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Association Between Residential Greenness, Cardiometabolic Disorders, and Cardiovascular Disease Among Adults in China

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Abstract

IMPORTANCE Living in areas with more vegetation (referred to as residential greenness) may be associated with cardiovascular disease (CVD), but little data are available from low- and middle-income countries. In addition, it remains unclear whether the presence of cardiometabolic disorders modifies or mediates the association between residential greenness and CVD.

OBJECTIVE To evaluate the associations between residential greenness, cardiometabolic disorders, and CVD prevalence among adults in China.

DESIGN, SETTING, AND PARTICIPANTS This analysis was performed as part of the 33 Communities Chinese Health Study, a large population-based cross-sectional study that was conducted in 33 communities (ranging from 0.25-0.64 km²) in 3 cities within the Liaoning province of northeastern China between April 1 and December 31, 2009. Participants included adults aged 18 to 74 years who had resided in the study area for 5 years or more. Greenness levels surrounding each participant's residential community were assessed using the normalized difference vegetation index and the soiladjusted vegetation index from 2010. Lifetime CVD status (including myocardial infarction, heart failure, coronary heart disease, cerebral thrombosis, cerebral hemorrhage, cerebral embolism, and subarachnoid hemorrhage) was defined as a self-report of a physician diagnosis of CVD at the time of the survey. Cardiometabolic disorders, including hypertension, diabetes, dyslipidemia, and overweight or obese status, were measured and defined clinically. Generalized linear mixed models were used to evaluate the association between residential greenness levels and CVD prevalence. A 3-way decomposition method was used to explore whether the presence of cardiometabolic disorders mediated or modified the association between residential greenness and CVD. Data were analyzed from October 10 to May 30, 2020.

MAIN OUTCOMES AND MEASURES Lifetime CVD status, the presence of cardiometabolic disorders, and residential greenness level.

RESULTS Among 24 845 participants, the mean (SD) age was 45.6 (13.3) years, and 12 661 participants (51.0%) were men. A total of 1006 participants (4.1%) reported having a diagnosis of CVD. An interquartile range (1-IQR) increase in the normalized difference vegetation index within 500 m of a community was associated with a 27% lower likelihood (odds ratio [OR], 0.73; 95% CI, 0.65-0.83; *P* < .001) of CVD prevalence, and an IQR increase in the soil-adjusted vegetation index within 500 m of a community was associated with a 26% lower likelihood (OR, 0.74; 95% CI, 0.66-0.84; *P* < .001) of CVD prevalence. The presence of cardiometabolic disorders was found to mediate the association between residential greenness and CVD, with mediation effects of 4.5% for hypertension, 4.1% for type 2 diabetes, 3.1% for overweight or obese status, 12.7% for

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residential greenness, associated with cardiovascular disease among adults, and does the presence of cardiometabolic disorders mediate or modify the association between residential greenness and cardiovascular disease?

Question Is the general vegetation level

of a residential area, referred to as

Key Points

Findings In this cross-sectional study of 24 845 adults in China, residential areas with higher greenness levels were associated with a lower likelihood of cardiovascular disease. The presence of cardiometabolic disorders partially mediated the association between residential greenness and cardiovascular disease.

Meaning The study's findings may be helpful for health care professionals and policy makers in the development of strategies, such as planning for green spaces in residential areas, to mitigate the burden of cardiovascular disease.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Abstract (continued)

hypercholesterolemia, 8.7% for hypertriglyceridemia, and 11.1% for high low-density lipoprotein cholesterol levels.

CONCLUSIONS AND RELEVANCE In this cross-sectional study, higher residential greenness levels were associated with lower CVD prevalence, and this association may be partially mediated by the presence of cardiometabolic disorders. Further studies, preferably longitudinal, are warranted to confirm these findings.

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Introduction

Cardiovascular disease (CVD) remains the primary cause of death and disability worldwide, especially in low- and middle-income countries.¹ Between 1990 and 2016, the estimated number of individuals with CVD in China increased from 40.6 million to 93.8 million.² Interventions and control strategies are therefore needed to mitigate this increase in CVD prevalence.

Accumulating data indicate that a higher amount of neighborhood vegetation (referred to as residential greenness) is associated with a range of beneficial health outcomes.^{3,4} A large number of studies have examined the cardiovascular associations of greenness,⁵⁻³⁷ but more than 50% of those focused on CVD mortality. In addition, most of the previous studies were conducted in middle- and high-income countries, and only a few studies were performed in low-income countries.^{23,27,30,31} It is unclear if the results of studies from high-income countries are generalizable to lower-income settings because a number of cultural, sociodemographic, and environmental factors differ between high-income nations vs lower-income nations.

Cardiometabolic disorders, including hypertension, type 2 diabetes, overweight or obese status, and dyslipidemia, are documented preclinical factors associated with CVD risk.³⁸ In environmental epidemiologic studies, these cardiometabolic disorders have often been suggested as intervening variables in the association between environmental exposures and CVD. A systematic review and meta-analysis³ as well as previous findings from the 33 Communities Chinese Health Study³⁹⁻⁴¹ have indicated that higher residential greenness levels were associated with a lower risk of cardiometabolic disorders. Two studies within the past 5 years have reported that the presence of cardiometabolic disorders partially mediated the association between greenness and CVD prevalence.^{28,36} However, it is also plausible that the presence of cardiometabolic disorders may modify the health outcomes associated with residential greenness because individuals with these disorders may change their lifestyles (eg, engage in physical activity or visit parks more frequently) as part of a treatment plan. Therefore, the associations between residential greenness, cardiometabolic disorders, and CVD remain unclear. To address these research gaps, we aimed to (1) examine the association between residential greenness levels and CVD prevalence in a general population of Chinese adults and (2) explore whether the presence of cardiometabolic disorders mediated or modified the association between residential greenness levels and CVD using an advanced 3-way decomposition method.

Methods

Participants and Procedures

The 33 Communities Chinese Health Study, a large population-based cross-sectional investigation, was conducted in the Liaoning province of northeastern China between April 1 and December 31, 2009. The province is a large industrial center that is highly urbanized. The prevalence rates of CVD and cardiometabolic disorders have been reported to be high in this region.⁴²⁻⁴⁴ This study followed

the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies. The Human Studies Committee of Sun Yat-sen University approved the study protocols. All participants provided written informed consent.

We used a 4-stage stratified cluster sampling strategy to randomly recruit study participants³⁹⁻⁴¹ (**Figure**). First, 3 cities (Shenyang, Anshan, and Jinzhou) were randomly selected among 14 total cities in the Liaoning province. Second, 3 residential communities were randomly selected from each of the 11 total districts (5 districts in Shenyang and 3 districts each in Anshan and Jinzhou), generating 33 communities that ranged in size from 0.25 km² to 0.64 km². Third, 700 to 1000 households were randomly selected from each community. Fourth, 1 adult was randomly selected from each household. A total of 28 830 individuals were initially invited to participate in the study. Of those, 3985 individuals (13.8%) were excluded for the following reasons: (1) 3634 individuals did not complete the study questionnaire; (2) 233 individuals had resided in the study community for less than 5 years; (3) 79 individuals were pregnant; (4) 27 individuals were younger than 18 years or older than 74 years; and (5) 12 individuals had a serious preexisting disease, such as terminal cancer. After exclusions, 24 845 participants (86.2%) were included in the analysis, and 15 477 participants (53.7%) provided venous blood samples after fasting. Sociodemographic characteristics were similar between the participants who provided blood samples and the participants who did not (n = 9368) (eTable 2 in the Supplement).

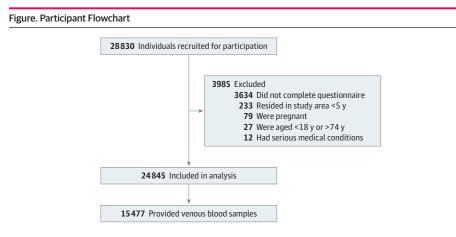
Cardiovascular Disease and Cardiometabolic Disorders

We assessed CVD status using a study questionnaire. A CVD case was defined as an affirmative response to the question: "Has a physician ever diagnosed you with myocardial infarction, heart failure, coronary heart disease, cerebral thrombosis, cerebral hemorrhage, cerebral embolism, or subarachnoid hemorrhage?"⁴⁵

Using a standard mercuric-column sphygmomanometer, trained and certified nurses measured systolic blood pressure and diastolic blood pressure according to procedures recommended by the American Heart Association.⁴⁶ We defined hypertension as mean systolic blood pressure higher than 140 mm Hg, mean diastolic blood pressure higher than 90 mm Hg, and/or reported receipt of antihypertensive medication in the 2 weeks before the interview.⁴⁷

Using protocols recommended by the World Health Organization,⁴⁸ we measured height and weight and calculated body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) for each participant. Based on Asian criteria,⁴⁸ obese status was defined as a BMI of 27.5 or higher, overweight status as a BMI of 23.0 to 27.5, and normal weight (including underweight) status as a BMI of less than 23.0.

After an overnight fast, peripheral venous blood samples were obtained. The levels of total cholesterol, triglycerides, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol were determined using a Hitachi Autoanalyzer, type 717OA (Hitachi). We defined



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hypercholesterolemia as a total cholesterol level of 240 mg/dL or higher, hypertriglyceridemia as a triglyceride level of 200 mg/dL or higher, low HDL cholesterol as an HDL cholesterol level of 40 mg/dL or higher, and high LDL cholesterol as an LDL cholesterol level of 160 mg/dL or higher.⁴⁹

We performed a standard 75-g oral glucose tolerance test and obtained blood samples at 0 hours and 2 hours after glucose intake. We measured fasting and 2-hour glucose levels using an enzymatic colorimetric method. Type 2 diabetes was defined based on American Diabetes Association guidelines as a fasting blood glucose level of 126 mg/dL or higher (to convert to mmol/L, multiply by 0.0555), a 2-hour glucose level of 200 mg/dL or higher, or the reported receipt of antidiabetic medication.⁵⁰

Residential Greenness Levels

We applied 2 satellite-based vegetation indices, the normalized difference vegetation index (NDVI)⁵¹ and the soil-adjusted vegetation index (SAVI),⁵² to characterize residential greenness levels. Both indices are derived based on the difference of surface reflectance and absorbance in 2 vegetation-informative light bands, visible red and near-infrared. The NDVI is calculated by subtracting visible red light from near-infrared light and dividing the difference by the sum of near-infrared light and visible red light. For SAVI, a correction factor was added to minimize factors associated with the soil background. Therefore, the SAVI was calculated by subtracting visible red light, and the correction factor; the dividend was then multiplied by the sum of the correction factor and 1.0. The resulting NDVI and SAVI values were unitless and ranged from -1.0 to 1.0, with higher values indicating greener areas, negative values indicating bodies of water, and values close to 0 indicating barren areas.

The 2 indices were calculated using Landsat 5 Thematic Mapper (National Aeronautics and Space Administration) satellite images at a spatial resolution of 30 m by 30 m, which were obtained during the greenest month (ie, August, which has the highest level of growing vegetation) and the year closest to the collection of health data (ie, 2010). Residential greenness was defined as the mean NDVI and SAVI levels in circular buffers of 500 m and 1000 m around each community's centroid. Greenness level was defined using the NDVI, with low greenness level defined as less than 0.40 m of vegetation per 500 m, and high greenness level defined as 0.40 m or more of vegetation per 500 m. All calculations were performed using ArcGIS, version 10.4 (Esri).

Confounding and Mediating Factors

We developed a directed acyclic graph to select confounding variables and potential mediating factors using the DAGitty package, version 2.16.3 for R software (R Foundation for Statistical Computing) (eFigure 1 in the Supplement). The following confounding variables were retained: age, sex, ethnicity, annual mean household income, educational level, physical activity level, district-level gross domestic product,³⁹ and particulate matter with an aerodynamic diameter of 2.5 µm or less.⁵³

Cardiometabolic disorders were selected as potential mediating factors (eFigure 1 in the Supplement). We developed an additional directed acyclic graph to identify potential confounding variables of exposure-mediator associations (eFigure 2 in the Supplement) and mediator-outcome associations (eFigure 3 in the Supplement). We incorporated the common confounding variables (ie, age, sex, ethnicity, household income, educational level, physical activity level, district-level gross domestic product, and particulate matter with an aerodynamic diameter of 2.5 µm or less) into the mediation analysis.

Statistical Analysis

We used generalized linear mixed models⁵⁴ to assess the association between residential greenness levels and CVD prevalence, with communities considered a random effect. The effect estimates were expressed as odds ratios (ORs) and 95% CIs per interquartile range (IQR) increase in NDVI and SAVI levels. We estimated unadjusted models and main models that were adjusted for the confounding variables selected using the directed acyclic graph (including age, sex, ethnicity, household income,

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educational level, physical activity level, district-level gross domestic product, and particulate matter with an aerodynamic diameter of 2.5 µm or less) (eFigure 1 in the Supplement). Informed by findings from previous studies, ^{55,56} we focused on a 500-m exposure buffer for the main analysis.

We also performed several sensitivity analyses. First, we estimated NDVI and SAVI levels in a larger exposure buffer of 1000 m to assess the impact of exposure misclassification. Second, we categorized NDVI and SAVI levels per 500 m into quartiles (for NDVI levels, quartile 1 comprised 0.18-0.23, quartile 2 comprised 0.24-0.29, quartile 3 comprised 0.30-0.40, and quartile 4 comprised 0.41-0.80; for SAVI levels, quartile 1 comprised 0.10-0.13, quartile 2 comprised 0.14-0.16, quartile 3 comprised 0.17-0.24, and quartile 4 comprised 0.25-0.48), and we used a natural spline-smoothing function to test for nonlinear associations. Third, we built models using sequential adjustments, and we adjusted the main models for alcohol consumption, cigarette smoking, physical activity level, controlled diet with low calories and low fat, consumption of sugar-sweetened soft drinks, and family history of CVD to assess their potential impact. We performed stratified analyses by age (<50 years vs \geq 50 years), sex, annual household income (<10 000 yuan vs \geq 10 000 yuan [\$1 was equivalent to 6.84 yuan in 2009]), and educational level (<9 years vs \geq 9 years) to examine whether the associations were consistent among different subpopulations.

We used a 3-way decomposition method to apportion the association between residential greenness and each cardiometabolic disorder with which the greenness level may have interacted with CVD prevalence. The 3 nonoverlapping components included (1) variables associated with greenness that were directly controlled for potential mediating factors (direct effect), (2) variables associated with additive interaction but not mediation (interactive effect), and (3) variables associated with mediation but not interaction (pure indirect effect) (eFigure 4 in the Supplement).⁵⁷ Standard errors were calculated using the delta method.⁵⁸ We also estimated the mediation effect of combined cardiometabolic disorders using the lavaan package, version 3.4.3 for R software (R Foundation for Statistical Computing). All other statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc). All tests were 2-tailed and paired, with a significance threshold of P < .05.

Results

Among 24 845 adult participants, the mean (SD) age was 45.6 (13.3) years, and 12 661 participants (51.0%) were men (Table 1). Most of the participants (94.5%) were of Han ethnicity and had a high educational level (78.0% of participants had >9 years of education) and high household income (76.8% of participants had a mean household income of >10 000 yuan per year). A total of 1006 participants (4.1%) reported having a diagnosis of CVD. Participants with CVD were more likely to be male (743 participants [73.9%]), 50 years or older (749 participants [75.5%]), of Han ethnicity (980 participants [97.4%]), have an educational level of 9 years or less (836 participants [93.1%]), and have an annual household income of more than 10 000 yuan (640 participants [63.6%]) (eTable 3 in the Supplement). Participants living in communities with higher greenness levels were more likely to be female (3106 participants [59.4%]), younger than 50 years (3662 participants [70.0%]), have an educational level of 9 years or less (3932 participants [75.2%]), have an annual household income of more than 10 000 yuan (4193 participants [80.2%]), exercise less than 180 minutes per week (3547 participants [67.8%]), and live in communities with lower concentrations of particulate matter with an aerodynamic diameter of 2.5 µm or less (71 participants [30.5%]). The prevalence of cardiometabolic disorders ranged from 1333 participants (8.6%) with high LDL cholesterol to 15 459 participants (62.2%) with overweight or obese status.

Greenness levels varied across the communities. For instance, NDVI levels per 500 m ranged from 0.18 to 0.80, with a median of 0.29 (IQR, 0.23-0.40), and SAVI levels per 500 m ranged from 0.10 to 0.48, with a median of 0.16 (IQR, 0.13-0.24) (eTable 4 in the Supplement). In addition, NDVI levels were consistent with SAVI levels. For example, the lowest Spearman correlation coefficient was 0.88 for the correlation between NDVI levels per 500 m and SAVI levels per 1000 m, and the

highest Spearman correlation coefficient was 0.98 for the correlation between NDVI levels per 500 m and SAVI levels per 500 m (eTable 4 in the Supplement).

In the adjusted models, an IQR increase in both NDVI and SAVI levels per 500 m was associated with a lower likelihood of CVD prevalence, with ORs of 0.73 (95% CI, 0.65-0.83; *P* < .001) for NDVI levels and 0.74 (95% CI, 0.66-0.84; *P* < .001) for SAVI levels (**Table 2**). Similar results were observed for NDVI levels per 1000 m (OR, 0.79; 95% CI, 0.71-0.89; *P* < .001) and SAVI levels per 1000 m (OR, 0.78; 95% CI, 0.69-0.87; *P* < .001). The effect estimates were similar to those of the main models

Table 1. Participant Characteristics					
	No. (%)				
		Residential greenness level			
Characteristic	Total	Low ^a	High ^a		
Total participants	24845 (100)	19616 (79.0)	5229 (21.0)		
Age, y					
<50	15 503 (62.4)	11 841 (60.4)	3662 (70.0)		
≥50	9342 (37.6)	7775 (39.6)	1567 (30.0)		
Sex					
Male	12 661 (51.0)	10 538 (53.7)	2123 (40.6)		
Female	12 184 (49.0)	9078 (46.3)	3106 (59.4)		
Ethnicity					
Han	23 470 (94.5)	18 552 (94.6)	4918 (94.1)		
Other	1375 (5.5)	1064 (5.4)	311 (5.9)		
Educational level, y					
≤9	19 370 (78.0)	15 438 (78.7)	3932 (75.2)		
>9	5475 (22.0)	4178 (21.3)	1297 (24.8)		
Annual household income, yuan ^b					
≤10 000	5761 (23.2)	4725 (24.1)	1036 (19.8)		
>10 000	19084 (76.8)	14891 (75.9)	4193 (80.2)		
Physical activity ≥180 min/wk					
Yes	7647 (30.8)	5965 (30.4)	1682 (32.2)		
No	17 198 (69.2)	13 651 (69.6)	3547 (67.8)		
District-level per capita GDP, median (IQR), yuan ^b	70 352 (47 639-100 423)	70 352 (47 639-100 423)	74 266 (25 561-100 423)		
PM $\leq 2.5 \ \mu m/m^3$, median (IQR), $\mu g/m^3$	73.00 (71.00-97.00)	72.82 (72.26-97.74)	70.97 (63.87-94.39)		
Cardiometabolic disorder					
Hypertension	8657 (34.8)	7099 (36.2)	1558 (29.8)		
Overweight/obese	15 459 (62.2)	12 473 (63.6)	2986 (57.1)		
Type 2 diabetes	1694 (10.9) ^c	1429 (11.5) ^d	265 (8.8) ^e		
Hypercholesterolemia	1717 (11.1) ^c	1456 (11.7) ^d	261 (8.7) ^e		
Hypertriglyceridemia	3494 (22.6) ^c	2931 (23.5) ^d	563 (18.7) ^e		
Low HDL cholesterol	2836 (18.3) ^c	2400 (19.3) ^d	436 (14.5) ^e		
High LDL cholesterol	1333 (8.6) ^c	1147 (9.2) ^d	186 (6.2) ^e		
Cardiovascular disease ^f	1006 (4.1)	871 (4.4)	135 (2.6)		

Abbreviations: GDP, gross domestic product; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; PM, particulate matter.

^a Greenness level was based on normalized difference vegetation index values. Low greenness level was defined as less than 0.40 m of vegetation per 500 m, and high greenness level was defined as 0.40 m or more of vegetation per 500 m.

^b \$1.00 was equivalent to 6.84 yuan in 2009.

^c Based on 15 477 participants.

^d Based on 12 470 participants.

^e Based on 3007 participants.

^f A total of 417 participants had heart disease, 529 participants had stroke, and 60 participants had heart disease and stroke.

Table 2. Association Between Residential Greenness Measures and Cardiovascular Disease Prevalence

Greenness measure ^a	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI) ^b	P value
NDVI per 500 m	0.57 (0.51-0.64)	<.001	0.73 (0.65-0.83)	<.001
NDVI per 1000 m	0.63 (0.57-0.70)	<.001	0.79 (0.71-0.89)	<.001
SAVI per 500 m	0.58 (0.51-0.65)	<.001	0.74 (0.66-0.84)	<.001
SAVI per 1000 m	0.62 (0.56-0.69)	<.001	0.78 (0.69-0.87)	<.001

Abbreviations: NDVI, normalized difference vegetation index; OR, odds ratio; SAVI, soil-adjusted vegetation index.

^a Greenness level per interquartile range increase.

^b Adjusted for age, sex, ethnicity, household income, educational level, district-level gross domestic product, physical activity level, and air pollution level.

when we adjusted for alcohol use (for NDVI: OR, 0.74; 95% CI, 0.65-0.83; P < .001; for SAVI: OR, 0.74; 95% CI, 0.66-0.84; P < .001), cigarette smoking (for NDVI: OR, 0.73; 95% CI, 0.64-0.86; P < .001; for SAVI: OR, 0.73; 95% CI, 0.65-0.83; P < .001), low-calorie and low-fat diet (for NDVI: OR, 0.73; 95% CI, 0.65-0.82; P < .001; for SAVI: OR, 0.73; 95% CI, 0.65-0.83; P < .001), low-calorie and low-fat diet (for NDVI: OR, 0.73; 95% CI, 0.65-0.82; P < .001; for SAVI: OR, 0.73; 95% CI, 0.65-0.83; P < .001), consumption of sugar-sweetened soft drinks (for NDVI: OR, 0.73; 95% CI, 0.64-0.82; P < .001; for SAVI: OR, 0.73; 95% CI, 0.65-0.83; P < .001), and family history of CVD (for NDVI: OR, 0.73; 95% CI, 0.65-0.82; P < .001; for SAVI: OR, 0.74; 95% CI, 0.65-0.83; P < .001) and when we incorporated sequential adjustments (eg, in model 1, which was adjusted for age, sex, ethnicity, and community size, the OR for NDVI was 0.71; 95% CI, 0.63-0.80; P < .001; for SAVI, 0.72; 95% CI, 0.64-0.81; P < .001) (eTable 5 in the Supplement).

We found similar linear dose-response patterns when using NDVI and SAVI levels per 500 m categorized into quartiles (eg, for quartile 2, the adjusted OR for NDVI was 1.03; 95% CI, 0.86-1.23; for quartile 3, the adjusted OR for NDVI was 0.66; 95% CI, 0.55-0.80; for quartile 4, the adjusted OR for NDVI was 0.63; 95% CI, 0.50-0.79; with P < .001 for trend) (eTable 6 in the Supplement) and when using a restrictive cubic spline analysis (for NDVI, P for nonlinear association = 0.74; for SAVI, P for nonlinear association = 0.62) (eFigure 5 in the Supplement). We found no significant interaction by age, sex, household income, or educational level (eTable 7 in the Supplement).

The mediation analyses examining the association between NDVI level per 500 m and CVD prevalence indicated mediation effects of 4.5% (95% CI, 0.6%-8.3%; P = .02) for hypertension, 3.1% (95% CI, 1.1%-5.1%; P = .002) for overweight or obese status, 4.1% (95% CI, 0.7%-7.4%; P = .02) for type 2 diabetes, 12.7% (95% CI, 4.6%-20.8%; P = .002) for hypercholesterolemia, 8.7% (95% CI, 2.9%-14.4%; P = .003) for hypertriglyceridemia, and 11.1% (95% CI, 3.8%-18.4%; P = .003) for high LDL cholesterol. No significant mediation effect was found for low HDL cholesterol (1.9%; 95% CI, -0.3% to 4.0%; P = .004) of the association between NDVI level per 500 m and CVD prevalence (eTable 8 in the Supplement). Similar results were obtained when we used SAVI level per 500 m as the exposure measure, with a significant mediation effect for all cardiometabolic disorders (eg, for hypercholesterolemia, 13.0%; 95% CI, 5.0%-21.0%; P = .001) with the exception of low HDL cholesterol (2.0%; 95% CI, -0.2% to 4.2%; P = .08). No significant interactive effect was found between residential greenness and any cardiometabolic disorder (Table 3).

Table 3. Association Between Residential Greenness, Cardiometabolic Disorders, and Cardiovascular Disease Prevalence

			Decomposition method, % (95% CI) ^a					
Exposure	Potential mediator	Participants, No.	Mediation effect	P value	Interactive effect	P value	Direct effect	P value
NDVI per 500 m	Hypertension	24 845	4.5 (0.6 to 8.3)	.02	7.0 (-18.4 to 32.4)	.59	88.5 (62.9 to 114.1)	<.001
	Type 2 diabetes	15 477	4.1 (0.7 to 7.4)	.02	-5.5 (-19.4 to 8.5)	.44	101.4 (86.4 to 116.4)	<.001
	Overweight/obese	24845	3.1 (1.1 to 5.1)	.002	38.1 (-6.6 to 82.7)	.10	58.8 (13.2 to 104.4)	.01
	Hypercholesterolemia	15 477	12.7 (4.6 to 20.8)	.002	-4.8 (-26.9 to 17.2)	.67	92.1 (68.9 to 125.4)	<.001
	Hypertriglyceridemia	15 477	8.7 (2.9 to 14.4)	.003	-0.8 (-32.4 to 30.7)	.96	92.2 (59.6 to 124.7)	<.001
	Low HDL cholesterol	15 477	1.9 (-0.3 to 4.0)	.09	-27.7 (-58.9 to 3.4)	.08	125.9 (94.7 to 157.1)	<.001
	High LDL cholesterol	15 477	11.1 (3.8 to 18.4)	.003	-7.2 (-25.3 to 10.8)	.43	96.1 (76.9 to 115.4)	<.001
SAVI per 500 m	Hypertension	24845	5.1 (1.2 to 9.0)	.01	9.3 (-15.3 to 33.9)	.46	85.6 (60.6 to 110.6)	<.001
	Type 2 diabetes	15 477	4.3 (0.9 to 7.7)	.01	-3.3 (-16.4 to 9.7)	.62	99.0 (84.7 to 113.4)	<.001
	Overweight/obese	24845	3.0 (1.1 to 5.0)	.002	41.9 (-2.8 to 86.6)	.07	55.0 (9.4 to 100.7)	.02
	Hypercholesterolemia	15 477	13.0 (5.0 to 21.0)	.001	-1.1 (-21.4 to 19.3)	.92	88.0 (65.7 to 110.3)	<.001
	Hypertriglyceridemia	15 477	8.1 (2.8 to 13.4)	.003	2.3 (-26.7 to 31.3)	.88	89.6 (59.4 to 119.)	<.001
	Low HDL cholesterol	15 477	2.0 (-0.2 to 4.2)	.08	-22.0 (-50.4 to 6.4)	.13	120.0 (91.3 to 148.7)	<.001
	High LDL cholesterol	15 477	11.6 (4.2 to 18.9)	.002	-4.1 (-20.7 to 12.5)	.63	92.5 (74.0 to 111.1)	<.001

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; NDVI, normalized difference vegetation index; SAVI, soil-adjusted vegetation index.

^a Adjusted for age, sex, ethnicity, household income, educational level, district-level gross domestic product, physical activity level, and air pollution level.

Discussion

In this study, we found that participants living in greener communities had a lower likelihood of receiving a diagnosis of CVD. The association between residential greenness and CVD was robust in a series of sensitivity analyses. The presence of cardiometabolic disorders (with the exception of low HDL cholesterol) partially mediated the association between residential greenness levels and CVD prevalence.

Many previous studies have documented an association between greenness levels and CVD (eTable 1 in the Supplement),⁵⁻³⁷ which is consistent with our current findings. For example, a crosssectional study of 11 404 Australian adults reported that higher neighborhood greenness levels (measured as the mean NDVI level per 1600 m) and variability (measured as the SD of the NDVI level per 1600 m) were associated with a lower prevalence of heart disease or stroke.¹³ Another crosssectional study of Chinese adults reported a substantial reduction in the likelihood of coronary heart disease and stroke among populations residing in areas with higher NDVI levels.³⁰ Similar results were reported by cross-sectional studies from the US,³⁶ Israel,²⁸ New Zealand,¹⁴ and Brazil.²³

Although our study was cross-sectional and used NDVI levels to estimate exposure, our findings may support those from 2 prospective cohort studies^{15,32} that used different green space measures and 1 natural experiment study.¹⁸ The first cohort study followed up 5112 Lithuanian adults for 4.4 years. The investigators found that a greater distance from green spaces was associated with an increased risk of CVD.¹⁵ The second cohort study found that a larger tree canopy percentage was associated with a lower risk of incident CVD among 46 786 Australian adults.³² In the natural experiment study, Donovan et al²¹ analyzed longitudinal data from 156 146 women and examined the association between the loss of trees owing to an invasive forest pest and incident CVD. They reported that women living in areas with greater tree loss had an increased risk of CVD.²¹

We observed that all of the explored cardiometabolic disorders (with the exception of low HDL cholesterol) substantially mediated the association between residential greenness and CVD prevalence, indicating that the disorders might be involved in the pathways by which greenness is associated with CVD. Our findings were consistent with those of a US study,³⁶ which found that the associations between NDVI levels and CVD were attenuated when regression models were adjusted for the presence of hypertension, type 2 diabetes, and dyslipidemia. Partially consistent with our findings, another study reported that the association of myocardial infarction with NDVI levels was partially mediated by the presence of dyslipidemia and type 2 diabetes but not hypertension.²⁸ Combined with our findings, the data extended our understanding of potential biological mechanisms underlying the association between residential greenness and CVD prevalence. Because cardiometabolic disorders are reported to be precursors to clinical CVD, the results of our mediation analysis suggest that future research and health care decisions that focus on the association of greenness with these earlier disorders may be useful for reducing future CVD events.

An earlier study suggested several pathways, such as reduction in air pollution and heat, encouragement of physical activity, increases in social cohesion, and decreases in mental fatigue and stress,⁵⁹ to explain the association between greenness and health. However, accumulating data do not provide support for an association between substantial air pollution reductions or increases in physical activity and a greater number of urban greenness areas.^{60,61} Because data on social cohesion and mental health were not available for our study, we did not investigate those potential factors. Future studies are needed to explore potential mechanisms, preferably through the inclusion of more mediators and the performance of serial mediation tests.

To our knowledge, this is one of a few epidemiologic studies to report an association between residential greenness and CVD in a low- or middle-income country. Our results may have public health importance, especially considering the fact that many low-income countries are experiencing rapid urbanization and subsequent decreases in greenness. A major strength of our study is its large population-based sample, which was randomly selected from communities across 3 different cities, and its high response rate, which minimized selection bias and provided sufficient statistical power

to detect modest effects. In addition, we used 2 greenness exposure measures and 2 different exposure buffers, and we adjusted for a parsimonious yet comprehensive set of covariates to control confounding without overadjustment. Furthermore, we performed mediation analyses using a 3-way decomposition method, which incorporates interactive effects and typically provides greater validity and higher statistical power than traditional approaches.⁵⁷

Limitations

This study has several limitations. First, the cross-sectional design did not allow us to assess temporality between greenness exposure and CVD, although the likelihood of reverse-association is low. In addition, the cross-sectional design may have overestimated the mediation effects.⁶² Second, we assessed greenness exposure based on communities and not individuals, which might have produced measurement error (ie, Berkson error⁶³). Although this error did not bias our effect estimates, it could have reduced statistical power. In addition, we have not specifically collected data on limited mobility. Third, although we objectively measured greenness exposure using NDVI and SAVI levels, these 2 measures reflect general vegetation levels and cannot differentiate the structure, type, and quality of greenness. Thus, we were unable to examine aspects of greenness that are most relevant to CVD prevalence.

Fourth, data on antidyslipidemia medication receipt were not available and were not used to define dyslipidemia, which might have reduced the prevalence of dyslipidemia and biased the results of our mediation analysis. Fifth, CVD diagnosis and several potential confounding variables were self-reported; therefore, false-positive findings and recall bias are possible. In addition, we assessed socioeconomic status using a limited number of variables, and other environmental factors, such as noise, walkability, and air temperature, were not considered in our model; thus, our results might have been affected by residual confounding.

Conclusions

Higher community greenness levels were associated with a lower likelihood of CVD prevalence in an industrial and highly urbanized setting within China. The association might be partly mediated by the presence of cardiometabolic disorders. Although the findings require confirmation in longitudinal studies, they contribute to the limited data available to policy makers who are interested in designing population-level interventions to mitigate the prevalence of CVD in China and other low- and middle-income countries.

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REFERENCES

1. World Health Organization. Cardiovascular diseases (CVDs): key facts. World Health Organization. Published May 17, 2017. Accessed December 5, 2019. https://www.who.int/mediacentre/factsheets/fs317/en/

2. Liu S, Li Y, Zeng X, et al. Burden of cardiovascular diseases in China, 1990-2016: findings from the 2016 Global Burden of Disease study. *JAMA Cardiol*. 2019;4(4):342-352. doi:10.1001/jamacardio.2019.0295

3. Twohig-Bennett C, Jones A. The health benefits of the great outdoors: a systematic review and meta-analysis of greenspace exposure and health outcomes. *Environ Res.* 2018;166:628-637. doi:10.1016/j.envres.2018.06.030

4. Fong KC, Hart JE, James P. A review of epidemiologic studies on greenness and health: updated literature through 2017. *Curr Environ Health Rep.* 2018;5(1):77-87. doi:10.1007/s40572-018-0179-y

5. Hu Z, Liebens J, Rao KR. Linking stroke mortality with air pollution, income, and greenness in northwest Florida: an ecological geographical study. *Int J Health Geogr.* 2008;7:20. doi:10.1186/1476-072X-7-20

6. Mitchell R, Popham F. Effect of exposure to natural environment on health inequalities: an observational population study. *Lancet*. 2008;372(9650):1655-1660. doi:10.1016/S0140-6736(08)61689-X

7. Maas J, Verheij RA, de Vries S, Spreeuwenberg P, Schellevis FG, Groenewegen PP. Morbidity is related to a green living environment. *J Epidemiol Community Health*. 2009;63(12):967-973. doi:10.1136/jech.2008.079038

8. Richardson E, Pearce J, Mitchell R, Day P, Kingham S. The association between green space and cause-specific mortality in urban New Zealand: an ecological analysis of green space utility. *BMC Public Health*. 2010;10:240. doi: 10.1186/1471-2458-10-240

9. Dominguez-Berjon MF, Gandarillas A, Segura del Pozo J, et al. Census tract socioeconomic and physical environment and cardiovascular mortality in the region of Madrid (Spain). *J Epidemiol Community Health*. 2010; 64(12):1086-1093. doi:10.1136/jech.2008.085621

10. Coutts C, Horner M, Chapin T. Using geographical information system to model the effects of green space accessibility on mortality in Florida. *Geocarto Int*. 2010; 25(6): 471-484. doi:10.1080/10106049.2010.505302

11. Richardson EA, Mitchell R. Gender differences in relationships between urban green space and health in the United Kingdom. *Soc Sci Med.* 2010;71(3):568-575. doi:10.1016/j.socscimed.2010.04.015

12. Richardson EA, Mitchell R, Hartig T, de Vries S, Astell-Burt T, Frumkin H. Green cities and health: a question of scale? J Epidemiol Community Health. 2012;66(2):160-165. doi:10.1136/jech.2011.137240

13. Pereira G, Foster S, Martin K, et al. The association between neighborhood greenness and cardiovascular disease: an observational study. *BMC Public Health*. 2012;12:466. doi:10.1186/1471-2458-12-466

14. Richardson EA, Pearce J, Mitchell R, Kingham S. Role of physical activity in the relationship between urban green space and health. *Public Health*. 2013;127(4):318-324. doi:10.1016/j.puhe.2013.01.004

15. Tamosiunas A, Grazuleviciene R, Luksiene D, et al. Accessibility and use of urban green spaces, and cardiovascular health: findings from a Kaunas cohort study. *Environ Health*. 2014;13(1):20. doi:10.1186/1476-069X-13-20

16. Lachowycz K, Jones AP. Does walking explain associations between access to greenspace and lower mortality? *Soc Sci Med.* 2014;107(100):9-17. doi:10.1016/j.socscimed.2014.02.023

17. Wilker EH, Wu C-D, McNeely E, et al. Green space and mortality following ischemic stroke. *Environ Res.* 2014; 133:42-48. doi:10.1016/j.envres.2014.05.005

18. Donovan GH, Butry DT, Michael YL, et al. The relationship between trees and human health: evidence from the spread of the emerald ash borer. *Am J Prev Med*. 2013;44(2):139-145. doi:10.1016/j.amepre.2012.09.066

19. Bixby H, Hodgson S, Fortunato L, Hansell A, Fecht D. Associations between green space and health in English cities: an ecological, cross-sectional study. *PLoS One*. 2015;10(3):e0119495. doi:10.1371/journal.pone.0119495

20. Chum A, O'Campo P. Cross-sectional associations between residential environmental exposures and cardiovascular diseases. *BMC Public Health*. 2015;15:438. doi:10.1186/s12889-015-1788-0

21. Donovan GH, Michael YL, Gatziolis D, Prestemon JP, Whitsel EA. Is tree loss associated with cardiovasculardisease risk in the Women's Health Initiative? a natural experiment. *Health Place*. 2015;36:1-7. doi:10.1016/j. healthplace.2015.08.007

22. James P, Hart JE, Banay RF, Laden F. Exposure to greenness and mortality in a nationwide prospective cohort study of women. *Environ Health Perspect*. 2016;124(9):1344-1352. doi:10.1289/ehp.1510363

23. Massa KHC, Pabayo R, Lebrao ML, Chiavegatto Filho ADP. Environmental factors and cardiovascular diseases: the association of income inequality and green spaces in elderly residents of Sao Paulo, Brazil. *BMJ Open*. 2016;6 (9):e011850. doi:10.1136/bmjopen-2016-011850

24. Ngom R, Gosselin P, Blais C, Rochette L. 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*. 2016;13(4):423. doi:10.3390/ijerph13040423

25. Picavet HSJ, Milder I, Kruize H, de Vries S, Hermans T, Wendel-Vos W. Greener living environment healthier people?: exploring green space, physical activity and health in the Doetinchem cohort study. *Prev Med*. 2016; 89:7-14. doi:10.1016/j.ypmed.2016.04.021

26. Vienneau D, de Hoogh K, Faeh D, Kaufmann M, Wunderli JM, Roosli M; SNC Study Group. More than clean air and tranquillity: residential green is independently associated with decreasing mortality. *Environ Int*. 2017;108: 176-184. doi:10.1016/j.envint.2017.08.012

27. Wang D, Lau KK-L, Yu R, Wong SYS, Kwok TTY, Woo J. Neighbouring green space and mortality in communitydwelling elderly Hong Kong Chinese: a cohort study. *BMJ Open*. 2017;7(7):e015794. doi:10.1136/bmjopen-2016-015794

28. Yitshak-Sade M, Kloog I, Novack V. Do air pollution and neighborhood greenness exposures improve the predicted cardiovascular risk? *Environ Int*. 2017;107:147-153. doi:10.1016/j.envint.2017.07.011

29. Crouse DL, Pinault L, Balram A, et al. Urban greenness and mortality in Canada's largest cities: a national cohort study. *Lancet Planet Health*. 2017;1(7):e289-e297. doi:10.1016/S2542-5196(17)30118-3

30. Jia X, Yu Y, Xia W, et al. Cardiovascular diseases in middle aged and older adults in China: the joint effects and mediation of different types of physical exercise and neighborhood greenness and walkability. *Environ Res.* 2018;167:175-183. doi:10.1016/j.envres.2018.07.003

31. da Silveira IH, Junger WL. Green spaces and mortality due to cardiovascular diseases in the city of Rio de Janeiro. *Rev Saude Publica*. 2018;52:49.

32. Astell-Burt T, Feng X. Urban green space, tree canopy and prevention of cardiometabolic diseases: a multilevel longitudinal study of 46 786 Australians. *Int J Epidemiol*. 2020;49(3):926-933. doi:10.1093/ije/dyz239

33. Orioli R, Antonucci C, Scortichini M, et al. Exposure to residential greenness as a predictor of cause-specific mortality and stroke incidence in the Rome longitudinal study. *Environ Health Perspect*. 2019;127(2):27002. doi: 10.1289/EHP2854

34. Kim S, Kim H, Lee J-T. Interactions between ambient air particles and greenness on cause-specific mortality in seven Korean metropolitan cities, 2008-2016. *Int J Environ Res Public Health*. 2019;16(10):1866. doi:10.3390/ ijerph16101866

35. Servadio JL, Lawal AS, Davis T, et al. Demographic inequities in health outcomes and air pollution exposure in the Atlanta area and its relationship to urban infrastructure. *J Urban Health*. 2019;96(2):219-234. doi:10.1007/s11524-018-0318-7

36. Wang K, Lombard J, Rundek T, et al. Relationship of neighborhood greenness to heart disease in 249 405 US Medicare beneficiaries. *J Am Heart Assoc.* 2019;8(6):e010258. doi:10.1161/JAHA.118.010258

37. Zijlema WL, Stasinska A, Blake D, et al. The longitudinal association between natural outdoor environments and mortality in 9218 older men from Perth, Western Australia. *Environ Int*. 2019;125:430-436. doi:10.1016/j. envint.2019.01.075

38. Forouzanfar MH, Alexander L, Anderson HR, et al; GBD 2013 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease study 2013. *Lancet*. 2015;386(10010):2287-2323. doi:10.1016/S0140-6736(15)00128-2

39. Yang B-Y, Markevych I, Bloom MS, et al. Community greenness, blood pressure, and hypertension in urban dwellers: the 33 Communities Chinese Health Study. *Environ Int*. 2019;126:727-734. doi:10.1016/j.envint.2019. 02.068

40. Yang B-Y, Markevych I, Heinrich J, et al. Residential greenness and blood lipids in urban-dwelling adults: the 33 Communities Chinese Health Study. *Environ Pollut*. 2019;250:14-22. doi:10.1016/j.envpol.2019.03.128

41. Yang B-Y, Markevych I, Heinrich J, et al. Associations of greenness with diabetes mellitus and glucosehomeostasis markers: the 33 Communities Chinese Health Study. *Int J Hyg Environ Health*. 2019;222(2):283-290. doi:10.1016/j.ijheh.2018.12.001

42. Wang W, Jiang B, Sun H, et al; NESS-China Investigators. Prevalence, incidence, and mortality of stroke in China: results from a nationwide population-based survey of 480 687 adults. *Circulation*. 2017;135(8):759-771. doi:10.1161/CIRCULATIONAHA.116.025250

43. Li Y, Wang L, Feng X, et al. Geographical variations in hypertension prevalence, awareness, treatment and control in China: findings from a nationwide and provincially representative survey. *J Hypertens*. 2018;36(1): 178-187. doi:10.1097/HJH.00000000001531

44. Zhang L, Wang Z, Wang X, et al; China Hypertension Survey Investigators. Prevalence of abdominal obesity in China: results from a cross-sectional study of nearly half a million participants. *Obesity (Silver Spring)*. 2019;27(11): 1898-1905. doi:10.1002/oby.22620

45. Qin X-D, Qian Z, Vaughn MG, et al. Gender-specific differences of interaction between obesity and air pollution on stroke and cardiovascular diseases in Chinese adults from a high pollution range area: a large population based cross sectional study. *Sci Total Environ*. 2015;529:243-248. doi:10.1016/j.scitotenv.2015.05.041

46. Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Circulation*. 2005;111(5):697-716. doi:10.1161/01.CIR.0000154900.76284.F6

47. Chobanian AV, Bakris GL, Black HR, et al; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42(6):1206-1252. doi:10.1161/01.HYP.0000107251.49515.c2

48. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363(9403):157-163. doi:10.1016/S0140-6736(03)15268-3

49. Joint Committee for Developing Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults. [Chinese guidelines on prevention and treatment of dyslipidemia in adults]. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2007;35(5):390-419.

50. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014; 37(suppl 1):S81-S90. doi:10.2337/dc14-S081

51. Tucker CJ. Red and photographic infrared linear combinations for monitoring vegetation. *Remote Sens Environ*. 1979;8(2):127-150. doi:10.1016/0034-4257(79)90013-0

52. Huete AR. A soil-adjusted vegetation index (SAVI). *Remote Sens Environ*. 1988;25(3):295-309. doi:10.1016/ 0034-4257(88)90106-X

53. Chen G, Li S, Knibbs LD, et al. A machine learning method to estimate PM_{2.5} concentrations across China with remote sensing, meteorological and land use information. *Sci Total Environ*. 2018;636:52-60. doi:10.1016/j. scitotenv.2018.04.251

54. Wong GY, Mason WM. The hierarchical logistic regression model for multilevel analysis. *J Am Stat Assoc*. 1985; 80(391):513-524. doi:10.1080/01621459.1985.10478148

55. Dadvand P, Villanueva CM, Font-Ribera L, et al. Risks and benefits of green spaces for children: a crosssectional study of associations with sedentary behavior, obesity, asthma, and allergy. *Environ Health Perspect*. 2014;122(12):1329-1335. doi:10.1289/ehp.1308038

56. Markevych I, Tiesler CMT, Fuertes E, et al. Access to urban green spaces and behavioural problems in children: results from the GINIplus and LISAplus studies. *Environ Int.* 2014;71:29-35. doi:10.1016/j.envint.2014.06.002

57. VanderWeele TJ. A three-way decomposition of a total effect into direct, indirect, and interactive effects. *Epidemiology*. 2013;24(2):224-232. doi:10.1097/EDE.0b013e318281a64e

58. VanderWeele TJ, Vansteelandt S. Conceptual issues concerning mediation, interventions and compositions. *Stat Interface*. 2009;2(4):457-468. doi:10.4310/SII.2009.v2.n4.a7

59. Markevych I, Schoierer J, Hartig T, et al. Exploring pathways linking greenspace to health: theoretical and methodological guidance. *Environ Res.* 2017;158:301-317. doi:10.1016/j.envres.2017.06.028

60. Kumar P, Druckman A, Gallagher J, et al. The nexus between air pollution, green infrastructure and human health. *Environ Int*. 2019;133(pt A):105181. doi:10.1016/j.envint.2019.105181

61. Persson A, Moller J, Engstrom K, Sundstrom ML, Nooijen CFJ. Is moving to a greener or less green area followed by changes in physical activity? *Health Place*. 2019;57:165-170. doi:10.1016/j.healthplace.2019.04.006

62. Maxwell SE, Cole DA, Mitchell MA. Bias in cross-sectional analyses of longitudinal mediation: partial and complete mediation under an autoregressive model. *Multivariate Behav Res*. 2011;46(5):816-841. doi:10.1080/00273171.2011.606716

63. Keogh RH, Shaw PA, Gustafson P, et al. STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: part 1–basic theory and simple methods of adjustment. *Stat Med.* 2020;39(16):2197-2231. doi:10.1002/sim.8532

SUPPLEMENT.

eTable 1. Previous Human Epidemiological Studies of Greenness Exposure and CVD Mortality and Morbidity

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