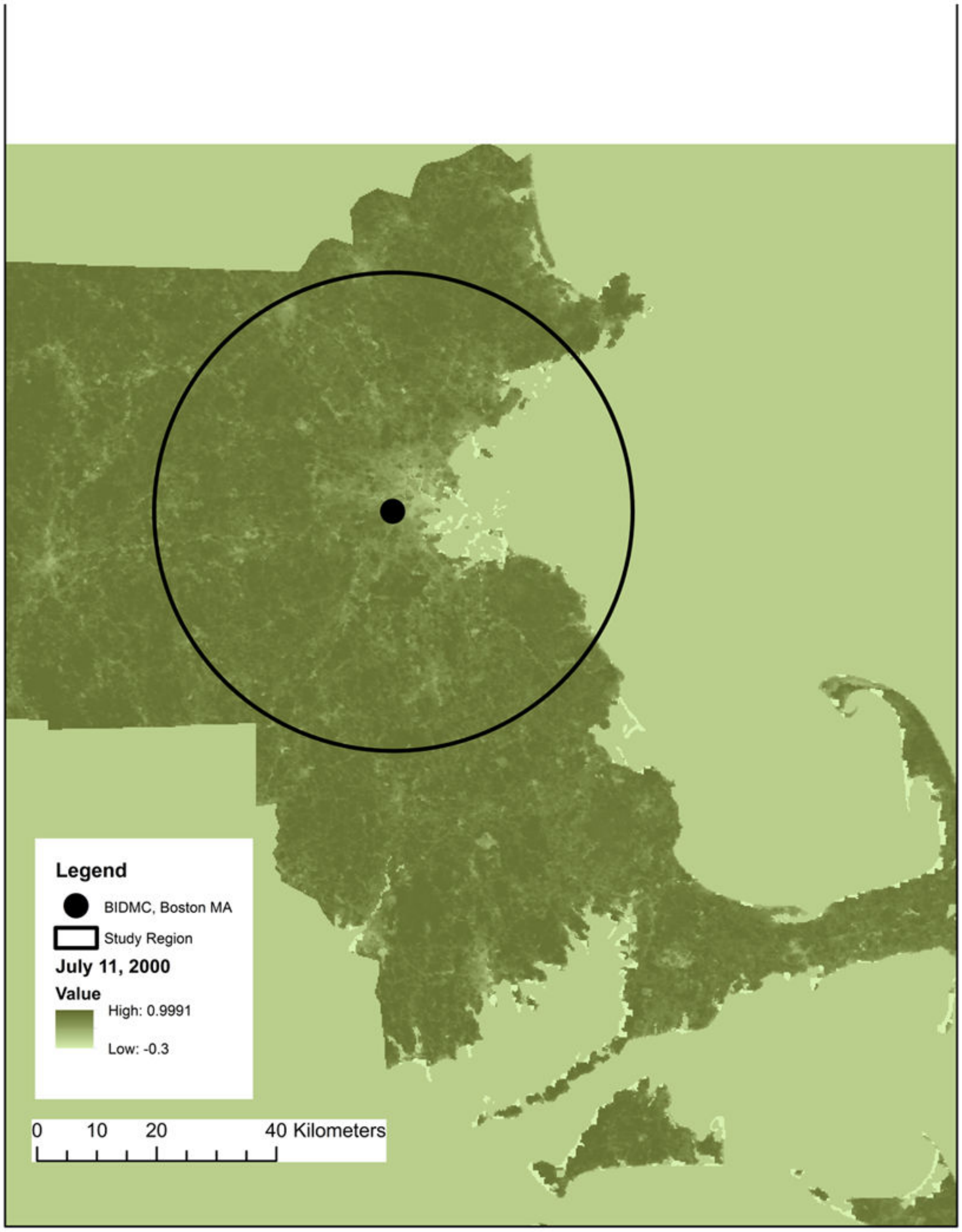

Figure 1.
NDVI predictions for the study region: July 11, 2000.

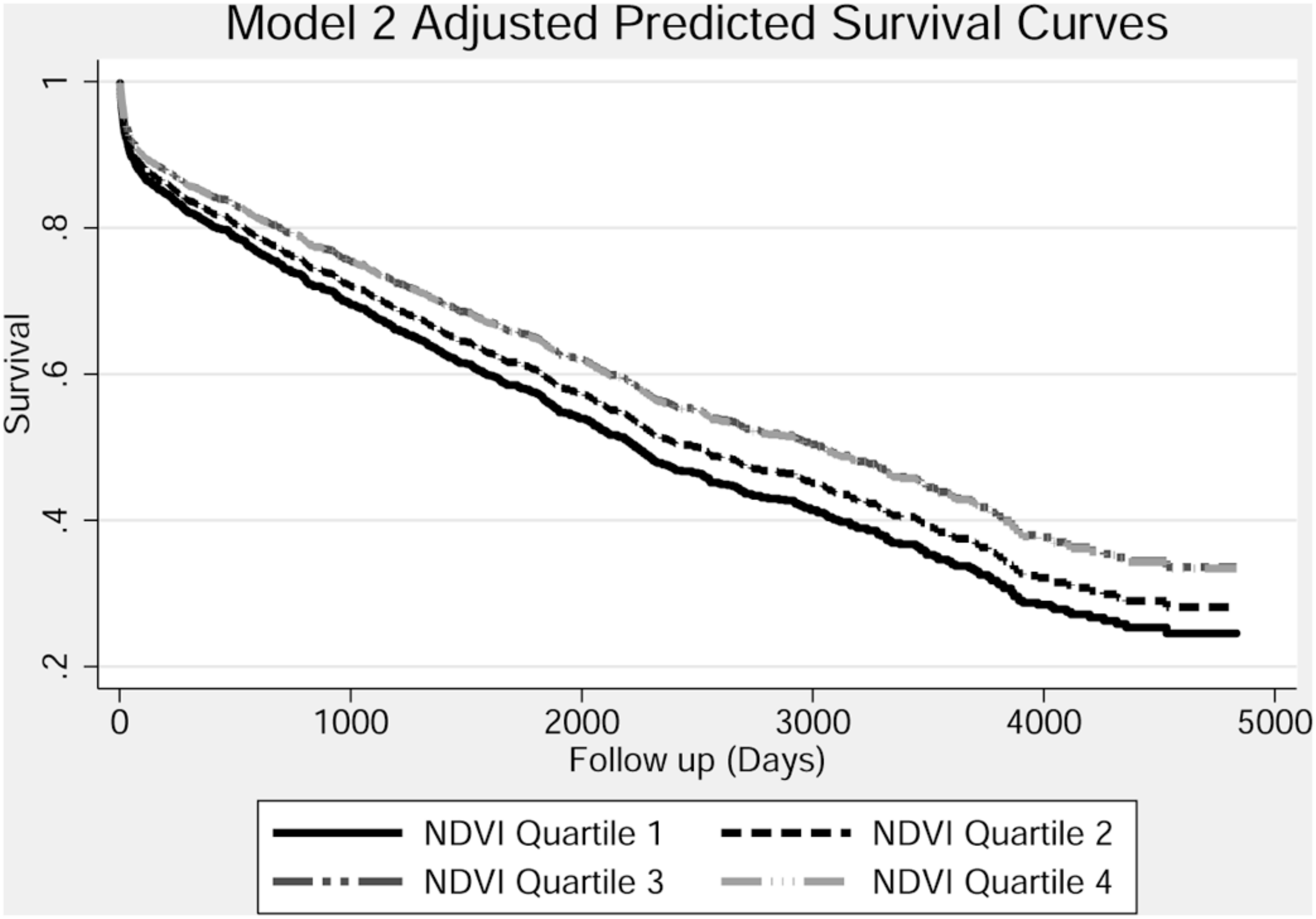

Figure 2.

Predicted survival curves based on Model 2 results. Living in the lowest quartile of exposure to green space was associated with the lowest predicted survival over follow-up. A less steep slope was observed for living in the second quartile and the association for living in the third quartile was indistinguishable from background levels.

Table 1

Population characteristics (n=1645) by Green Space (median [IQR] or n(%)).

NDVI range	Quartile 1 (n=409) (0.119 -0.533)	Quartile 2 (n=413) (0.534 -0.647)	Quartile 3 (n=410) (0.648 -0.753)	Quartile 4 (n=413) (0.754-0.893)
Age (years)	73 [21]	75 [22]	76 [19]	77 [20]
Follow up (years)	4.8 [6.5]	4.8 [6. 9]	5.0 [6.2]	4.9 [6.0]
Male	190 (46%)	171 (41%)	192 (47%)	191 (46%)
Black	70 (17%)	82 (20%)	33 (8%)	7 (2%)
Hispanic	23 (6%)	17 (4%)	10 (2%)	6 (1%)
Current smokers	68 (17%)	60 (15%)	53 (13%)	44 (11%)
Former smokers	104 (25%)	87 (21%)	123 (30%)	123 (30%)
Percent without high school diploma in census block group	20 [22]	15 [15]	8 [10]	6 [7]
Median income in census block group	40,598 [23,062]	45,114 [24,761]	62,639 [29,394]	77,431 [37,490]
Stroke History	122 (30%)	118 (29%)	115 (28%)	109 (26%)
Past CAD	108 (26%)	101 (25%)	99 (24%)	107 (26%)
AF History	98 (24%)	86 (21%)	109 (27%)	121 (29%)
HF History	46 (11%)	63 (15%)	55 (13%)	50 (12%)
Diabetes	129 (32%)	143 (35%)	109 (27%)	92 (22%)
Dyslipidemia	183 (45%)	157 (38%)	181 (44%)	163 (39%)
Hypertension	302 (74%)	301 (73%)	292 (71%)	279 (67%)

CAD=coronary artery disease; AF=Atrial Fibrillation; HF=Heart Failure

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Table 2

Hazard Ratios (HR) and confidence intervals for NDVI by quartile in multivariable adjusted models.

	Model 1[a]			Model 2[b]			Model 3[c]		
NDVI	**HR**	**95%CI**	**P-trend**	**HR**	**95%CI**	**P-trend**	**HR**	**95%CI**	**P-trend**
Quartile 1	--	--	.001			0.009			0.02
Quartile 2	0.90	(0.75, 1.08)		0.90	(0.75, 1.08)		0.91	(0.76, 1.10)	
Quartile 3	0.79	(0.65, 0.94)		0.78	(0.64, 0.95)		0.79	(0.65, 0.96)	
Quartile 4	0.77	(0.64, 0.92)		0.78	(0.63, 0.97)		0.80	(0.65,0.99)	
NDVI[d]	0.87	(0.78, 0.97)	.009	0.91	(0.80,1.03)	0.12	0.92	(0.81,1.05)	0.22

[a]adjusted for age and sex.

[b]adjusted for age, sex, race (black/other), hispanic, smoking status (current, former, never), history of coronary artery disease, history of stroke, atrial fibrillation, heart failure, diabetes, dyslipidemia, hypertension, percent of people age 25+ without a high school diploma (tertiles) and median household income (quartiles).

[c]adjusted for model 2 covariates and the log of distance to a road with >10,000 cars/day.

[d]scaled to an IQR difference in NDVI (0.22).