Health & Place 79 (2023) 102960

Contents lists available at ScienceDirect

Health and Place

journal homepage: www.elsevier.com/locate/healthplace

Neighborhood greenspace and cognition: The cardiovascular health study

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ARTICLE INFO

Keywords:
Alzheimer's disease
Environment
Epidemiology

ABSTRACT

Objectives: We examined whether greenspace measures (overall percent greenspace and forest, and number of greenspace types) were associated with clinically adjudicated dementia status.
Methods: In a sample of non-demented older adults (n = 2141, average age = 75.3 years) from the Cardiovascular Health and Cognition Study, Cox proportional hazard and logistic regression analyses were used to estimate associations of baseline greenspace with risks of incident dementia and MCI, respectively, while adjusting for demographics, co-morbidities, and other neighborhood factors. We derived quartiles of percent greenness (greenspace), forest (percent tree canopy cover), and tertiles of greenspace diversity (number of greenspace types) for 5-km radial buffers around participant's residences at study entry (1989–1990) from the 1992 National Land Cover Dataset. Dementia status and mild cognitive impairment (MCI) over 10 years was clinically adjudicated.
Results: We observed no significant association between overall percent greenspace and risk of mild cognitive impairment or dementia and mostly null results for forest and greenspace diversity. Forest greenspace was associated with lower odds of MCI (OR quartile 4 versus 1: 0.54, 95% CI: 0.29–0.98) and greenspace diversity was associated with lower hazard of incident dementia (HR tertile 2 versus 1: 0.70, 95% CI = 0.50–0.99).
Discussion: We found divergent results for different types of greenspace and mild cognitive impairment or dementia. Improved greenspace type and diversity measurement could better characterize the association between greenspace and cognition.

1. Introduction

The prevalence of Alzheimer's Disease and Related Dementias (ADRD) has increased, drawing increased attention among clinical and research communities, as ADRD poses significant burden nationally and globally (Brookmeyer et al., 2018; Global et al., 2019; Alzheimer's Association, 2020). Critically, ADRD is uneven across geographies. Higher prevalence of AD has been found in the Southeastern and Midwestern US. (Fowler et al., 2019) Conversely, mortality from AD is highest in the West and Northwest of the US and lowest in the Northeast (Akushevich et al., 2018). These geographic variations in ADRD describe high risk populations but fail to identify specific pathways through which to intervene to reduce disparities. Previous research has identified individual risk factors for cognitive decline, such as cardiovascular disease, diabetes, and smoking (Baumgart et al., 2015; Farrer et al., 1997). Even after accounting for such individual-level risk factors for ADRDs, there is a significant proportion (estimated over two-thirds) of unexplained risk that remains; further exploration of environmental factors might explain

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https://doi.org/10.1016/j.healthplace.2022.102960
Received 21 July 2022; Received in revised form 4 November 2022; Accepted 14 December 2022

some of this remaining risk (Killin et al., 2016). A growing body of literature focused on social determinants of health (SDOH) has started to investigate the role of group-level environmental risk factors on cognitive trajectories and risk of developing ADRDs (Killin et al., 2016; Besser et al., 2017; Clarke et al., 2012; Yen et al., 2009). The built environment includes all human-made entities that comprise the physical characteristics of communities in which individuals live, work, and recreate including land use patterns, transportation, buildings, infrastructure, and design (Centers for Disease Control and Prevention, 2013). A specific concept within the built environment, "greenspace," often includes undeveloped, open land with natural vegetation (e.g. grass, trees) (Centers for Disease Control and Prevention, 2013). It further encompasses urban parks, open public spaces, and residential vegetation (Twohig-Bennett and Jones, 2018). Greenspace is a facet of the built environment that is highly modifiable, both promotion and improvement of residential greenspaces represent potential interventions that could provide multiple benefits to community health (Kingsley, 2019).

Increased access to residential greenspace has been shown to have a protective association with cognitive decline and prevalence of Alzheimer's Disease in some studies (Brown et al., 2018; Cherrie et al., 2018; de Keijzer et al., 2016, 2018; Zijlema et al., 2017; Besser et al., 2021a), but not others (Clarke et al., 2012; Slawsky et al., 2019; Wang et al., 2017; Wu et al., 2015; Yu et al., 2018). Several mechanisms underlying the relationship between greenspace and cognition have been proposed in previous work. Overall greenspace may impact cognition via cardiorespiratory, inflammatory, or hypothalamic-pituitary-adrenal (HPA) axis pathways, due to increased opportunity for physical activity, stress abatement and social interaction, respectively (de Keijzer et al., 2016, 2018; Maas et al., 2009; Daniels et al., 2022; Roe et al., 2020; Ulrich et al., 1991). Past physiological impacts, exposure to greenspaces are also associated with improvements in mental health, including depression, levels of stress, and quality of life (Piva et al., 2022). Increased greenspace has shown a negative association with exposure to air pollutants, and higher levels of air pollution have been found to be associated with cognitive decline and dementia (de Prado Bert et al., 2018; Kilian and Kitazawa, 2018; Power et al., 2016). Trees and forest canopy are a specific component, or type, of greenspace found to be protective against the risk of dementia, potentially through improvements in air quality and pollution reduction (Power et al., 2016; Astell-Burt et al., 2020; Nowak et al., 2014). Additionally, forest tree canopy is a type of greenness that provides shade and temperature regulation, increasing the comfort of being active outdoors and might promote social recreation for older adults (Kabisch et al., 2017). Further, increasing the number of different types of vegetation within a space (greenspace diversity) may be protective against cognitive decline due to the association between more diverse gut microbiota and improved immune status and/or decreased inflammation (Hanski et al., 2012; Donovan et al., 2018).

Prior research linking greenspace to cognition is limited by poor measures of cognition and ADRD outcomes, restricted geographic scope, and failure to consider type or diversity of greenspace (de Keijzer et al., 2016; Besser and Mitsova, 2021). Prior studies of greenspace and ADRD outcomes have not employed clinically adjudicated diagnosis data, and instead have used cognitive testing or medical claims data to classify diagnosis, which can be prone to misclassification and have significant issues with measurement error and bias (Lee et al., 2019; Ranson et al., 2019). Spatial variability of natural environmental exposures both within and between different geographic locations is necessary to better characterize the impact of such exposures, and to address the homogeneity of measurement seen in past studies (Hajat et al., 2015). As such, use of multi-center, population-based, regionally diverse samples is warranted. Frequently, environmental studies derive a composite percent "greenspace" in a given area, based on summing individual land cover class types indicative of "greenspace" (forest, shrubland, fields) present in an area of interest (Wickham et al., 2014). While this summed global metric is useful and widely used, use of the composite "greenspace" measure limits our insights into which aspects of greenspace are most important to cognition. To best inform future intervention strategies, exploration of types of greenspace (i.e., forest) and diversity of greenspace types is needed to better characterize the specific aspects of greenspace that are most important for cognition.

To address these gaps, we used a retrospective cohort study design to evaluate the association between measures of environmental greenspace (overall, type, and diversity) and clinically adjudicated cognitive status using data from the ancillary Cardiovascular Health Study-Cognition Study (CHS-CS). We hypothesized individuals living in areas with greater greenspace measures (overall, type, and diversity) at baseline would have a reduced risk of dementia and/or mild cognitive impairment compared to individuals living in areas with less greenspace. Importantly, by utilizing such a large population sample in which ADRD outcomes are carefully measured, we will have the ability to detect possibly small effects related to greenspace and be able to assess new, innovative measures of greenspace, including diversity.

2. Methods

2.1. Study sample

We used data from the Cardiovascular Health Study-Cognition Study (CHS-CS) an ancillary study conducted to examine the prevalence of mild cognitive impairment (MCI) and dementia in the Cardiovascular Health Study, a cohort with detailed assessment of risk factors and health outcomes (Lopez et al., 2003a). Baseline recruitment from 1989 to 1990 included randomly sampling individuals from the Health Care Financing Administration's Medicare eligibility lists in four U.S. field centers: Sacramento, California (CA); Hagerstown, Maryland (MD); Winston-Salem, North Carolina (NC); and Pittsburgh, Pennsylvania (PA). In 1992–1993, an additional cohort of African Americans ($n = 687$) were similarly recruited, at three of four field centers (CA, NC, PA). Participants completed a baseline exam, consisting of a home interview and clinic exam. Annual follow-up occurred from baseline until 1999, when semi-annual follow-up via phone was introduced. A total of 3608 (58% female, 16% African American) individuals completed repeated neuropsychological testing, including the Modified Mini-Mental State Examination (3MS), and neuroimaging via magnetic resonance imaging (MRI) of the brain (Fitzpatrick et al., 2004). In 1998–1999, CHS-CS participants received detailed neurological and neuropsychological examinations and possible cases of dementia and MCI were clinically adjudicated by a review committee of neurologists and psychiatrists (Fitzpatrick et al., 2004). For the present study, we restricted to 2141 CHS-CS participants with (1) 5-km greenspace data available; (2) no prevalent dementia prior to MRI (1991–1993); (3) APOE genotype data available; and (4) individuals who self-identified as belonging to the racial/ethnic groups of "White" or "Black" (Fig. 1).

2.2. Environmental buffers

All greenspace data used in this study are available upon request through the Retail Environment and Cardiovascular Disease (RECVD) project (Drexel University Urban Health Collaborative, 2022). The RECVD study selected 1-km circular buffers as they are a common choice when studying walking environments and destinations, and also considered a larger radius of 5-km for other types of neighborhood amenities (e.g., food stores and medical facilities) likely to be accessed by private vehicle (Berke et al., 2007; Duncan and Mummery, 2005; Frank et al., 2007; Lovasi et al., 2009; Moudon et al., 2006; Sallis et al., 1990). Individuals in CHS were a functional sample of older adults, ambulatory and physically fit enough to attend clinic sites for repeat evaluations. As such, we did not expect them to be limited to walkable greenspace in their surrounding neighborhood and considered they might drive to a nearby designated greenspace, and benefit from a larger buffer size. Thus, 5-km buffers were selected as our primary exposure

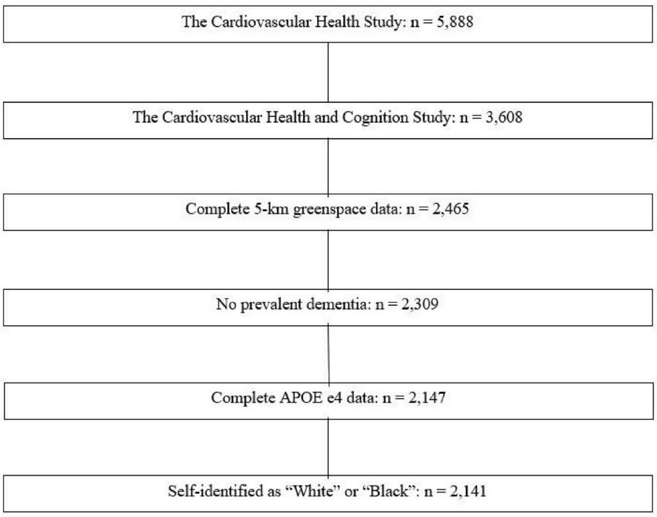

Fig. 1. Flow chart of selection of included participants (n = 2141), the Cardiovascular Health and Cognition Study, United States, 1992–1993 (n = 2141).

buffer as we believe greenspace operates at a larger environmental and spatial scale and tested the sensitivity of a smaller 1-km "neighborhood" buffer.

2.3. Greenspace measures

Greenspace measures for the CHS cohort at baseline were assessed using the 1992 National Land Cover Dataset (NLCD). The NLCD classifies land use for a given area based on 30 m satellite images augmented by ancillary data, such as maps (Vogelmann et al., 2001; National Land Cover Database |, 2022). Similar to other studies (Besser and Mitsova, 2021), we used these data to calculate overall greenspace as the percent of land uses consistent with greenspace (13 land uses included: deciduous, evergreen, or mixed forest, shrubland, orchards/vineyards, grassland/herbaceous, pasture/hay, row crops, small grains, fallow, urban/recreational grasses, woody wetlands, emergent herbaceous wetlands) within the 1-km and 5-km Euclidean radial buffers surrounding each participant's residential address (e.g., as a proxy for their neighborhoods). Overall greenspace was characterized into quartiles based on the distribution in the study sample. We developed additional measures to assess diversity and greenspace type in relation to cognition, including percent forest and an index of diversity. Forest greenspace was created by summing the percent of each forest types (deciduous, evergreen, and mixed) and like percent greenspace, characterized into quartiles. Diversity was defined as the total number of greenspace landcover types within the buffer; the index ranged from 2 to 13. For all greenspace measures, we chose quantiles based on distribution. Diversity was tertiled (unlike the other two quartiled measures) because it had a much narrower distribution and range of values (range: 2–13), compared to overall greenspace and forest greenspace (range: 0–96).

2.4. Environmental characteristics

Environmental characteristics included urbanicity, socioeconomic status (SES), and CHS clinic site. Urbanicity was dichotomized as metropolitan or micropolitan area, based on census-defined core-based statistical areas. Neighborhood SES was measured by summing z-scores derived from 1990 Census data on 6 variables that represented dimensions of wealth and income: median household income; median value of housing units; percentage of households receiving interest; dividend or net rental income; percentage of adults who completed high school; percentage of adults who completed college; percentage of persons in managerial or professional specialty occupations (Diez-Roux et al., 2001).

2.5. Dementia, mild cognitive impairment, and cognitive function

The CHS-CS included yearly measures of cognitive function and, from 1998 to 2000, participants were evaluated for mild cognitive impairment (MCI) and dementia by detailed neurological, and neuropsychological examinations. The possible cases of dementia and MCI were clinically adjudicated by a review committee of neurologists and psychiatrists (Lopez et al., 2003b). Prevalent MCI status was dichotomized as "normal" or "MCI." Follow-up time was available for cases of incident dementia. In addition, the Modified Mini-Mental State Examination (3MS), was used to assess global cognitive functioning (Barnes et al., 2006). The 3MS test evaluates a broad variety of cognitive functions, covers a wider range of difficulty levels, and has established reliability and validity. The 3MS test has a score range of 1–100 with higher scores indicative of better cognition.

2.6. Participant characteristics

Demographics included age, self-identified race/ethnicity (White or Black), sex, education (<high school, high school degree or Tests of General Educational Development (GED), some college/vocational school, college degree and above), and income (<\$25,000/year, ≥ \$25,000/year). Risk factor and clinical characteristics included: cigarette smoking (never/current/former, pack-years), hypertension (systolic >140mmg, diastolic >90mmg, medication use), diabetes (fasting glucose >125 mg/dL, non-fasting ≥ 200 mg/dL, or medication use), body mass index (kg/m^2, calculated from height and weight), and apolipoprotein E (APOE e4) allele (genetic risk factor for Alzheimer's disease) (≥1 e4 allele, no e4 alleles). A co-morbidity index was calculated by summing the total number of conditions reported, including depression (self-report or medication use), arthritis (self-report or medication use), chronic obstructive pulmonary disease (self-report of diagnosis of chronic bronchitis, asthma, emphysema), cardiovascular disease (coronary heart disease, myocardial infarction, congestive heart failure), and cerebrovascular disease (stroke, transient ischemic attack).

2.7. Statistical analyses

We evaluated differences in sample characteristics (demographic, clinical, and environmental characteristics) by quartile of greenspace in unadjusted analyses (i.e., chi-square tests, t-tests).

Unadjusted and adjusted Cox proportional hazard and logistic regression analyses were used to examine associations of greenspace with risk of incident dementia (time variable defined as follow-up years) and dichotomous risk of mild cognitive impairment (MCI). All included confounders were based on prior greenspace & cognition work in the Cardiovascular Health Study Cognition Study (Besser et al., 2021b). Variables that were either 1) significantly different across greenspace quartiles at $p < 0.05$ and/or 2) associated with greenspace, dementia status, or both in unadjusted regression at $p < 0.10$ were controlled for in models. To observe the impact of increasing confounder adjustment, nested multivariable models were run (1) controlled for demographics (age, race, sex, education, income); (2) demographics and co-morbidities (hypertension, diabetes, co-morbid index, BMI, smoking status, APOE e4 allele); (3) demographics, co-morbidities, and environmental factors (neighborhood SES, urbanicity, CHS site). In further analyses, the unadjusted and adjusted Cox proportional hazard and logistics regression models were re-run using quartiles of forest greenspace and tertiles of greenspace diversity index. Finally, we tested for trend across quartiles/tertiles in all final models to evaluate evidence for a dose response relationship between increasing levels of greenness and cognition. To better understand the attenuation of effect estimates after full model adjustment for environmental factors, in ad hoc exploratory analyses we evaluated addition of each environmental factor to the model separately, and CHS clinic site appeared to be the factor driving the association.

In sensitivity analyses, we re-ran unadjusted and adjusted models using 1-km buffers for all greenspace measures (overall greenspace, forest greenspace, and greenspace diversity index) to examine whether variation in the size of neighborhood buffer affected associations with mild cognitive impairment or dementia. In further analyses, we used a continuous measure of all exposures (overall greenspace, forest greenspace, and greenspace diversity index) to examine the sensitivity of conclusions to categorization methods based on quartile or tertile cutpoint. Finally, to explore whether greenspace is associated with clinically relevant changes in cognitive function but not ADRD diagnosis, generalized linear mixed models accounting for within-subject correlations were used to examine the association between percent greenspace at baseline and continuous 3MSE score (1991–1999). For example, individuals might show substantial decline over time but still be considered "cognitively normal" given a high 3MSE score at baseline. Consistent results between the association of greenspace, ADRD diagnosis and 3MSE score would support our conclusions, and understanding of the strength and direction of the relationship.

3. Results

Individuals living in the highest quartile of greenspace were more likely to be White, have less than a high school education, and have never smoked, compared to other greenspace quartiles (Table 1). Individuals living in the lowest quartile of greenspace had higher neighborhood SES, and urbanicity, compared with individuals living in higher quartiles. Differences in age, hypertension, diabetes, BMI, index of comorbidities, and >1 APOE e4 allele were not statistically significant. Compared to participants in CHS-CS that were not included as part of the analytical sample, individuals in the current sample were more likely to be White and have a higher neighborhood SES (Supplemental Table 1).

In the CHS-CS full sample, there were 480 (13.3%) cases of incident dementia, 227 (6.3%) prevalent dementia, 577 (16.0%) prevalent MCI, and 2318 (64.4%) cognitively normal. The average age of participants at baseline was approximately 75 and individuals were followed for up to 10 years. Unadjusted and adjusted Cox proportional hazards regression models for quartile of greenspace, forest and tertile of diversity and risk of incident dementia are presented in Table 2. In unadjusted models, there was a higher hazard of dementia for higher as compared to lower quartiles of overall greenspace. These associations were attenuated with increasing confounder adjustment, and in fully adjusted models, overall greenspace was not associated with incident dementia across all quartile contrasts (Quartile (Q)2 vs. Q1 OR = 1.01, 95% CI: 0.68, 1.50; Q3 vs. Q1 OR = 1.01, 95% CI: 0.70, 1.51; Q4 vs. Q1 OR = 0.99, 95% CI: 0.65, 1.51). Similarly, all quartiles of forest greenspace were associated with a higher hazard of dementia in unadjusted models and the association was frequently attenuated with confounder adjustment. As with percent greenspace, in fully adjusted models, forest greenspace was positively associated with dementia (trend test p = 0.0477), although none of the individual hazard estimates were statistically significant (Q2 vs. Q1 HR = 1.01, 95% CI: 0.65, 1.56; Q3 vs. Q1 OR = 1.37, 95% CI: 0.82, 2.25; Q4 vs. Q1 OR = 1.48, 95% CI: 0.91, 2.43). In unadjusted analyses, more diversity (types of greenspace) was associated with reduced hazard of incident dementia. In final models, compared to the lowest diversity, only moderate diversity of greenspace types was significantly associated with a reduced hazard of dementia (Tertile (T)2 vs. T1 HR = 0.70, 95% CI: 0.50, 0.99; T3 vs. T1 HR = 0.71, 95% CI: 0.38, 1.31; trend test p = 0.0585).).

Unadjusted and adjusted logistic regression models for quartile of greenspace, forest and tertile of diversity and odds of MCI are presented in Table 3. In unadjusted models, there were non-significant higher odds of MCI for lower (Q1 vs. Q2 OR = 2.49, 95% CI: 1.75, 3.53) as compared

Table 1

Participant characteristics, by quartiles of neighborhood greenspace (5 km), the Cardiovascular Health and Cognition Study, United States, 1992–1993 (n = 2141).

	Quartile of Greenspace (5 km)					p-value
	Total (n = 2141)	Q1 (n = 535)	Q2 (n = 517)	Q3 (n = 538)	Q4 (n = 551)	
Demographics						
Age, mean (SD)	75.3 (4.8)	75.5 (4.9)	75.4 (4.5)	75.0 (4.9)	75.4 (4.8)	0.4391
White race, n (%)	2039 (95.2%)	515 (96.3%)	459 (88.8%)	521 (96.8%)	544 (98.7%)	<0.0001
Female, n (%)	1217 (56.8%)	275 (51.4%)	289 (55.9%)	328 (61.0%)	325 (59%)	0.0097
Education, n (%)						
Less than high school	516 (24.1%)	65 (12.2%)	121 (23.5%)	138 (25.7%)	192 (34.9%)	<0.0001
High school or GED	626 (29.2%)	137 (25.7%)	136 (26.4%)	181 (33.6%)	172 (31.3%)	
Some vocational	513 (24.0%)	177 (33.2%)	119 (23.1%)	123 (22.9%)	94 (17.1%)	
College and above	483 (22.6%)	155 (29.0%)	140 (27.1%)	96 (17.8%)	92 (16.7%)	
Income, >$25k/year, n (%)	855 (39.9%)	267 (49.9%)	207 (40.0%)	190 (35.3%)	191 (34.7%)	<0.0001
Clinical characteristics						
Smoking status, n (%)						0.0008
Never smoker	918 (42.9%)	210 (39.3%)	202 (39.1%)	229 (42.6%)	277 (50.3%)	
Former smoker	1017 (47.5%)	279 (52.2%)	257 (49.7%)	262 (48.7%)	219 (39.8%)	
Current smoker	206 (9.6%)	46 (8.6%)	58 (11.2%)	47 (8.7%)	55 (10.0%)	
Hypertension, n (%)	965 (45.1%)	238 (44.5%)	211 (40.81%)	242 (45.0%)	274 (49.7%)	0.1170
Diabetes, n (%)	329 (15.4%)	74 (13.8%)	78 (15.1%)	86 (16.0%)	91 (16.5%)	0.6330
BMI (kg/m^2), mean (SD)	26.5 (4.4)	26.3 (4.2)	26.3 (4.3)	26.5 (4.6)	26.8 (4.5)	0.2067
≥2 co-morbidities[a], n (%)	480 (22.4%)	118 (22.1%)	131 (25.3%)	115 (21.4%)	116 (21.1%)	0.4656
≥1 APOE e4 allele, n (%)	487 (22.7%)	119 (22.2%)	111 (21.5%)	117 (21.8%)	140 (25.4%)	0.3789
Neighborhood						
Neighborhood SES,[b] mean (SD)	0.5 (3.2)	2.1 (3.5)	0.6 (3.8)	−0.2 (3.0)	−0.6 (2.4)	<0.0001
Urban vs. suburban/rural, n (%)	2106 (98.4%)	535 (100%)	513 (99.4%)	532 (98.9%)	526 (97.4%)	0.0003
CHS clinic site, n (%)						<0.0001
Winston-Salem, NC	470 (21.9%)	20 (3.7%)	167 (32.3%)	154 (28.6%)	129 (23.4%)	
Hagerstown, MD	587 (27.4%)	10 (1.9%)	12 (2.3%)	247 (45.9%)	318 (57.7%)	
Sacramento, CA	607 (28.4%)	393 (73.5%)	76 (14.7%)	73 (13.6%)	65 (11.8%)	
Pittsburgh, PA	477 (22.3%)	112 (20.9%)	262 (50.7%)	64 (11.9%)	39 (7.1%)	

Note. QX = quartile X, BMI = body mass index.

[a] Co-morbidities include: depression (self-report or medication use), arthritis (self-report or medication use), chronic obstructive pulmonary disease (self-report of diagnosis of chronic bronchitis, asthma, emphysema), cardiovascular disease (coronary heart disease, myocardial infarction, congestive heart failure), and cerebrovascular disease (stroke, transient ischemic attack).

[b] Z-score; higher scores represent higher neighborhood SES.

Table 2
Cox proportional hazards regression estimating the association between measures of neighborhood greenspace (5 km) and risk of incident dementia.

	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Overall greenspace				
Quartile 1	REF	REF	REF	REF
Quartile 2	1.20 (0.86, 1.67)	1.10 (0.78, 1.54)	1.06 (0.75, 1.48)	1.01 (0.68, 1.50)
Quartile 3	1.28 (0.93, 1.77)	1.26 (0.90, 1.75)	1.23 (0.89, 1.72)	1.01 (0.70, 1.51)
Quartile 4	1.51 (1.10, 2.06)	1.39 (1.01, 1.92)	1.31 (0.95, 1.82)	0.99 (0.65, 1.51)
Trend[e]				p = 0.9413
Forest				
Quartile 1	REF	REF	REF	REF
Quartile 2	1.33 (0.96, 1.83)	1.25 (0.90, 1.73)	1.17 (0.84, 1.63)	1.01 (0.65, 1.56)
Quartile 3	1.22 (0.88, 1.68)	1.19 (0.86, 1.66)	1.15 (0.83, 1.60)	1.37 (0.82, 2.25)
Quartile 4	1.38 (1.01, 1.90)	1.40 (1.01, 1.93)	1.28 (0.93, 1.78)	1.48 (0.91, 2.43)
Trend[e]				p = 0.0477
Diversity				
Tertile 1	REF	REF	REF	REF
Tertile 2	0.87 (0.67, 1.11)	0.87 (0.68, 1.12)	0.84 (0.65, 1.08)	0.70 (0.50, 0.99)
Tertile 3	0.71 (0.53, 0.95)	0.72 (0.54, 0.97)	0.73 (0.54, 0.98)	0.71 (0.38, 1.31)
Trend[e]				p = 0.0585

[a] Control only for greenspace.
[b] Controlling for age, race, sex, education, income.
[c] Controlling for demographics + co-morbidities (diabetes, hypertension, index of co-morbidities, BMI, smoking status, APOE e4 allele).
[d] Controlling for demographics, co-morbidities + neighborhood SES, urban vs. rural, CHS site.
[e] p-value for trend test across quantiles for Model 4.

to higher (Q1 vs. Q4 OR = 1.15, 95% CI: 0.78, 1.69) quartiles of overall greenspace. These associations were partially attenuated with increasing confounder adjustment, and in fully adjusted models, overall greenspace was not associated with MCI across all quartile contrasts (Q2 vs. Q1 OR = 1.40, 95% CI: 0.91, 2.17; Q3 vs. Q1 OR = 1.38, 95% CI: 0.86, 2.20; Q4 vs. Q1 OR = 1.00, 95% CI: 0.62, 1.72). In unadjusted models, forest greenspace was associated with a non-significant increased odds of MCI, across two quartile contrasts (Q2 vs. Q1 OR = 1.35, 95% CI: 0.93, 1.95; Q3 vs. Q1 OR = 1.95, 95% CI: 1.37, 2.77; Q4 vs. Q1 OR = 1.42, 95% CI: 0.98, 2.05). As previously, after adjusting for environmental characteristics these associations were attenuated. Living in the highest quartile of forest greenspace was associated with a significant reduced odds of MCI (Q4 vs. Q1 OR = 0.54, 95% CI: 0.29, 0.98; trend test p = 0.0147) but a non-significant and mixed results for quartile two and three (Q2 vs. Q1 OR = 1.10, 95% CI: 0.66, 1.84; Q3 vs. Q1 OR = 0.64, 95% CI: 0.35, 1.15). In crude analyses and in analyses adjusting for demographics and co-morbidities, more greenspace diversity was significantly associated with a reduced odds of MCI. However, in fully adjusted models, increasing greenspace diversity was non-significantly associated with an increased odds of MCI (T2 vs. T1 OR = 1.25, 95% CI: 0.78, 2.00; T3 vs. T1 OR = 1.86, 95% CI: 0.96, 3.61).

Table 3
Multivariable logistic regression estimating the association between measures of neighborhood greenspace (5 km) and risk of Mild Cognitive Impairment (MCI).

	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Overall greenspace				
Quartile 1	REF	REF	REF	REF
Quartile 2	2.49 (1.75, 3.53)	2.03 (1.40, 2.94)	1.99 (1.37, 2.89)	1.40 (0.91, 2.17)
Quartile 3	1.55 (1.07, 2.24)	1.38 (0.94, 2.03)	1.36 (0.93, 2.02)	1.38 (0.86, 2.20)
Quartile 4	1.15 (0.78, 1.69)	0.95 (0.63, 1.43)	0.96 (0.64, 1.45)	1.00 (0.62, 1.72)
Trend				p[e] = 0.9014
Forest				
Quartile 1	REF	REF	REF	REF
Quartile 2	1.35 (0.93, 1.95)	1.26 (0.85, 1.86)	1.24 (0.83, 1.83)	1.10 (0.66, 1.84)
Quartile 3	1.95 (1.37, 2.77)	1.80 (1.24, 2.63)	1.79 (1.22, 2.62)	0.64 (0.35, 1.15)
Quartile 4	1.42 (0.98, 2.05)	1.36 (0.92, 2.02)	1.31 (0.88, 1.94)	0.54 (0.29, 0.98)
Trend				p[e] = 0.0147
Diversity				
Tertile 1	REF	REF	REF	REF
Tertile 2	0.70 (0.53, 0.92)	0.71 (0.53, 0.96)	0.71 (0.52, 0.96)	1.25 (0.78, 2.00)
Tertile 3	0.54 (0.39, 0.75)	0.61 (0.43, 0.86)	0.60 (0.42, 0.86)	1.86 (0.96, 3.61)
Trend				p[e] = 0.0616

[a] Control only for greenspace.
[b] Controlling for age, race, sex, education, income.
[c] Controlling for demographics + co-morbidities (diabetes, hypertension, index of co-morbidities, BMI, smoking status, APOE e4 allele).
[d] Controlling for demographics, co-morbidities + neighborhood SES, urban vs. rural, CHS site.
[e] p-value for trend test across quantiles for Model 4.

In sensitivity analyses, no associations with incident dementia were found in fully adjusted Cox proportional hazard regression models for continuous or categorical measures of greenspace, forest, or diversity using 1- and 5-km neighborhood buffers (Supplemental Tables 2–3), in contrast to some of the diversity findings in the primary 5-km analyses. Similar to the primary 5-km analyses, in fully adjusted logistic regression models, the highest quartile of forest (1-km) was associated with a reduced odds of MCI (OR = 0.55, 95% CI: 0.30, 0.94), and non-significant protection for quartiles 2 and 3 (Supplemental Table 4). No other associations with continuous or categorical measures of overall greenspace, forest, or diversity were found for 1-km buffers (Supplemental Table 4). In fully adjusted logistic models, a continuous index of diversity was associated with higher odds of MCI (OR = 1.15, 95% CI: 1.02, 1.30) for 5-km buffers (Supplemental Table 5). Finally, no association between continuous or categorical measures of percent greenspace, forest, or diversity index and 3MSE score (1991–1999) were found in fully adjusted generalized linear mixed models for 5-km buffers (Supplemental Table 6).

The distribution of greenspace measures and dementia status across

CHS clinics was investigated (Supplemental Tables 7–8). The highest proportion of cognitively normal individuals and approximately 73.5% of individuals in the lowest quartile of greenspace were from the Sacramento, CA clinic site. The highest proportion of individuals with incident dementia and approximately 57.7% of individuals living in the highest quartile of greenspace were from the Hagerstown, MD clinic site. The highest proportion of individuals with MCI and approximately half of individuals in the second quartile of greenspace were from the Pittsburgh, PA clinic site.

4. Discussion

In a large cohort of regionally diverse US older adults, aspects of environmental greenspace were weakly associated with protection against incident dementia and MCI, although findings varied for different types of greenspace. In fully adjusted models, overall greenspace was not associated with MCI or dementia. Associations of forest and greenspace diversity and cognitive outcomes were largely null. However, increased greenspace diversity was marginally significantly associated with lower hazard of incident dementia, but not with odds of MCI. More forest space was significantly associated with lower odds of MCI but higher hazard of dementia.

Our finding that overall greenspace was not protective against incident dementia and MCI aligns with several previous studies (Wu et al., 2015; Wu et al., 2017; Yuchi et al., 2020). Consistent with the body of literature on this topic, our findings are mixed. Similarly, they suggest that while overall greenspace may not be significant, specific types/aspects of greenspace may impact cognitive outcomes. A small but growing body of work has investigated the association between specific types and diversity of greenspace and cognitive outcomes in older adults. Unlike in our study, a recent large epidemiologic cohort from Australia found a decreased risk of dementia with increasing tree canopy (forest) (Astell-Burt et al., 2020). However, similar to our study, there were inconsistencies, wherein forest showed an association with cognitive outcomes, but not total green space (Astell-Burt et al., 2020). Similar to our finding that increased forest showed different associations with MCI and dementia, increased overall greenspace has been shown to be both protective against non-AD dementia, but increased the risk of AD dementia (Yuchi et al., 2020). In another study, the first aforementioned group also studied tree canopy and subjective memory, again finding a positive association between tree canopy and self-reported memory (Astell-Burt and Feng, 2020). The diverse etiology of MCI (medication use, psychiatric syndromes, metabolic problems, vascular disease, etc.) may explain greenspace diversity being associated with dementia, but forest with MCI. Supportive of our main analyses, we did not find any association between any of our measures of greenspace and change in cognitive function, as measured by the 3MSE, in the current analysis. Previous work supports an association between increased greenspace diversity and favorable psychological and physical health outcomes, however studies on cognitive outcomes are scarce and methodological differences make direct comparisons challenging, and further attention is warranted in future work (Aerts et al., 2018).

Specific components of overall greenspace, percent forest and diversity, may be more relevant to cognitive outcomes than overall greenspace based on our findings in the current study. In order to elucidate the components of greenspace important to favorable cognitive outcomes and to expand our understanding of potential mechanisms of these associations, greenspace should be evaluated by type and diversity in future research. We do not have a rationale to explain the unexpected increased risk for mild cognitive impairment we observed in association with increased greenspace diversity, although this association did not reach statistical significance. While prior research supports health benefits for plant diversity, potentially working through immune related pathways (Hanski et al, 2012), our study is the first to evaluate greenspace diversity in relation to cognitive function. These findings may support future work into examining whether greenspace impacts cognition through inflammatory and immune pathways. Interestingly, we did not find evidence of a negative dose-response relationship between greenspace diversity and incident dementia, as estimates for the second and third tertile of diversity were similar, however only the second tertile was significantly associated with reduced risk. Prior studies of greenspace biodiversity and health outcomes typically consider the total number of plant or tree species in a defined area or use a count of different land-cover types, similar to the present study (Aerts et al., 2018). In our sensitivity analyses, only one continuous exposure measure was significantly associated with the outcomes of interest. This finding could be due to multiple testing or could support our choice to quantile our measures according to distribution, as the associations are not necessarily linear. Future research could use flexible modeling approaches such as smoothing splines to further characterize nonlinearity (Marx and Eilers, 1998).

As found in post-hoc descriptive analyses, an important consideration is how the distribution of both the overall composite greenspace measure and baseline cognitive status largely differed by site. At baseline, the largest proportion of participants with normal cognition lived in Sacramento, CA, which was the CHS site with the lowest amount of greenspace. The CHS site with the highest amount of greenspace, Hagerstown, MD, had the largest proportion of individuals with incident dementia. This confounding by CHS clinic site is difficult to untangle because it is so closely associated with exposure of interest. In the current analysis, we did not have adequate power to evaluate CHS site as an effect modifier, but our findings suggest that associations may depend on local distribution of greenspace and/or other environmental characteristics and therefore, site-specific analyses are also of value in future work. In unadjusted models, we observed non-protective effects of greenspace measures on mild cognitive impairment or dementia. However, we observed an attenuation of the effect in the hypothesized direction with increasing covariate adjustment. This finding underscores the importance of properly addressing confounders in observational studies of greenspace and cognition. A lack of consideration of confounder adjustment and adjustment for location might explain the discrepancies and inconsistencies found between the current and previous work. Carefully designed quasi-experimental studies, leveraging changing greenspace or participant moves, may be a useful approach to addressing this limitation in future research (Donovan et al., 2015). While the mechanisms linking greenness and cognition remain unclear, they may include improved air quality, reduced stress and increased social activity, all of which may operate as an environmental impact, and not just a neighborhood (walkable) one (de Keijzer et al., 2016; de Keijzer et al., 2018; Maas et al., 2009; Daniels et al., 2022; Roe et al., 2020; Ulrich et al., 1991). As we hypothesized greenspace operates at a larger environmental and spatial scale, we utilized a larger 5-km buffer for primary analyses. Given that the size of the spatial area that an older adult moves through in daily life, or life-space mobility, is associated with cognitive decline (Caldas et al., 2020), we tested the sensitivity of changing our definition of exposure geography on our findings by estimating effects for a smaller 1-km buffer. In sensitivity analyses, we found our results differed with variations in the definition of neighborhood based on buffer size but were generally similar in pattern of effect size. While results of the current work for both 5-km and 1-km buffer size were largely null, there was suggestion of forest and diversity supporting cognition at the 5-km scale, and protective associations for forest greenspace and MCI were consistent across buffer size. If replicated, these results suggest improvements in air pollution or promotion of social recreation are mechanisms to explore in the future. Buffer size used to define greenspace in cognitive studies varies across previous work, complicating comparisons. Emergent novel methodologies to eliminate the need for buffers and estimate associations across a continuous spatial scale can help address such measurement issues in the future (Peterson et al., 2021).

Strengths of the current study include use of a large, population-based cohort with clinically adjudicated cognitive status outcomes and consideration of type and diversity of greenspace. Several limitations of the current study warrant discussion. While the four geographic regions present in the CHS sample have differing topographic and population features, all four are relatively urban, metropolitan areas, with less rural representation in the study. Individuals with prevalent dementia at baseline were excluded, as we were interested in incident cases. Although the parent CHS cohort has ~15% Black participants, through exclusions in the current study, over 95% of our sample was White, again limiting generalizability and pertinence to racially/ethnically diverse populations including Black individuals. Selection criteria might have influenced our findings, as our study sample differed from the source population (the full cohort), and this induced selection bias might have induced residual confounding or collider stratification bias. The resolution of the NLCD is considered medium to coarse resulting in potential measurement error and bias, which may also explain the weak and inconsistent findings (Nowak and Greenfield, 2010). Exposure misclassification is possible, as the NLCD measurement only allows for a single land use per pixel, when several land uses might be present within the 30-m resolution, and the NLCD has been shown to underestimate tree canopy especially in developed lands (Nowak and Greenfield, 2010). Additionally, the NLCD does not provide any information about the quality of greenspaces which may also be relevant for protecting cognitive health (van Dillen et al., 2012). Use of "street-level" tools to measure greenspace may be helpful in future work to overcome the limitations of satellite imagery (O'Regan et al., 2021). Further, the greenspace buffer used does not account for an individual's interactions with greenspace outside of their neighborhood, nor does it consider any barriers (e.g. mobility, neighborhood walkability, etc) that might prevent older adults from accessing greenspace even if they live in an area with a high percent greenspace. Only baseline greenness was considered in the current study, and consideration of moving to a more or less green residential area is warranted in future work. We also did not consider changes in address over time. As change of addresses among older individuals were more likely to be prompted by changes in health status (move to a long-term care facility, etc.), bias would be an issue if people were systematically moving to areas that were of higher or lower greenness. As this is unlikely, bias associated with residential relocation was likely small. Additionally, while the current work included longitudinal outcome measurement, it was limited by lack of longitudinal exposure measurement over time. As the end goal of such research is to change environments to impact health outcomes, future work will need to examine how shifts in the environment impact individuals over time. Finally, the current findings may be a result of reverse causation or self-selection into neighborhoods, and methods to address such bias, including quasi-experimental and longitudinal study designs should be considered in future work (Besser et al., 2021c).

5. Conclusions

Our study suggests forest greenspace and greenspace diversity may be relevant to risk of dementia and MCI among older adults, though results are not conclusive. Future research, carefully designed to minimize confounding, should consider type and diversity of greenspace to help clarify mechanisms whereby greenspace may lower risk of dementia. Continued research can better inform future preventive interventions for healthy brain aging and public health recommendations.

Study funding

Sara Godina is supported by NIH awards (5-T32-AG-55381-2 and 1R36AG076741-01) and the K. Leroy Irvis Fellowship at the University of Pittsburgh Graduate School of Public Health. Lilah Besser is supported by NIH/NIA award K01AG063895 and the Alzheimer's Association (AARG-21-850963). Jana Hirsch and Gina Lovasi are supported by the National Institute on Aging (1R01AG049970, 3R01AG049970-04S1), Commonwealth Universal Research Enhancement (C.U.R.E) program funded by the Pennsylvania Department of Health—2015 Formula award—SAP #4100072543, the Urban Health Collaborative at Drexel University, and the Built Environment and Health Research Group at Columbia University. Jana Hirsch is supported by National Institute on Aging (R01AG072634). Yvonne Michael is supported by National Institute on Aging (3R01AG049970-04S1). Jana Hirsch and Yvonne Michael are supported by the National Institute on Aging (1R01AG072634). The remaining authors have no funding to disclose.

Author contribution

S.L. Godina wrote the paper and performed all statistical analyses. Y. L. Michael supervised the data analysis. A.L. Rosso, J.A. Hirsch, L.M. Besser, G.S. Lovasi, G.H. Donovan, P.K. Garg, J.M. Platt, A.L. Fitzpatrick, O.L. Lopez, M.C. Carlson, and Y.L. Michael all planned the study and contributed to revising the paper.

Declaration of competing interest

No conflicts of interest.

Acknowledgements

This work was supported by contracts HHSN268201200036C, HHSN268200800007C, HHSN268201800001C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, 75N92021D00006, and grants U01HL080295 and U01HL130114 from the National Heart, Lung, and Blood Institute (NHLBI), with additional contribution from the National Institute of Neurological Disorders and Stroke (NINDS). Additional support was provided by R01AG15928, R01AG20098, R01AG023629, and R01AG055404 from the National Institute on Aging (NIA). A full list of principal CHS investigators and institutions can be found at CHS-NHLBI.org. Incorporation of geographic characteristics was supported by the National Institute of Aging (grants 1R01AG049970, 3R01AG049970-04S1), Commonwealth Universal Research Enhancement (C.U.R.E) program funded by the Pennsylvania Department of Health—2015 Formula award—SAP #4100072543, the Urban Health Collaborative at Drexel University, and the Built Environment and Health Research Group at Columbia University, *Columbia University Robert N Butler Center for Aging, and a generous gift from Dana and David Dornsife to the Drexel University Dornsife School of Public Health.* The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.healthplace.2022.102960.

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