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Long-term exposure to residential greenness and cardiovascular disease and all-cause mortality in China

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Abstract

Background Influence of residential greenness on CVD risk has garnered increasing attention, however, evidence from large-scale cohort studies in developing nations, such as China, remains sparse. This study aimed to evaluate the association of residential greenness with CVD and mortality, and explore the potential mediating role of modifiable risk factors in the associations.

Methods A total of 22,702 participants aged 35 years and above were enrolled between October 2012 and December 2015. Residential greenness was assessed using Normalized Difference Vegetation Index (NDVI) within radii of 300 m, 500 m, and 1000 m from participants' residential address ($NDVI_{300\,m}$, $NDVI_{500\,m}$, and $NDVI_{1000\,m}$). Primary outcomes comprised CVD events and all-cause mortality, with follow-up from 2018 to 2019. Multivariable Cox regression models were employed to estimate hazard ratios (HRs), and causal mediation analysis was conducted to assess the role of modifiable risk factors in the observed associations.

Results Residential greenness demonstrated a significant association with the risk of CVD, with HRs per tertile increment of 0.84 (95% confidential interval [CI]: 0.77–0.92) for $NDVI_{300\,m}$, 0.86 (95% CI: 0.79–0.94) for $NDVI_{500\,m}$, and 0.90 (95% CI: 0.82–0.98) for $NDVI_{1000\,m,}$ separately. Compared to areas with the lowest $NDVI_{500\,m}$, the HR for CVD incidence in areas with medium and high $NDVI_{500\,m}$ were 0.89 (95% CI: 0.76–1.06), and 0.74 (95% CI: 0.62–0.89), respectively. Utilizing a newly proposed two-stage regression method in mediation analysis, approximately 16.18%, 5.34%, 4.04%, and 2.45% of the total effect of $NDVI_{500\,m}$ on CVD risk were mediated by high-density lipoprotein cholesterol, physical activity, body mass index, and diabetes mellitus, respectively.

Conclusion This study provides compelling evidence that higher residential greenness is associated with a reduced risk of CVD among the adult Chinese population, with specific modifiable risk factors playing a mediating role. These findings underscore the significance of incorporating green space interventions into CVD prevention strategies.

Keywords Cardiovascular disease, Greenness, Mediation analysis, Epidemiology

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Introduction

Cardiovascular diseases(CVD) remain a major causes of death in the world, particularly in low- and middle-income countries [1]. In 2020, there were 4.58 million deaths attributed to CVD in China [2], with a predicted growth rate of CVD events exceeding 50% between 2010 and 2030, solely based on population aging and growth, assuming that risk factors remain unchanged [3]. Moreover, prior studies have already demonstrated that some common and well known risk factors, such as smoking, obesity and hypertension, are associated with the risk of CVD incidence and deaths [4], and effective intervention concerning lifestyle modifications can significantly improve the control rate of blood pressure [5, 6]. At the same time, there is an increasing recognition that environmental elements, such as built environment and air pollution, can influence individual behavioral and metabolic factors, as well as the CVD incidence, also potentially serving as significant factors in accurate CVD risk assessment and prediction.

In recent years, residential greenness has attracted significant global attention for its potential to enhance public health. Scientific study showed that living in greener areas, or even brief exposure to vegetation, can improve both physical and mental well-being [7]. These benefits stem from several factors, including reducing stress and air pollution, increasing convenience of engaging in physical activities, and enhancing social cohesion [8–10]. Collectively, these effects contribute to a lower risk of chronic diseases, particularly cardiovascular conditions. Previous research has indicated that individuals residing in areas characterized by higher residential greenness face a reduced risk of myocardial infarction, heart failure, ischemic stroke, high blood pressure, and dyslipidemia [11–18]. However, most investigations were conducted in middle- and high-income developed countries, resulting in a scarcity of evidence from large-scale population-based cohort studies in developing nations, such as China, where the prevalence of CVD and cardiometabolic disorders have surged. Furthermore, to our knowledge, only a limited number of studies within the Chinese population has explored the association between residential greenness and CVD risk [19, 20]. Nonetheless, those investigations adopted cross-sectional designs. Moreover, only a few studies have explored the potential mediation effect of hypertension, diabetes, lipid levels, body mass index (BMI), physical activity, and air pollution on the association between greenness and CVD risk, yielding inconsistent findings [19–22]. In the context of China's rapid economic development and the accelerated surge in certain modifiable risk factors and the associated burden of CVD, it becomes particularly imperative to scrutinize the association between greenness and both CVD incidence and mortality risk. This necessitates a comprehensive investigation based on a large-scale population-based cohort study, focusing on discerning potential factors that may influence this association.

Therefore, in this present study, we aimed to evaluate the association of residential greenness with CVD and mortality among Chinese adults based on a large-scale longitudinal study, and explore whether modifiable risk factors could mediate the relationship between residential greenness and CVD.

Methods

Data source and study population

In this study, individuals were selected from the China Hypertension Survey (CHS), a nationally representative population-based survey conducted from October 2012 to December 2015. Briefly, a stratified multistage random sampling method was used to recruit nearly 0.5 million participants aged 15 years and older from 31 provinces in mainland China, more information was provided elsewhere [23]. For this sub-study, all selected urban and rural areas were further stratified into eastern, central, and western regions based on geographical location and economic levels. Then a total of 16 cities and 17 counties were selected using simple random sampling (SRS), and at least three communities or villages were randomly selected from each region [24, 25]. Ultimately, 30,036 individuals aged ≥ 35 years, with essential baseline information at baseline (including gender, name, and valid blood samples), were enrolled initially. The followed up was conducted in 2018 and in 2019, and the outcomes were identified from baseline (2012–2015) to the follow-up survey (2018–2019).

In this current study, we first excluded participants lost to follow-up (n = 4,726). Next, we further removed 2,135 subjects with a history of CVD and 473 participants with incomplete baseline covariate data. Finally, 24.4% participants were excluded from the original population, and 22,702 participants with no CVD and had complete baseline information on hypertension, diabetes, and blood lipid levels were included in the final analysis. (Figure S1 in supplementary materials 1). This study was approved by the ethics committee of Fuwai Hospital, Beijing, China, and all participants provided written informed consent.

Assessment of residential greenness levels

Normalized Difference Vegetation Index (NDVI) was used to quantify residential greenness in the 300 m, 500 m and 1000 m radius around the participant's residential addresses. The NDVI is a vegetation indicator, which is defined as (NIR—RED)/(NIR + RED), where NIR represents the near-infrared reflectance and RED signifies red reflectance. The NDVI ranges from −1 to 1, with positive values indicating vegetation, zero indicating bare soil, and negative values representing non-vegetated surfaces, such as blue spaces or water bodies. The higher the positive NDVI values, the greater the level of green vegetation. Monthly satellite-derived NDVI datasets across China, archived in the SPOT/VEGETATION PROBA-V 100 m products [26], were used in this study. These datasets have a spatial resolution of 100 m × 100 m and were derived by calculating the monthly maximum values. We assessed the residential greenness levels via averaging the values within each participant's boundaries. Furthermore, regarding that water surfaces or blue spaces may have independent beneficial effects on health, negative NDVI values were removed in our analysis [27]. We calculated the three-year average NDVI before baseline survey to reflect their long-term exposure to green environments. To take into account seasonal variability in greenspace, in the sensitivity analysis, the average NDVI values between May and September were also computed to maximise the contrast in estimated exposure since the summer months are the greenest months in China. Additionally, NDVI of 500 m radii around participant's residential addresses were stratified into tertiles based on established research practice [27], with ranges of < 0.33 (Q1, Low), 0.33–0.44 (Q2, Medium), and > 0.44 (Q3, High), respectively.

Mediating factors and covariates

Hypertension, diabetes mellitus, overweight/obesity, dyslipidemia, physical activity and fine particulate matter concentration ($PM_{2.5}$, particles with an aerodynamic diameter of ≤ 2.5 μm) were considered as potential mediators of greenness and CVD incidence. In this study, hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg, and/or a diastolic blood pressure (DBP) ≥ 90 mmHg, and/or self-reported taking antihypertensive medication at baseline. According to the 2017 standards of the Chinese Medical Association's Diabetes Study Group, diabetes was defined as a fasting plasma glucose (FPG) level reaching or exceeding 7.0 mmol/L (126 mg/dL), or a self-reported diagnosis of type 2 diabetes by a healthcare professional, or being on anti-diabetic medication [28]. Overweight and obesity were defined as a body mass index (BMI) of 24.0 and ≥ 28.0 kg/m^2, respectively. Participants with total cholesterol (TC) ≥ 6.22 mmol/L, triglyceride (TG) ≥ 2.26 mmol/L, low-density lipoprotein cholesterol (LDL-C) > 4.14 mmol/L, or high-density lipoprotein cholesterol (HDL-C) < 1.04 mmol/L were considered as having dyslipidemia based on the Chinese Guidelines for Lipid Management (2023) [29]. Additionally, physical activity was defined by metabolic equivalent tasks (METs) based on the participants'occupation/housework, commuting, and leisure time activities, and low physical activity was defined as < 600 METs/week. Average $PM_{2.5}$ concentrations in the year before CVD incidence or death were also included. By linking each participant's residence by residential counties/districts to average $PM_{2.5}$concentrations in a 1 km × 1 km grid, which has been cross-validated [30]. Drinker was defined as consuming at least 1 alcoholic beverage per week in the past month. Daily maximum temperature data was obtained from meteorological station within each district or county. Heatwaves were defined as daily maximum temperatures exceeding the 92.5 th percentile of the warm season for at least three consecutive days.

We adjusted the following variables that were likely to confound the association based on the questionnaire, including age, sex, level of education (junior high school or below and high school or above), urbanization (urban/rural), and geographic region (eastern, central, or western), alcohol consumption (drinker or non-drinker), smoking status (never smoked, former smoker, or current smoker), family history of CVD, and anti-dyslipidemia medication receipt. Moreover, we also included per capita Gross Domestic Product (GDP) to represent socioeconomic status (SES) at district/county levels, which were collected from statistic yearbooks, national bureau of statistics and China national knowledge infrastructure.

Outcome measures

The primary outcomes were composite of CVD events and mortality at any point before the follow-up survey conducted in 2018–2019, including coronary heart disease (CHD, International Classification of Diseases 10 th Revision [ICD-10) codes I20-I25), stroke (I60-I61 and I63-I64), chronic heart failure (I50), and deaths attributable to CVD (I00-I25, I27-I88, and I95-99). Specifically, CHD was defined as having one of the following conditions or treatments: myocardial infarction, coronary artery bypass graft surgery, or percutaneous coronary intervention coronary heart disease-related deaths, or CHD-related deaths. Stroke encompassed both non-fatal and fatal stroke, including subarachnoid hemorrhage, intracerebral hemorrhage, ischemic stroke, and unspecified stroke. During the follow-up, we tracked CVD events by contacting participants or their proxies through face-to-face interviews, telephone calls, or mailed questionnaires. and further verified these events by reviewing medical records or death certification. More detailed information on the questionnaires is in the supplementary materials 2.

Statistical analysis

In this study, descriptive statistics were carried out for all variables of interest. Continuous variables were represented by means with standard deviations (SDs), and categorical data by frequency and percentages. The association of greenness levels with CVD and mortality was estimated by multivariable Cox proportional hazards models, adjusting for age, sex, level of education, geographical region, urbanization, alcohol consumption, smoking status, family history of CVD, and per GDP. Hazard ratios (HRs) and 95% confidential interval (CI) were computed. Moreover, the Cox proportional hazard assumption was tested by weighted Schoenfeld residuals and *P*-values were greater than 0.05 for all outcomes. The survival time was measured in years from the date of initial interview administration to the occurrence date of study endpoint events. Subjects meeting any of the following criteria were treated as censored observations: (1) documented history of CVD at baseline assessment; (2) loss to follow-up during the study period; or (3) incomplete baseline covariate measurements essential for analysis. Median values were earmarked to each group of NDVI levels and were treated as continuous variables when performing trend testing. Exposure–response curves between $NDVI_{500\ m}$ and incident CVD and mortality risk were plotted using penalized splines with two degrees of freedom. Furthermore, stratified analyses were conducted to explore variation in the association of greenness levels per tertile increment with CVD by sex, age and urbanization, and we also added a cross-product term between green and stratified variables into the fully adjusted model to test for interaction on the multiplicative scale.

Finally, we conducted mediation analysis to evaluate the effect of NDVI levels in 500 m radii on outcomes (expressed as the HR per tertile increase in NDVI) described by VanderWeele for Cox proportional hazards regression, keeping cardiometabolic risk factors, physical activity, $PM_{2.5}$concentration, and heatwave days as mediator variables [31, 32]. Regarding that the 500 m buffer can cover more green space the participants may use, we used it as the main exposure to explore the mediation analyses. Briefly, the total effect was decomposed into the natural direct effect (NDE) and natural indirect effect (NIE), where NDE represents the effect size of NDVI unexplained through the mediator, while NIE is interpreted as the effect size of NDVI resulting from mediation through the specified mediators. The proportion of the association of NDVI with CVD events and all-cause mortality mediated via the designated mediator, was computed as a metric of the contribution of the natural indirect association to the overall association, employing the following formula: [32]

$$Proportionmediated = HR^{NDE} \times (HR^{NIE} - 1)/(HR^{NDE} \times HR^{NIE} - 1)$$

Moreover, all of the 95% CIs for the total effect, NDE, NIE and the proportion mediated were calculated using the delta method, and the mediation effects of each potential mediator were assessed separately in this current study.

Penalized splines analysis was conducted using the *survival* package, version 3.4.2 for R software (R Foundation for Statistical Computing, Vienna, Austria). All other analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC USA). *Mediation* macro for SAS was applied to perform the mediation analysis. All statistical tests were 2-sided at a significance level of $P < 0.05$.

Results

Baseline characteristics

The baseline characteristics according to different levels of NDVI (low, medium, high) are presented in Table 1. Among 22 702 adult participants initially free of CVD, the mean baseline age was 56.1 ± 13.1 years. During the follow-up, 993 participants developed fatal or nonfatal CVD and 1096 died from all causes (Figure S1 in supplementary materials 1). The cumulative incidence of CVD and all-cause mortality were 9.45 and 10.81 per 1000 person-years, respectively (Table 2). Participants resided in areas with higher greenness were more likely to lower BMI levels, and from rural areas. The median (inter-quartile range) of average 3-year NDVI exposure in circular buffers of 300 m, 500 m and 1000 m around each address's centroid were 0.39 (0.18), 0.39 (0.19), and 0.38 (0.20), respectively. Figure 1 displays the geographical distributions of average NDVI levels from 2012–2015 in China, with substantial variations in greening across the entire surveyed region.

Association of greenness with CVD and all-cause mortality

Table 2 presents the association between different levels of NDVI and CVD incidence as well as all-cause mortality. In the multivariate adjustment model, we found that higher levels of greenness (measured by NDVI) were associated with greater protective effects (i.e. beneficial effect) for CVD. Specifically, for per tertile increment in $NDVI_{300\ m}$, $NDVI_{500\ m}$, and $NDVI_{1000\ m}$, the risk of total CVD reduced by 16% (HR =0.84 [95% CI: 0.77–0.92]), 14% (HR =0.86 [95% CI: 0.79–0.94)), and 10% (HR =0.90 [95% CI: 0.82–0.98]), respectively. This trend towards reducing the CVD risk was significant for the classes with elevated levels of NDVI ($P_{trend} < 0.05$).

Table 1 Characteristics of study participants

Characteristic	Total (N = 22,702)	$NDVI_{500\ m}$			P value
		Low (N = 7458)	Medium (N = 7712)	High (N = 7532)	
Socio-demographics					
Age, years	56.1 ± 13.1	55.7 ± 13.3	55.3 ± 12.7	57.4 ± 13.2	<.001
Gender, %					0.558
Male	10,505 (46.3)	3489 (46.8)	3546 (46.0)	3470 (46.1)	
Female	12,197 (53.7)	3969 (53.2)	4166 (54.0)	4062 (53.9)	
Educational level, %					<.001
Elementary middle School or lower	11,593 (51.1)	2537 (34.0)	4246 (55.1)	4810 (63.9)	
High school or above	11,109 (48.9)	4921 (66.0)	3466 (44.9)	2722 (36.1)	
Residence, %					<.001
Urban	10,130 (44.6)	5300 (71.1)	2556 (33.1)	2274 (30.2)	
Rural	12,572 (55.4)	2158 (28.9)	5156 (66.9)	5258 (69.8)	
Region, %					<.001
East	9263 (40.8)	3149 (42.2)	3313 (43.0)	2801 (37.2)	
Central	9460 (41.7)	2322 (31.1)	3426 (44.4)	3712 (49.3)	
West	3979 (17.5)	1987 (26.6)	973 (12.6)	1019 (13.5)	
Lifestyle behaviors					
Consumption of Alcohol, %	6318 (27.8)	2081 (27.9)	2123 (27.5)	2114 (28.1)	0.749
Smoking types, %					<.001
Current	5731 (25.2)	1599 (21.4)	2068 (26.8)	2064 (27.4)	
Former	1216 (5.4)	379 (5.1)	448 (5.8)	389 (5.2)	
Never	15,755 (69.4)	5480 (73.5)	5196 (67.4)	5079 (67.4)	
Mediators					
Low physical activity (< 600 METs/week)	4860 (21.4)	1951 (26.2)	1338 (17.3)	1571 (20.9)	<.001
Hypertension	8957 (39.5)	3037 (40.7)	2931 (38.0)	2989 (39.7)	0.003
Diabetes Mellitus	2286 (10.1)	908 (12.2)	707 (9.2)	671 (8.9)	<.001
BMI, Kg/m^2	24.5 ± 3.5	25.0 ± 3.5	24.4 ± 3.5	24.1 ± 3.4	<.001
Triglycerides, mmol/L	1.4 ± 1.0	1.5 ± 1.0	1.5 ± 1.0	1.4 ± 1.0	
Cholesterol, mmol/L					
Total	4.8 ± 1.0	4.7 ± 1.0	4.8 ± 1.0	4.8 ± 1.0	<.001
HDL-C	1.4 ± 0.3	1.3 ± 0.3	1.4 ± 0.3	1.4 ± 0.4	<.001
LDL-C	2.8 ± 0.8	2.7 ± 0.8	2.8 ± 0.8	2.8 ± 0.8	<.001
FPG, mmol/L	5.6 ± 1.5	5.6 ± 1.7	5.6 ± 1.4	5.5 ± 1.4	<.001
$PM_{2.5}$, μg/m^3	53.4 ± 13.2	54.0 ± 12.7	50.8 ± 12.7	55.3 ± 13.8	<.001
GDP per capita, yuan	65,339.0 ± 36,929.8	70,443.6 ± 43,915.4	66,955.6 ± 36,939.3	58,629.2 ± 27,032.1	<.001

NDVI normalized difference vegetation index, *BMI* body mass index, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low density lipoprotein cholesterol, *FPG* fasting plasma glucose, *MET* metabolic equivalent tasks, *PM* particulate matter, *GDP* gross domestic product

Furthermore, compared to areas with the lowest of NDVI per 500 m, the HR for the incidence of total CVD in areas with medium and high $NDVI_{500\ m}$ were 0.89 (95% CI: 0.76–1.06), and 0.74 (95% CI: 0.62–0.89), respectively. For CHD outcome, we also found significant association, with estimated HRs of 0.55 (95% CI: 0.40–0.75) and 0.67 (95% CI: 0.49–0.90) for participant living in the medium and high NDVI in 500 m radii. Similar results were observed for NDVI levels per 300 m and 1000 m. Moreover, the correlation between greenness and stroke was interesting, because we found that residential greenness in the 300 m radius could reduce the risk of stroke, but no statistically significant difference was observed for $NDVI_{1000\ m}$. Also, no important associations were observed between overall greenness and all-cause mortality. The exposure–response curves based on penalized spline models revealed that the risk of CVD decreased with the increment of $NDVI_{500\ m}$, and the HR for the association between $NDVI_{500\ m}$ and total CVD, and

Table 2 Hazard ratio for CVD and all-cause mortality associated with residential greenness

Exposure		CVD		CHD		Stroke		All-cause mortality	
		Incidence/1000 person-years	HR (95%CI)	Incidence/1000 person-years	HR (95%CI)	Incidence/1000 person-years	HR (95%CI)	Incidence/1000 person-years	HR (95%CI)
$NDVI_{300\,m}$	Low	10.39	[Reference]	3.91	[Reference]	5.40	[Reference]	9.92	[Reference]
	Medium	9.00	0.79(0.66–0.93)	1.88	0.45(0.32–0.62)	6.20	1.02(0.81–1.27)	10.35	0.97(0.82–1.15)
	High	9.12	0.70(0.59–0.84)	2.84	0.60(0.44–0.81)	5.33	0.77(0.61–0.98)	12.09	0.88(0.74–1.04)
	Per tertile increment[a]	9.45	0.84(0.77–0.92)	2.86	0.79(0.67–0.92)	5.64	0.87(0.77–0.98)	10.81	0.93(0.86–1.01)
	P for trend		<.001		0.002		0.020		0.100
$NDVI_{500\,m}$	Low	10.02	[Reference]	3.70	[Reference]	5.20	[Reference]	9.73	[Reference]
	Medium	9.51	0.89(0.76–1.06)	2.07	0.55(0.40–0.75)	6.62	1.15(0.92–1.43)	10.92	1.05(0.89–1.25)
	High	8.84	0.74(0.62–0.89)	2.85	0.67(0.49–0.90)	5.06	0.80(0.63–1.02)	11.76	0.90(0.76–1.07)
	Per tertile increment[a]		0.86(0.79–0.94)		0.83(0.70–0.97)		0.88(0.79–0.99)		0.94(0.86–1.02)
	P for trend		<.001		0.016		0.038		0.125
$NDVI_{1000\,m}$	Low	9.97	[Reference]	3.63	[Reference]	5.24	[Reference]	9.68	[Reference]
	Medium	9.30	0.83(0.70–0.98)	1.93	0.50(0.36–0.68)	6.53	1.05(0.84–1.30)	10.73	1.01(0.86–1.20)
	High	9.10	0.80(0.66–0.96)	3.17	0.79(0.58–1.08)	5.00	0.82(0.64–1.04)	12.07	0.94(0.79–1.12)
	Per tertile increment[a]		0.90(0.82–0.98)		0.91(0.77–1.07)		0.90(0.80–1.01)		0.97(0.89–1.05)
	P for trend		0.017		0.217		0.077		0.426

Notes: All models were adjusted for age, sex, alcohol consumption, urbanization and geographical region, smoking, educational level, family history of CVD, CVD medication history, and per capita GDP

Abbreviations: *HR* hazard ratio, *CVD* cardiovascular disease, *NDVI* normalized difference vegetation index, *CHD* coronary heart disease, *HR* hazard ratio, *CI* confidential interval

[a] NDVI level per tertile increment

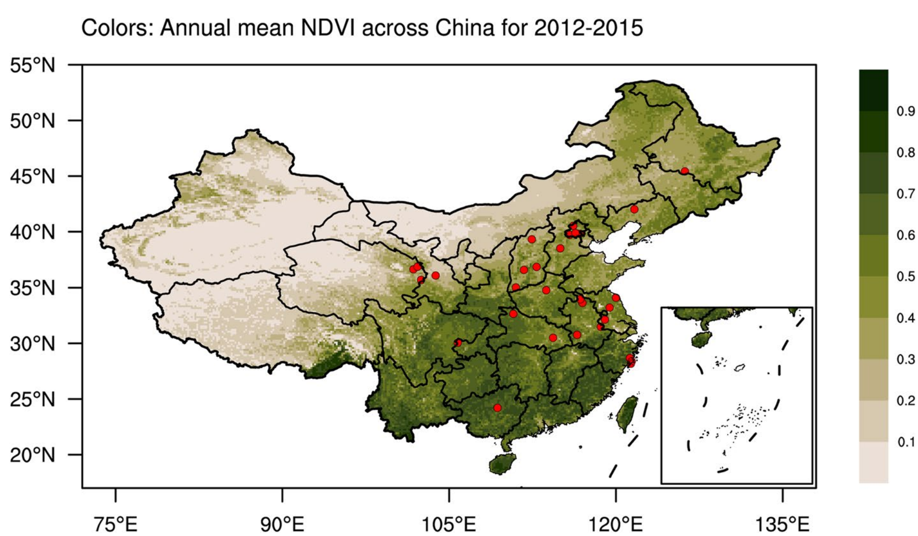

Fig. 1 Annual mean NDVI (colors) at baseline (2012–2015) and 38 China Hypertension Survey sites (red dots) across China. Insets: South China Sea. Abbreviations: NDVI, Normalized Difference Vegetation Index

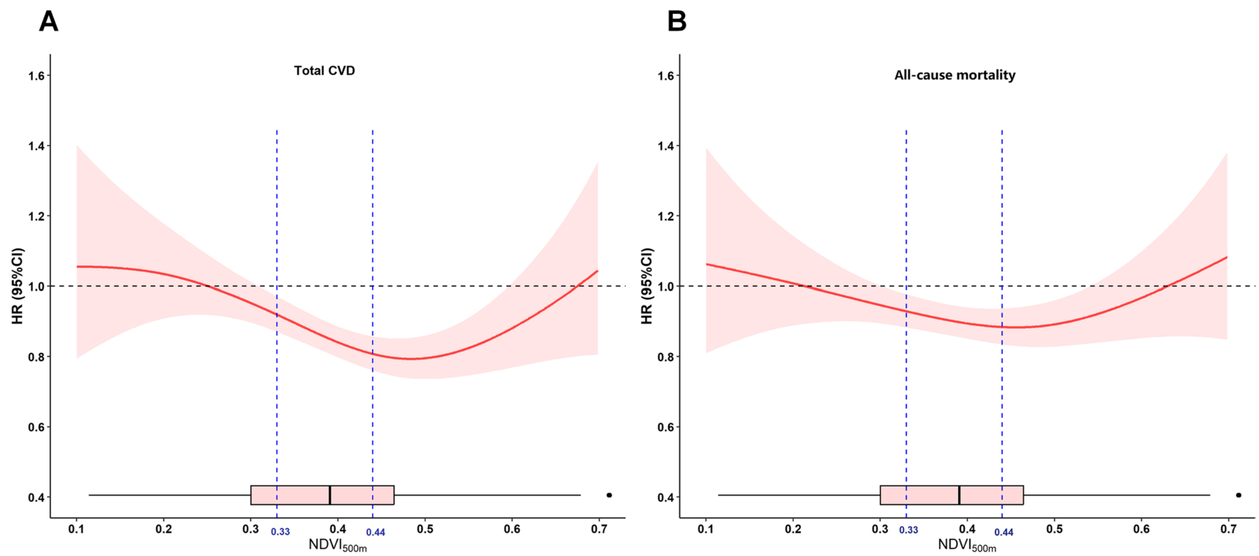

Fig. 2 Exposure–response relations between long term exposure to NDVI within the 500 m circular buffers around the participants'residential addresses and incidence of CVD and all-cause mortality. Solid line represents point estimate and dashed lines represent 95% confidence intervals. Boxplot represents distribution of NDVI exposure levels for participants. NDVI, normalized difference vegetation index; CVD, cardiovascular disease

all-cause mortality were non-linear (*P*-nonlinear <0.05), respectively (Fig. 2).

Stratified analysis

In the stratified analyses (Fig. 3), the association of a tertile increase in $NDVI_{300\ m}$ and $NDVI_{500\ m}$ with the risk of CVD did not differ substantially by age and sex. However, the association differed according to urbanization. In particular, we observed a different association between $NDVI_{300\ m}$ and CVD risk in the rural areas (HR $=0.71$; 95%CI:0.63, 0.80) and in urban area (HR $=0.97$;95%CI:0.85,1.11), and the *P* interaction lower than 0.001. Similar results were observed for $NDVI_{500\ m}$ and $NDVI_{1000\ m}$. Additionally, participants younger than 60 had a greater significant modification effect of $NDVI_{1000\ m}$, and the *P* value of multiplicative interaction was 0.034.

Mediation analysis

Mediation analysis showed that diabetes mellitus, BMI continuous, HDL-C, and physical activity played mediation effects on the association between $NDVI_{500\ m}$ and CVD. In contrast, no significant mediation effect was found for hypertension and $PM_{2.5}$ (Table 3). Specifically, an increase in per tertile for $NDVI_{500\ m}$ reduced the risk of CVD by 13% (HR [total association], 0.87; 95%CI, 0.79–0.95), and that approximately 16.18% of the total association was mediated through the HDL-C (HR [indirect association], 0.98; 95%CI, 0.96–0.99). Also, Table 3 showed that an increase in $NDVI_{500\ m}$ decreased the risk of CVD by 15% (HR [total association], 0.85; 95% CI, 0.78–0.93), and that 5.34% of the total association (95% CI, 2.01%−13.55%) was mediated through the physical activity (HR [indirect association], 0.99; 95% CI, 0.99–1.00, $P=$ 0.001). Moreover, proportions mediated were 4.04% for BMI, and 2.45%(95%CI, 35.5%−64.2%) for diabetes mellitus. Additionally, no mediation effects of hypertension, diabetes mellitus, and lipids were found to play a significant role in the association of $NDVI_{500\ m}$ with CHD and all-cause mortality ($P>$ 0.05) (Table S1−2 in supplementary materials 1). However, in the mediation analyses of NDVI and stroke risk, physical activity showed the most significant mediation effects (Table S1 in supplementary materials 1).

Discussion

In this prospective cohort study in China, we observed that individuals residing in higher residential greenness, as measured by satellite-derived $NDVI_{300\ m}$ and $NDVI_{500\ m}$, had a reduced risk of CVD incidence, whereas non-significant relationship was found between residential greenness and the risk of all-cause mortality. Additionally, the association between residential greenness and the risk of CVD was partially mediated by diabetes mellitus, BMI, HDL-C, and physical activity.

Findings in this study of negative associations between greenness level and the risk of CVD incidence were supported by previous research [11–13, 17, 18]. The longitudinal study conducted in Korea, enrolling 351 409 participant aged over 20 years, demonstrated that living in urban area with higher level of greenness may beneficially affect the risk of total CVD [18]. Another study combining four large population-based cohorts in

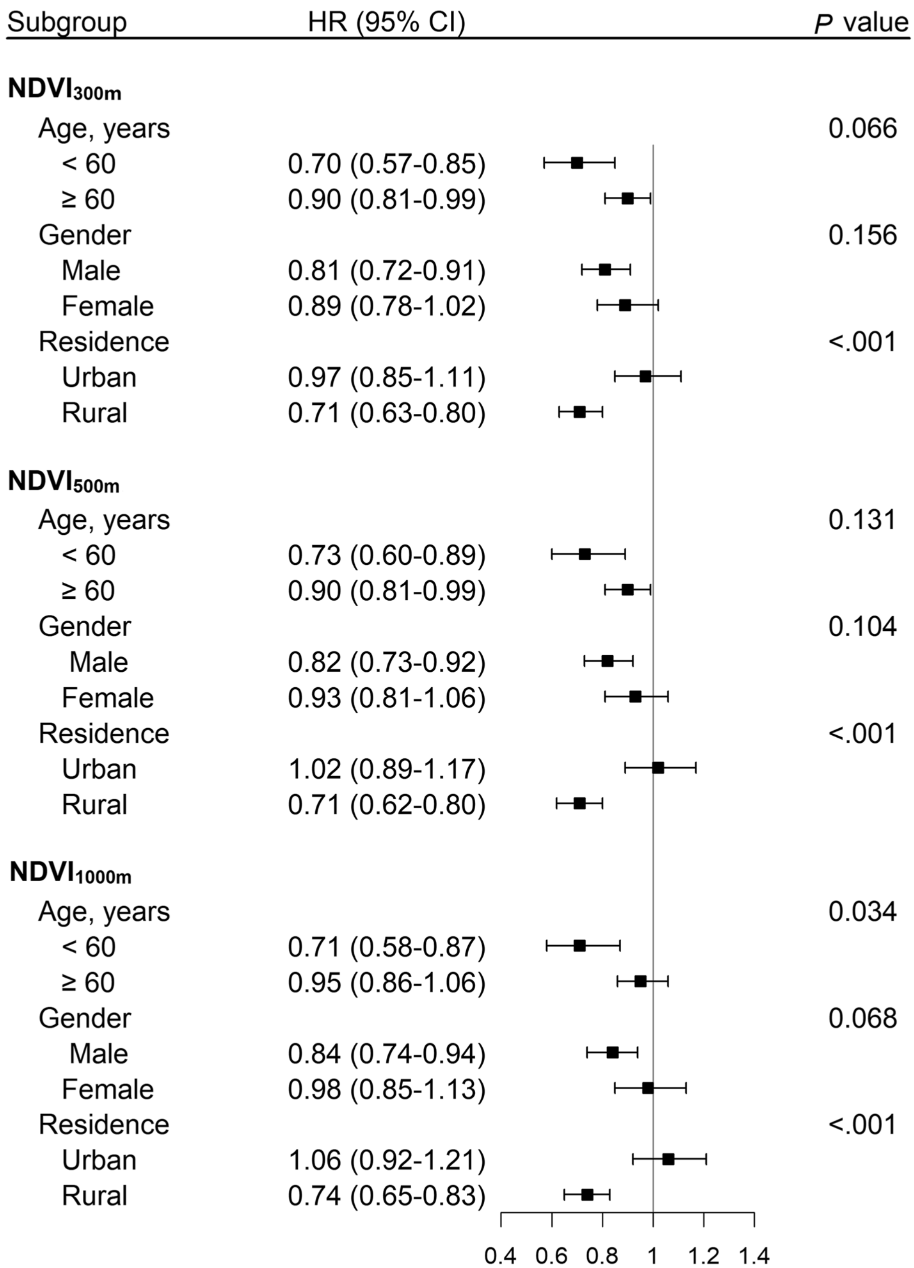

Fig. 3 Stratified analyses of association between greenness levels per tertile increment and the risk of cardiovascular events. NDVI, normalized difference vegetation index

Ontario revealed that the incidence risk of acute myocardial infarction and heart failure decreased by 6% and 7%, respectively, as an interquartile range increased in residential greenness (measured by NDVI level) [17]. To our knowledge, only a few studies conducted in in developing nations, such as China, that have examined the association between greenness exposure and incidence risk of CVD [19, 20]. For example, the 33 Communities Chinese Health Study, based on population-based cross-sectional study, and recruiting 24,845 participants aged from 18 to 74 years, suggested that an interquartile range increase in $NDVI_{500\ m}$of a community was associated with a 27% lower likelihood of CVD prevalence, with an OR being 0.73 (95% CI:0.65–0.83), which was similar to our findings [20]. Insights derived from these studies, combined with this current study, can offer valuable guidance to decision-makers involved in shaping development strategies aimed at improving cardiovascular health among

Table 3 Decomposition of the total association between NDVI within 500 m buffer and the risk of total CVD direct and indirect associations mediated by cardiometabolic risk factors

Variable	Associations[a]						Proportion mediated, % (95% CI)
	Total		Indirect		Direct		
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	
Hypertension	0.86(0.78–0.94)	0.001	1.00(0.99–1.00)	0.129	0.86(0.79–0.94)	0.001	2.52(−0.80,7.91)
Diabetes mellitus	0.86(0.79–0.94)	0.001	1.00(0.99–1.00)	0.020	0.86(0.79–0.94)	0.001	2.45(0.33,7.17)[*]
Overweight/Obesity	0.92(0.85–0.99)	0.036	1.00(0.99–1.01)	0.717	0.92(0.85–0.99)	0.034	−1.19(−28.24,9.43)
BMI continuous	0.86(0.79–0.94)	0.001	0.99(0.99–1.00)	0.024	0.87(0.79–0.95)	0.002	4.04(0.45,11.95)[*]
Dyslipidemia	0.86(0.79–0.94)	0.001	1.00(0.99–1.00)	0.302	0.86(0.79–0.94)	0.001	1.90(−2.02,7.35)
TC	0.86(0.79–0.94)	0.001	1.00(0.99–1.00)	0.048	0.87(0.79–0.95)	0.001	2.75(−0.07,8.46)
TG	0.87(0.79–0.95)	0.003	1.00(0.99–1.00)	0.507	0.87(0.80–0.96)	0.004	0.92(−2.33,4.89)
HDL-C	0.87(0.79–0.95)	0.002	0.98(0.96–0.99)	<.001	0.89(0.81–0.97)	0.011	16.18(7.37,47.96)[*]
LDL-C	0.86(0.79–0.94)	0.001	1.00(1.00–1.00)	0.283	0.86(0.79–0.94)	0.001	1.02(−0.98,3.98)
Physical activity	0.85(0.78–0.93)	0.001	0.99(0.99–1.00)	0.001	0.86(0.79–0.94)	0.001	5.34(2.01,13.55)[*]
$PM_{2.5}$	0.85(0.78–0.93)	0.001	0.99(0.99–1.00)	0.058	0.86(0.79–0.94)	0.001	4.16(−0.31,12.05)
Heatwave days	0.86(0.78–0.94)	<.001	1.02(1.00–1.04)	0.017	0.84(0.77–0.92)	<.001	−12.82(−48.79,−2.47)[*]

Abbreviations: *CVD* cardiovascular disease, *NDVI* normalized difference vegetation index, *HR* hazard ratio, *CI* confidential interval, *BMI* body mass index, *TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *PM* particulate matter

[a] Hazard ratios given per tertile increase for NDVI level

[*] $P < 0.05$

citizens. This includes acknowledging the pivotal influence of residential greenness and contemplating initiatives such as the expansion of green spaces. Most importantly, our findings provide evidence of the association between greenness levels and CVD in developing country, and highlight the importance of implementing greenness interventions at population level for primary prevention of CVD and the comprehensive management of modifiable risk factors. Moreover, our initiatives should not be exclusively focus on expanding the quantity of green spaces, rather, equal attention should be given to enhancing public perception of these environments to optimize health benefits.

Stratified analyses revealed that rural residents derived greater health benefits from green space exposure compared to their urban counterparts. While prior studies have predominantly focused on urban settings in high-income countries [18, 33–35], our findings align with a recent Chinese cohort study documenting stronger protective effects of rural greenness [36]. Three key factors may explain this disparity: First, rural regions typically exhibit higher vegetation density and structurally distinct green spaces (e.g., forests, farmland) compared to fragmented urban greenery, which may limit urban residents'exposure to meaningful vegetation [8, 37]. Second, accelerated urbanization in Chinese cities correlates with elevated air pollution levels, potentially counteracting green space benefits [38]. Third, urban parks—often prioritized in green space metrics—frequently lack dense vegetation; studies show minimal correlation between urban park coverage and actual greenness exposure [39]. These findings underscore the need to contextualize green space research within regional urbanization patterns and ecological characteristics.

Additionally, the evidence concerning the impact of residential greenness on specific CVD subgroups, particularly stroke was sparse. Several studies have investigated the relationship between residential greenness and the risk of stroke, however, they have yield inconsistent findings [18, 40]. Possible explanations may be the difference in exposure definitions and population selection. In this current large-scale cohort study, we found that residential greenness in the 300 m radius around the participant's residential addresses could reduce the risk of stroke, but no statistically significant difference between NDVI per 1000 m and stroke risk. It seems possible that vegetation appears decrease the risk of stroke via directly and efficiently reducing traffic related air pollution and noise, particularly within a small buffer size surrounding individual's residence address. Undoubtedly, future studies should shed light on whether these associations are sensitive to different buffer size around individual's neighbourhood, a factor which may be related to the accessibility of the greenspace.

Although some studies have suggested that greenspaces may enhance the cardiovascular health by diminishing exposure to air pollution and traffic noise, alleviating the heat, and promoting physical activity among nearby residents [19, 41, 42], the exact mechanisms remain incompletely delineated. A report has provided three potential functions of greenspace on health, including reducing harm, restoring capacities, and building capacities [42]. In this context, some studies have explored the association of residential greenness with CVD, focusing on the mediators such as physical activity, road proximity and air pollution [11, 12]. A recent analysis of data from five southwestern provinces of China based on a cross-sectional design indicated that higher physical activity level and lower BMI may partially mediate the benefit effect of greenspace on the risk of 10-year atherosclerosis cardiovascular disease (ASCVD), with physical activity and BMI mediating 44.73% and 35.15% of the total effect for Enhanced Vegetation Index per 500 m, respectively, in the medium-risk and low-risk groups compared [19]. These also accord with our finding, which showed that physical activity and BMI continuous mediated 5.34% and 4.04% of the total effects for $NDVI_{500\ m}$on CVD. A community-based study in eastern China also found that physical activity partially mediated the relationship between greenness exposure and CVD [43]. This observation may be explained by the fact that green environments offer an intrinsic motivation for individuals to engage in outdoor activities, fostering increased opportunities for walking and active transportation [44]. People living in greener areas may benefit from reduced pollution, less noise, lower stress levels, and enhanced psychological restoration, all of which can improve health outcomes [44, 45]. Additionally, growing evidence shows that higher greenness is associated with lower BMI, a known risk factor for CVD [46, 47]. It is plausible that greenness indirectly affects cardiovascular health by influencing BMI. Although some studies have shown that BMI mediates the relationship between residential greenness and hypertension or ASCVD [11, 37], the exact mechanisms remain unclear. Some research indicates that green environments may provide convenient spaces for physical activity, helping to reduce obesity and lower blood pressure [48]. Nevertheless, comparing the proportions mediated across various studies poses a challenge owing to variations in exposure assessment, the delineation of buffer zones around individual's residential address, and selection of analytical methods.

Additionally, we failed to find the mediation effect of $PM_{2.5}$on the association between greenness and the risk of CVD incidence in this current study, which was in accordance with prior research [19]. On the contrary, another study, enrolling 121,701 female registered nurses aged 30 to 55 years, has found support for the conclusion that air pollution might act as a mediator in the association between greenness and mortality [49]. This inconsistency could arise from variations in population selection and the metrics used to assess air pollution. Furthermore, the diversity, quality, and accessibility of greenspaces within residential neighborhoods may exert a substantial influence on the estimation of observed effects [14], thus warranting further investigation as potential factors contributing to the existing inconsistencies in epidemiological findings. We also found that the association of greenness with the risk of CVD was partially mediated by diabetes mellitus and HDL-C. To our best knowledge, only a few studies have indicated that cardiometabolic risk factors partially mediated the association between greenness and CVD risk [20, 21]. For example, partially consistent with our findings, the 33 Communities Chinese Health Study suggested that hypertension, type 2 diabetes mellitus, obesity and hypercholesterolemia mediated the association of residential greenness (NDVI) with CVD prevalence of 4.5%, 4.1%, 3.1% and 12.7%, respectively [20]. Another study revealed that the association of NDVI levels with myocardial infarction was partially mediated by dyslipidemia and type 2 diabetes mellitus but not hypertension [21]. Further studies are warranted to bridge the aforementioned gap and broaden our understanding of the mediation effect of modifiable risk factors on the association of residential green space with cardiovascular health.

This present study has several strengths. The findings of this current study are noteworthy because this study was based on a large-scale, representative longitudinal survey with standardized procedures and strict quality control, which is essential for accurate estimation of the association between greenness and CVD and mortality. Incorporating a large range of NDVI levels at individual-level enables us to estimate the associations with increased precision. Moreover, mediation analysis with proportional hazard models was applied based on the counterfactual approaches [31], which could provide a mathematical decomposition of the total association into direct and indirect associations with clear explanations. However, we acknowledge some specific limitations. First, although the greenness levels were obtained based on high resolution satellite images, the information on the types, quality and access of greenspace in residential neighbourhoods, and changes in residential greenness during the follow-up period were not distinguished in this present study, which may lead to misclassification of greenness exposure. Previous study also showed that higher access to greenspace and pocket park were associated with decreased all-cause mortality risk [14]. Second, information on the duration of greenness exposure, and noise were not available, which could confound the association of greenness with CVD events and all-cause mortality and have potential influence on the mediation analyses. Third, the information on subjects'residential mobility or length of time spent at reported baseline addresses was unavailable, which might be an important determinant of the association. Fourth, the relatively short follow-up duration limited the number of CVD-specific mortality observed, so this study did not examine the association between residential greenness and CVD-specific mortality. We will further investigate this relationship in future studies with extended follow-up durations. Finally, we didn't take into account seasonal variability in greenspace. We are currently designing a further analysis examining seasonal effect modification using monthly NDVI data. These findings will be reported in future work investigating temporal variations in greenness-health relationships.

Conclusion

In this prospective cohort study of adults in China, we observed that higher residential greenness level was independently associated with a reduced risk of CVD. This association appears to be partially mediated by some modifiable risk factors, such as diabetes mellitus, BMI continuous, HDL-C, and physical activity. These findings highlight the importance of interventions promoting green environments in the primary prevention, providing valuable insights for policymakers regarding the potential role of green spaces in mitigating cardiovascular health risks amidst challenges posed by climate change.

Abbreviations

CVD	Cardiovascular disease
NDVI	Normalized Difference Vegetation Index
CI	Confidential interval
HR	Hazard ratio
CHS	China Hypertension Survey
SRS	Simple random sampling
PM	Particulate matter
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
FPG	Fasting plasma glucose
BMI	Body mass index
TC	Total cholesterol
TG	Triglyceride
LDL-C	Low-density lipoprotein cholesterol
HDL-C	High-density lipoprotein cholesterol
METs	Metabolic equivalent tasks
GDP	Gross Domestic Product
CHD	Coronary heart disease
ICD-10	International Classification of Diseases 10th Revision
SD	Standard deviation
NDE	Natural direct effect
NIE	Natural indirect effect
ASCVD	Atherosclerotic Cardiovascular Disease

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Authors' contributions

Xue Cao, Nuerguli Tuerdi: Conceptualization, Methodology, Software, Formal analysis, Visualization, Writing—Original Draft. Haosu Tang, and Yujie Zhang: Methodology, Visualization, and Investigation. Xin Wang, Congyi Zheng, and Gang Huang: Validation, Investigation, and Writing—Review & Editing. Yixin Tian, Xue Yu, Xuyan Pei: Investigation. Zengwu Wang: Conceptualization, Resources, Writing—Review & Editing, and Project administration.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of Fuwai Hospital, Beijing, China, and all participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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