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The effect of residential greenness on cardiovascular mortality from a large cohort in South China: An in-depth analysis of effect modification by multiple demographic and lifestyle characteristics

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ABSTRACT

Background: The potential for residential greenness to improve cardiovascular health through both physical and psychological mechanisms is well recognized. However, evidence from rapidly urbanizing developing countries and cohort-based causal inference approaches, remains limited. We aim to examine the effect of residential greenness and time to cardiovascular mortality in South China.

Methods: We utilized data from a community-based population survey involving 748,209 participants at baseline from 2009 to 2015, followed up until 2020. Residential greenness exposure was assessed by the annual Normalized Difference Vegetation Index (NDVI) in the 500 m radius of each participant's residence. We used time-varying proportional hazard Cox models coupled with inverse probability weighting to fit marginal structural models and obtain hazard ratios (HRs) for cardiovascular disease (CVD) mortality after adjusting for confounders. Multiple effect modifiers on both additive and multiplicative scales were further explored.

Results: A total of 15,139 CVD-related deaths were identified during a median of 7.9 years of follow-up. A protective effect was found between higher greenness exposure and reduced CVD mortality, with a 9.3 % lower rate of total CVD mortality (HR 0.907, 95 % CI 0.859–0.957) based on a 0.1 increase in annual average NDVI. Demographic (age, marital status) and lifestyle factors (smoking, drinking status) were found to modify the association between residential greenness and CVD mortality (all *P* interaction values < 0.05 or 95 %CI for RERI excluded the value 0). Notably, this effect was more pronounced among older adults, married, and individuals having healthier lifestyles, indicating a greater benefit from greenness for these subgroups.

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Conclusions: Our findings support a causal link between increased residential greenness exposure and a reduced risk of CVD mortality in South China with marked heterogeneous effects, which has public health implications for cultivating greener urban environments to mitigate the impact of CVD within the context of rapid urbanization.

1. Introduction

Cardiovascular disease (CVD) has become the leading cause of premature death globally, including China, accounting for substantial disease burden and healthcare costs (Vaduganathan et al., 2022). In addition to conventional behavioral risk factors in CVD, such as smoking, alcohol consumption, physical activity, and diet, emerging evidence indicates that the living environment may significantly influence cardiovascular health, particularly in the context of rapid urbanization (Bhatnagar, 2017). Green spaces, or residential greenness, recognized as features of the living environment, have the potential to reduce urban heat, alleviate air pollution, and promote physical activity, social connection, and psychological health, hence contributing to improved cardiovascular outcomes (Dadvand et al., 2016; Nieuwenhuijsen, 2021). As urbanization advances, inadequate coverage and restricted availability of green spaces can have detrimental ramifications on public health at the population level.

Several observational studies support a protective association between greenness and CVD mortality in the general population (Chenet et al., 2020; Liuet al., 2022b). A recent meta-analysis, summarizing findings from cross-sectional and cohort studies, reported that a 0.1 increase in normalized difference vegetation index (NDVI), an indicator of greenness, was associated with 2–3 % lower odds of CVD mortality (Liuet al., 2022b). However, evidence from developing countries is scarce, particularly in China, where rapid urbanization has resulted in the fragmentation and loss of natural green spaces (Muhamad Noret al., 2021; Yanget al., 2014), and the impact of greenness has been confirmed to be significant in low and middle-income countries (Asriet al., 2020). Additionally, urbanization has caused a transformation in individual lifestyles, resulting in sedentary behaviors, increased susceptibility to tobacco use, and alcohol consumption (Liet al., 2016; Liuet al., 2016). However, the extent to which individual factors may modify the relationship between greenness and CVD mortality risk remains largely unknown. The research on these individual factors regarding demographics and lifestyles may help to identify subgroups of the population who are vulnerable to environmental factors (Munzelet al., 2022). For instance, people older than 65 years, and those with low education levels were more vulnerable to CVD-related mortality due to extreme heat (Liuet al., 2022a). Vulnerable subgroups, including drinkers and smokers, had increased risk for adverse CVD outcomes from exposure to air pollution (Luo et al., 2022). Additionally, in South China, significant aging population trends are evident, with the elderly dependency ratio—the number of individuals aged 65 and older per 100 individuals aged 15 to 64—in Guangdong Province increasing from 8.89 % in 2010 to 11.82 % in 2020 (Zhao and Wang, 2022). In 2015, the urbanization rate for permanent residents in Guangdong reached 68.7 % and showed an increasing trend (Wanget al., 2019). It is estimated that urbanization may increase the age-standardized CVD incidence by 73–81 per 100,000 from 2010 to 2030 (Chanet al., 2012). Therefore, given the escalating population aging, urbanization, and the continuously increasing burden of CVD, developing a deeper comprehension of the impact of greenness on cardiovascular health, particularly how it may unfold among subgroups with different demographics and lifestyles, can have broad public health implications.

It should be noted that the estimates of association based on traditional assessments (e.g., observational designs) cannot infer causality. Effect estimates derived from traditional assessments could be biased due to confounders and selection bias, whereas causal inference techniques help to determine the risk of CVD mortality related to a specific exposure. Causal inference approaches play a critical role in public

health, providing a rigorous framework to evaluate cause-and-effect relationships between residential greenness and CVD (Glasset al., 2013). Nevertheless, there remains a paucity of evidence on the causal links between greenness and the risk of CVD mortality, which is vital for designing effective interventions and guiding policy decisions for CVD prevention.

The aim of this present study is to examine the potential causal relationship between residential greenness and risk of mortality from CVD, including ischemic heart disease (IHD), myocardial infarction (MI), total stroke, ischemic stroke, and hemorrhagic stroke based on a large population-based prospective cohort of nearly 0.8 million individuals in South China. We further evaluate the effect modifications by multiple demographics (age, sex, ethnicity, marital status, education level) and lifestyles characteristics (physical activity, smoking status, drinking status) on this relationship.

2. Methods

2.1. Study population

Participants were selected from the subset of Guangzhou and Zhongshan cities, which was based on a community-based population survey in accordance with the Major Projects of Science Research China's 11th (2006–2010) and 12th (2012–2017) five-year plans. The available information ranged between 2009 and 2015 from a total of 844,368 participants. We excluded participants under 18 years of age, those with unknown residential address, and those who died within six months. Our final sample consisted of 748,209 adults. Demographic characteristics and lifestyle practices were collected using computer-based questionnaires administered through face-to-face interviews. Participants also underwent physical measurements and provided biological samples. Further details have been documented elsewhere (Ruanet al., 2019). This study obtained ethical approval from the Human Ethics Committee at Sun Yat-sen University. All participants provided written informed consent.

2.2. Assessment of exposure and covariates

During the interviews, each individual's home address was collected, which could be linked to the Autonavi Open platform (<https://lbs.amap.com/>) to obtain longitude and latitude coordinates. Residential greenness exposure was assessed by annual NDVI, obtained from the LPDAAC (Land Processing Distributed Active Archive Center) (<https://lpdaac.usgs.gov>). NDVI is a widely used satellite-image-based vegetation index that helps assess and monitor vegetation health and vigor across large areas. It ranges from -1.0 to 1.0 , with higher values indicating denser, healthier vegetation and greater levels of greenness. To minimize the estimation bias due to blue space, pixels with values below 0 were excluded from the analysis (McDougallet al., 2022; Wu and Asri, 2023). By linking the NDVI imagery to the longitude and latitude coordinates of each residential address, we calculated the greenness within a radial buffer of 500 m. Our main analyses focused on the 500 m buffer, as it represents areas reachable within a 15-minute walk from participants' residences, thus providing a practical depiction of nearby green spaces (Villeneuve et al., 2018). We also utilized different buffer sizes (i.e., 250 m and 1,000 m) to allow for comparisons with previous studies that employed these choices (Gullonet al., 2023; Jameset al., 2016b; Villeneuve et al., 2018). Several buffer sizes should be tested to better understand and explore the association between neighborhood greenness and health outcomes (Markevych et al., 2017).

In this study, covariates including demographics (age, sex, ethnicity, marital status, education level), medical insurance, family history of CVD, and lifestyles (physical activity, smoking status, drinking status) were collected through self-administrated questionnaires at baseline. Physical activity was assessed through the following question: 'How frequently do you engage in physical activity each week?', with categorized as never or having regular physical activity. Smoking and drinking status were obtained through the following questions: 'What is your smoking/drinking status?', with grouped as non-smoker and smoker/non-drinker and drinker. Additionally, air pollution was quantified as the annual mean PM_{2.5} (particulate matter with an aerodynamic diameter ≤ 2.5 μm) concentrations at a spatial resolution of 1- km². In detail, the hourly PM_{2.5} in situ observations, obtained from the China National Environmental Monitoring Center and measured using the tapered element oscillating microbalance or the β -attenuation method. Calculations of daily PM_{2.5} were estimated based on satellite data at a 1- km² resolution using space-time extremely randomized tree models, which can be obtained from the ChinaHighPM_{2.5} dataset (<https://weijing-rs.github.io/product.html>). Participants were allocated annual PM_{2.5} values spanning from 2009 to 2020, utilizing a nearest-neighbor matching methodology based on their residential addresses (Zhanget al., 2024b). We further used an existing global NO₂ (Nitrogen Dioxide) concentration dataset at a 1 km spatial resolution from a land use regression model (Mohegh, 2020). We also included exposure to light at night in our analysis given that it may serve as a potential indicator of urbanization and socioeconomic status (Morgan-Taylor, 2023; Nadybalet al., 2020; Xiao et al., 2023). The data on exposure to light at night were derived from a 1-km annual Prolonged Artificial Nighttime-light Dataset of China (PANDA-China) (Zhanget al., 2024a).

2.3. Ascertainment of outcomes

The outcomes for our study were mortality from CVD, including total CVD, IHD, MI, total stroke, ischemic stroke, and hemorrhagic stroke. Death data were obtained from Guangzhou Death Registry, Guangzhou Center for Disease Control and Prevention (GCDC) until December 31, 2020. According to the International Classification of Diseases, 10th edition (ICD-10), mortality from total CVD (I00–I99), IHD (I20–I25), MI (I21), stroke (I60–I64), ischemic stroke (I63), and hemorrhagic stroke (I60–I62) were evaluated. Person-years were estimated for patients from the start of the study until the date of death or 31 December 2020, whichever occurred first.

2.4. Statistical analysis

We used a Marginal Structural Cox Proportional Hazard (MS-Cox) model to estimate potential causal links between annual NDVI and total and specific CVD mortality. Specifically, generalized propensity scores (GPSs) were generated to then estimate stabilized inverse probability weights (IPW). Overall, this approach allows us to check the covariate balance across exposure levels (Wanget al., 2016). Furthermore, given the hypothesized role of PM_{2.5} as a time-varying confounder which can lead to exposure-confounder feedback when using traditional multi-variable approaches (Cole and Hernan, 2008; Moodie and Stephens, 2011), using MS model using IPW allows us to avoid such potential source of collider stratification bias, if present (Figure S1). We implemented a MS-Cox model with IPW. We considered three IPW methods including IPWs from generalized linear models (GLM-IPWs), entropy balancing (Ebal-IPWs), and Bayesian additive regression trees (Bart-IPWs) (Hughet al., 2010; Tübbicke, 2022). The average absolute correlation (AC) was calculated to assess the covariate balance on the weighted pseudo-population. Following traditional identification assumptions under the potential framework including consistency, positivity and exchangeability, the resulting hazard ratio (HR) can be interpreted as the potential effect of the time-varying NDVI exposure on mortality. Given the optimal balance of confounders (Figure S2), our

main Models used the method of Bart-IPWs to estimate the HRs for total and specific CVD mortality per 0.1 increase in annual average NDVI in the 500-m buffer. The confounders, including age, sex, ethnicity, marital status, medical insurance, education level, smoking status, drinking status, family history of CVD, physical activity, and time-varying annual mean PM_{2.5}, were determined using a directed acyclic graph (DAG) (Figure S3). Previous studies have identified physical activity as an effect modifier in the relationship between greenness and mortality (Coleman et al., 2022; James et al., 2016a). Therefore, in this study, we considered physical activity as a potential effect modifier to identify vulnerable populations or lifestyle behaviors that whether can derive greater benefits from green environments. Additional sensitivity analyses were conducted using a radial buffer of 250 m and 1,000 m around each participant's residence. Other sensitivity analyses involved further adjusting for time-varying annual mean NO₂ and exposure to light at night.

We also used different analytical approaches as sensitivity analyses to ensure that our conclusions were robust to the model specification. We implemented conventional Cox proportional hazards models with Model S1 and Model S2. In Model S1, we adjusted for sex (men and women), and age (continuous variable). In Model S2, we additionally adjusted for ethnicity (Han ethnicity and Minority), marital status (unmarried, married, and widowed/divorce), education level (primary school and below, second and high school, college degree or above), medical insurance (for urban workers, for urban residents, the new rural cooperative medical insurance, and others), family history of CVD (yes and no), smoking status (smoker and non-smoker), drinking (drinker and non-drinker), and physical activity (never and regular).

In addition, we evaluated effect modification (on the multiplicative scale) by conducting stratified analyses by age groups, sex, ethnicity, marital status, education level, physical activity, smoking status, and drinking status based on Model 3. We also conducted stratified analyses on exposure to PM_{2.5} and nighttime light to explore whether PM_{2.5} might attenuate the protective effects of greenness on CVD mortality. PM_{2.5} levels were stratified based on the median value, while exposure to nighttime light was stratified into quartiles based on the distribution of mortality cases. The presence of effect heterogeneity was evaluated by using a likelihood ratio test, which compared models with and without the interaction term between the categorical factors and the continuous variable of NDVI. To evaluate the effect modification on the additive scale, we calculated the relative risk due to interaction (RERI). A RERI value of 0 denotes the absence of additive interaction, whereas RERI ≥ 0 suggests a positive interaction. The interaction was deemed statistically significant when the 95 % confidence interval (CI) for RERI excluded the value 0 (Li and Chambless, 2007). While interactions on the multiplicative scale provide valuable information about relative risks, the additive scale offers additional context about absolute risk differences. The comprehensive approaches ensure that our findings are robust and relevant for both epidemiological research and practical public health applications (Knol and VanderWeele, 2012). All analyses were performed using R Software version 4.1.3 (The Foundation for Statistical Computing).

3. Results

3.1. Study population characteristics

Baseline characteristics stratified by total CVD mortality endpoints were showed in Table 1. The mean (standard deviation, SD) age of the total 748,209 participants was 45.8 (17.3) years; 366,949 (49.0 %) were men. During a median follow-up of 7.9 years, a total of 15,139 CVD deaths were detected. Compared to the control group, participants who died from CVD were inclined to be older, Han ethnicity, less educated, widowed, urban workers, have a family history of CVD, current smokers, ever drinkers, and exposed to a higher level of PM_{2.5}.

Table 1
Characteristics for the participants in the baseline (2009–2015) according to the follow-up total CVD mortality endpoints.

	Total (n = 748,209)	Control group (n = 733,070)	Mortality from CVD (n = 15,139)
Age, y	45.8 (17.3)	45.2 (16.9)	74.4 (12.3)
Sex			
Women	381,260 (51.0 %)	373,718 (51.0 %)	7,542 (49.8 %)
Men	366,949 (49.0 %)	359,352 (49.0 %)	7,597 (50.2 %)
Ethnic			
Han ethnicity	732,177 (97.9 %)	717,155 (97.8 %)	15,022 (99.2 %)
Minority	16,032 (2.1 %)	15,915 (2.2 %)	117 (0.8 %)
Education			
No school completed	7,564 (1.0 %)	6,641 (0.9 %)	923 (6.1 %)
Elementary school	74,030 (9.9 %)	69,538 (9.5 %)	4,492 (29.7 %)
Middle school	181,069 (24.2 %)	177,394 (24.2 %)	3,675 (24.3 %)
High school	364,178 (48.7 %)	358,849 (49.0 %)	5,329 (35.2 %)
College or above	121,368 (16.2 %)	120,648 (16.5 %)	720 (4.8 %)
Marital status			
Unmarried	161,888 (21.6 %)	160,755 (21.9 %)	1,133 (7.5 %)
Married	560,867 (75.0 %)	549,488 (75.0 %)	11,379 (75.2 %)
Widowed	17,837 (2.4 %)	15,428 (2.1 %)	2,409 (15.9 %)
Divorce	7,617 (1.0 %)	7,399 (1.0 %)	218 (1.4 %)
Medical insurance			
For urban workers	359,190 (48.0 %)	350,219 (47.8 %)	8,971 (59.3 %)
For urban residents	182,424 (24.4 %)	177,738 (24.2 %)	4,686 (31.0 %)
The new rural	40,229 (5.4 %)	40,063 (5.5 %)	166 (1.1 %)
Others	166,366 (22.2 %)	165,050 (22.5 %)	1,316 (8.7 %)
Family history of CVD			
No	631,007 (84.3 %)	619,950 (84.6 %)	11,057 (73.0 %)
Yes	117,202 (15.7 %)	113,120 (15.4 %)	4,082 (27.0 %)
Exercise frequency			
Never	320,598 (42.8 %)	312,955 (42.7 %)	7,643 (50.5 %)
Sometimes	243,432 (32.5 %)	240,736 (32.8 %)	2,696 (17.8 %)
Over once a week	71,178 (9.5 %)	69,657 (9.5 %)	1,521 (10.0 %)
Everyday	113,001 (15.1 %)	109,722 (15.0 %)	3,279 (21.7 %)
Smoking status			
Current smoker	34,101 (4.6 %)	33,071 (4.5 %)	1,030 (6.8 %)
Previous smoker	6,689 (0.9 %)	6,222 (0.8 %)	467 (3.1 %)
Non-smoker	707,419 (94.5 %)	693,777 (94.6 %)	13,642 (90.1 %)
Drinking status			
Drinker	65,319 (8.7 %)	63,676 (8.7 %)	1,643 (10.9 %)
Non-drinker	682,890 (91.3 %)	669,394 (91.3 %)	13,496 (89.1 %)
PM _{2.5} , µg/m ³	37.44 (8.72)	37.37 (8.71)	43.45 (7.39)
NDVI	0.22 (0.04)	0.22 (0.04)	0.21 (0.04)

*Values are presented as means (standard deviation) or n (percentage).

Abbreviations: CVD: cardiovascular disease, PM_{2.5}:particulate matter with an aerodynamic diameter ≤ 2.5 µm, NDVI: normalized difference vegetation index.

3.2. The effect of NDVI on cardiovascular mortality

Among the documented 15,139 CVD deaths, 6,800 were attributed to IHD, 3,181 to MI, 3,435 to stroke, 1,556 to ischemic stroke, and 1,317 to hemorrhagic stroke. In MS-Cox models, a potential casual protective association were detected between greenness and CVD mortality; for example, when using Bart-IPWs, 0.1 increase in annual average NDVI in the 500-m buffer led to a 9.3 % lower risk of total CVD mortality (HR 0.907, 95 % CI 0.859–0.957), 15.2 % lower risk of IHD mortality (HR 0.848, 95 % CI 0.782–0.919), 27.7 % lower risk of MI mortality (HR 0.723, 95 % CI 0.640–0.816), 9.9 % lower risk of stroke mortality (HR 0.901, 95 % CI 0.804–1.010), 18.5 % lower risk of ischemic stroke mortality (HR 0.815, 95 % CI 0.684–0.972), and 7.4 % lower risk of hemorrhagic stroke mortality (HR 0.926, 95 % CI 0.771–1.113). Results were consistent when using other different MS-Cox models: Ebal-IPWs, and GLM-IPWs (Fig. 1). Sensitivity analyses indicated results were similar for NDVI in the 250-m and 1,000-m buffer (Table S1). Based on the fully-adjusted models, further adjustment for time-varying annual mean NO₂ and exposure to light at night did not yield significant changes. When using Bart-IPWs, a 0.1 increase in annual average NDVI in the 500-meter buffer still corresponded to a 9.0 % lower risk of total CVD mortality (HR 0.910, 95 % CI 0.858–0.965) (Table S2). Additionally, conventional Cox models indicated an inverse association between greenness and CVD mortality, although the relationship was slightly attenuated in the fully-adjusted models (Model S2) in comparison to the age- and sex-adjusted model (Model S2) (Table S3).

3.3. Effect modification by demographics and lifestyles

The effect of NDVI on cardiovascular mortality was further accessed stratified by multiple demographics and lifestyles characteristics by using the MS-Cox models with Bart-IPWs. It was observed a higher protective effect of residential greenness on CVD mortality among people who were married (HR 0.881, 95 % CI 0.828–0.937) in comparison to those unmarried (HR 0.919, 95 % CI 0.721–1.170) and widowed/divorce (HR 1.128, 95 % CI 0.979–1.301) (*P* interaction < 0.001) (Table 2). With regard to the specific CVD mortality, it was shown a stronger protective effect of exposure to a higher level of NDVI on IHD and MI mortality among the non-smokers than the smokers (*P* interaction = 0.008 and < 0.001, respectively), where the protective associations of greenness with IHD and MI mortality was significantly stronger among the non-smokers (HR 0.828, 95 % CI 0.760–0.903 and HR 0.685, 95 % CI 0.603–0.779, respectively) compared with the smokers (Fig. 2A and Fig. 2B). Furthermore, drinking status may modify the association between greenness and MI mortality (*P* interaction = 0.038), where a potential casual protective link was observed among the non-drinkers, with 26.9 % lower risk of MI mortality (HR 0.681, 95 % CI 0.598–0.776) based on a 0.1 increase in annual average NDVI in the 500-m buffer (Fig. 2B). Furthermore, we calculated the RERIs of NDVI and multiple demographics and lifestyles on CVD mortality and found a negative additive interaction for NDVI and age, but a positive additive interaction for NDVI and marital status (Table 3).

We also performed a subgroup analysis for the association of NDVI with CVD mortality stratified by PM_{2.5} and exposure to light at night. Interaction analysis showed that PM_{2.5} may modify the association between greenness and total CVD (*P* interaction < 0.001). Only under the median value of PM_{2.5}, a potential casual protective association was observed between greenness and risk of CVD mortality, with 21.6 % lower risk of CVD mortality (HR 0.784, 95 % CI 0.665–0.925) based on a 0.1 increase in annual average NDVI in the 500-m buffer (Table S4). For total CVD, we found a positive additive interaction with a RERI of 5.72 (95 % CI: 3.94, 7.50) for increasing NDVI exposure assessed at a higher PM_{2.5} level. Similarly, we found that exposure to light at night may also modify the association between greenness and total CVD mortality (*P* interaction < 0.001), where a potential protective effect was observed for greenness under a high level of exposure to light at night (Table S5).

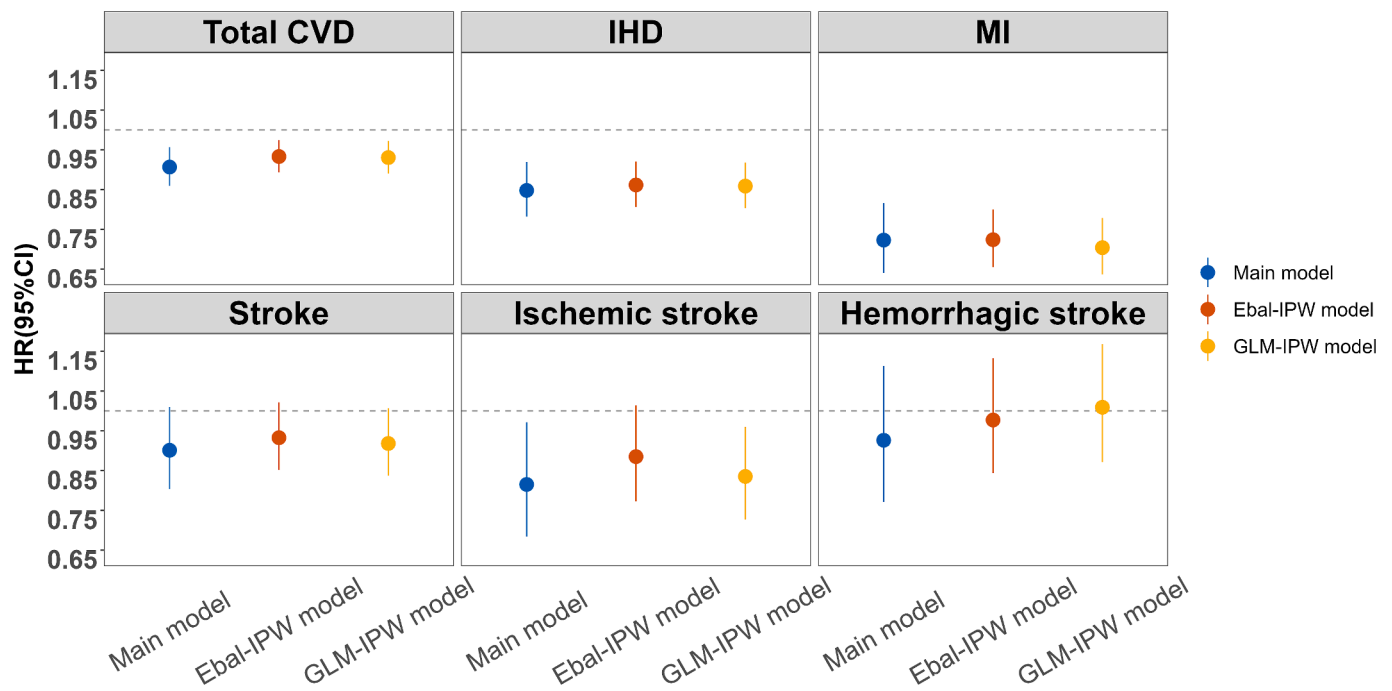


Fig. 1. Residential greenness (0.1 unit increase in 500 m annual average NDVI) and the risk of total and specific CVD mortality according to MS-Cox models. *Models were initially adjusted for age, sex, ethnic, education, marital status, medical insurance, family history of CVD, smoking status, drinking status, physical activity, and PM_{2.5}, and subsequently refitted with the marginal structural Cox model (MS-Cox model): Main model, MS-Cox model using IPWs based on Bayesian additive regression trees. Ebal-IPW model, MS-Cox model using inverse probability weights (IPWs) based on entropy balancing; GLM-IPW model, MS-Cox model using IPWs based on generalized linear models. Abbreviation: NDVI: Normalized Difference Vegetation Index; CVD: cardiovascular disease; IHD: ischemic heart disease; MI: myocardial infarction.

Table 2

Associations (Hazard Ratios and 95 % confidence intervals) between residential greenness (0.1 unit increase in 500 m annual average Normalized Difference Vegetation Index) and total cardiovascular mortality, stratified by demographics and lifestyle factors.

Variables	Cases (n)	HR (95 %CI)	P interaction
Age			0.714
<65 years	2,995	0.987 (0.872–1.117)	
≥65 years	12,144	0.854 (0.805–0.906)	
Sex			0.372
Men	7,597	0.932 (0.863–1.007)	
Women	7,542	0.891 (0.825–0.962)	
Marital status			<0.001
Unmarried	1,133	0.919 (0.721–1.170)	
Married	11,379	0.881 (0.828–0.937)	
Widowed/Divorce	2,627	1.128 (0.979–1.301)	
Education			0.378
Primary school and below	5,415	0.957 (0.871–1.052)	
Second and high school	9,004	0.889 (0.827–0.956)	
College degree or above	720	0.851 (0.651–1.112)	
Smoking status			0.215
Non-smoker	13,642	0.904 (0.853–0.957)	
Smoker	1,497	1.006 (0.849–1.191)	
Drinking status			0.907
Non-drinker	1,643	0.899 (0.848–0.953)	
Drinker	13,496	0.963 (0.840–1.103)	
Physical activity			0.300
Never	7,643	0.901 (0.834–0.973)	
Regular	7,496	0.915 (0.847–0.988)	

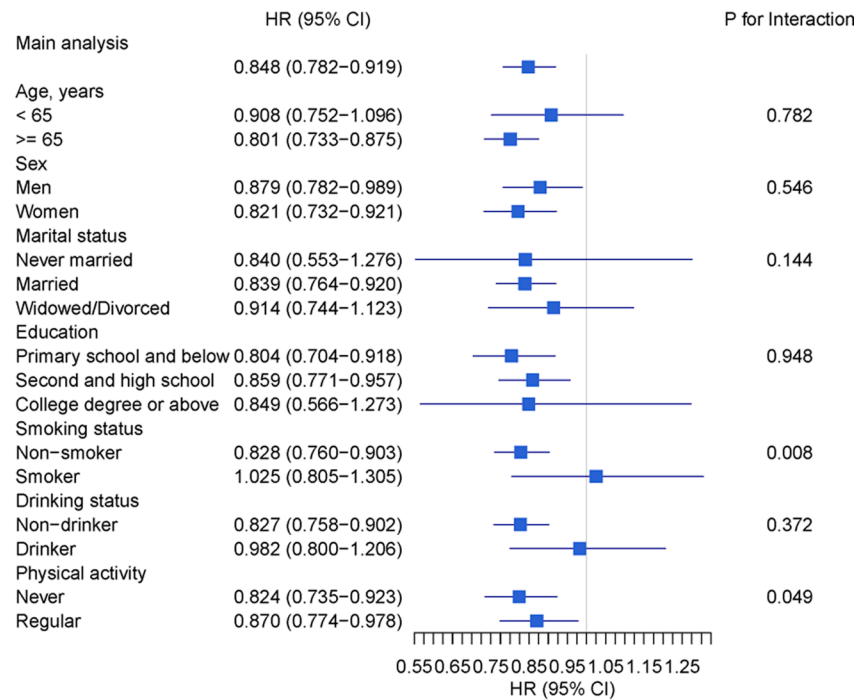
*Models were initially adjusted for age, sex, ethnic, education, marital status, medical insurance, family history of CVD, smoking status, drinking status, physical activity, and PM_{2.5}, and subsequently refitted with the marginal structural Cox model using inverse probability weights based on Bayesian additive regression trees. The P interaction shows the interaction effects between residential greenness and corresponding factors.

4. Discussion

Our study evaluated the possible causative links between residential greenness exposure and the risk of CVD mortality in China. In this prospective cohort study of Southern Chinese, we found a protective relationship between residential greenness and CVD mortality, with a 9.3 % lower risk for total CVD mortality based on a 0.1 increase in annual average NDVI in the 500-m buffer. These findings were strongest for MI, IHD, and ischemic stroke mortality. Demographics, including age and marital status may modify the association between greenness and CVD mortality. Lifestyle factors, including smoking and drinking may be modifiers, where the protective effect was higher among non-smokers and non-drinkers for MI mortality and ischemic stroke mortality, respectively. The results remained robust on the causal link between residential greenness exposure and risk of CVD mortality through multiple modeling approaches and sensitivity analyses.

Our study indicated a protective association between residential greenness and CVD mortality in China, a developing country, is consistent with most previous studies conducted in developed regions, such as Hong Kong, Swiss, Dutch, Canada, and Spain (Crouse et al., 2017; Gullonet et al., 2023; Klompaker et al., 2021; Vienneuet et al., 2017; Wanget al., 2017). For example, evidence from Hong Kong Chinese showed that every 0.1 increase in green space coverage within a 300 m radius buffer associated with 11.2 % decrease in risk of CVD mortality (HR 0.888, 95 % CI 0.817–0.964) (Wanget al., 2017). Another cross-sectional study from Spain observed that for every increase in 0.1 units of NDVI at 1000 m there was a 16 % reduction in CVD risk (Gullonet et al., 2023). In developed regions, individuals with higher socioeconomic status tend to reside in areas with more greenness. However, the situation in China is often the opposite due to rapid urbanization, where individuals with lower socioeconomic status often live in rural areas with more greenness. By stratifying results based on exposure to light at night, we found that this association was particularly significant in areas with high light exposure. Since nighttime light is an

(A)



(B)

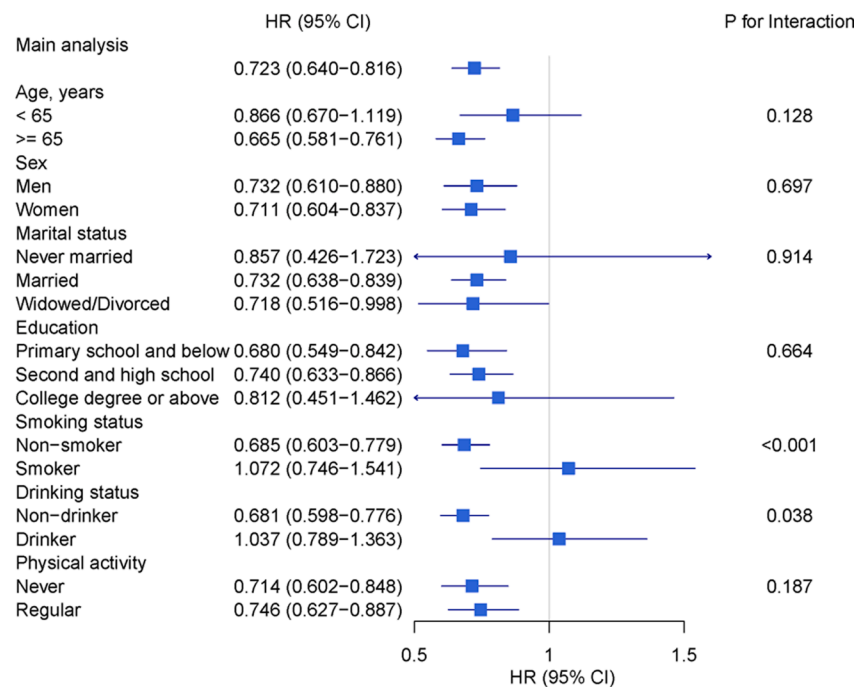


Fig. 2. Associations (Hazard Ratios and 95 % confidence interval) between residential greenness (0.1 unit increase in 500 m annual average NDVI) and mortality form IHD (A), MI (B), stroke (C), stratified by demographics and lifestyle factors. *Models were initially adjusted for age, sex, ethnic, education, marital status, medical insurance, family history of CVD, smoking status, drinking status, physical activity, and PM_{2.5}, and subsequently refitted with the marginal structural Cox model using inverse probability weights based on Bayesian additive regression trees. The P interaction shows the interaction effects between residential greenness and corresponding factors. **Abbreviation:** NDVI: Normalized Difference Vegetation Index; IHD: ischemic heart disease; MI: myocardial infarction.

(C)

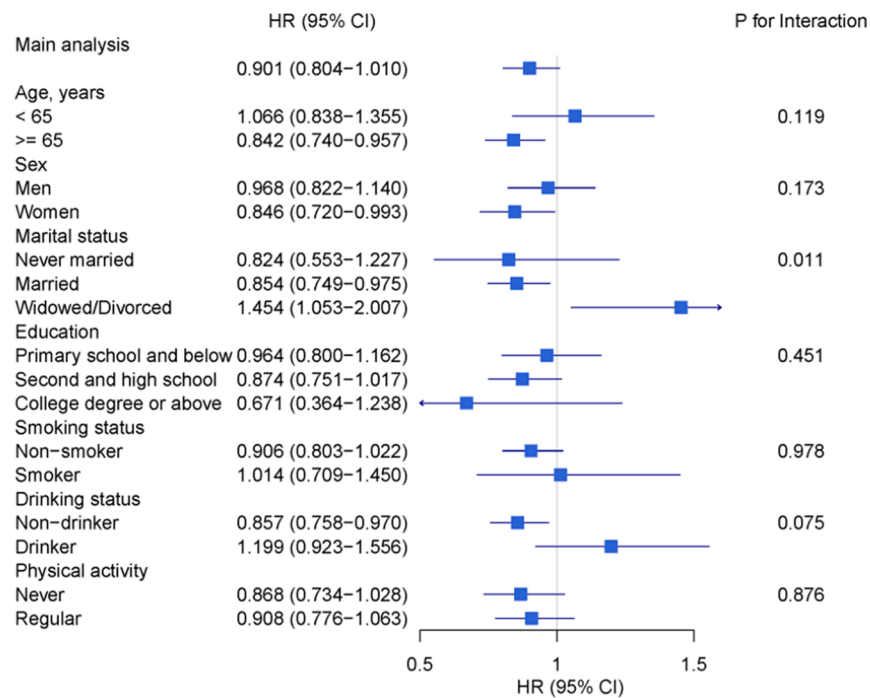


Fig. 2. (continued).

Table 3
RERI of NDVI and multiple demographics and lifestyles characteristics on total and specific CVD mortality.

	RERI (95 % CI)					
	Total CVD	IHD	MI	Stroke	Ischemic stroke	Hemorrhagic stroke
Demographics						
Age	-7.64 (-10.57, -4.71)	-10.83 (-15.18, -6.47)	-13.31 (-18.84, -7.77)	-8.59 (-13.87, -3.31)	-6.79 (-15.58, 2.01)	-12.94 (-20.14, -5.74)
Sex	-0.02 (-0.57, 0.53)	0.04 (-0.71, 0.80)	0.21 (-0.70, 1.13)	-0.22 (-1.42, 0.98)	-0.12 (-1.79, 1.55)	-0.37 (-2.37, 1.64)
Marital status	3.35 (1.61, 5.09)	2.08 (-0.39, 4.55)	-0.92 (-5.35, 3.51)	8.89 (4.73, 13.05)	18.87 (10.05, 27.7)	7.12 (0.24, 14.00)
Education	0.04 (-1.12, 1.20)	0.41 (-1.04, 1.85)	0.71 (-0.84, 2.27)	-0.18 (-2.87, 2.51)	-2.92 (-7.98, 2.13)	2.10 (-3.16, 7.35)
Lifestyles						
Smoking status	0.31 (-0.54, 1.16)	1.02 (-0.13, 2.17)	1.39 (0.06, 2.73)	-0.08 (-1.86, 1.69)	-0.22 (-2.70, 2.27)	0.08 (-2.73, 2.90)
Drinking status	0.05 (-0.70, 0.79)	0.29 (-0.65, 1.22)	0.63 (-0.42, 1.68)	0.91 (-0.64, 2.46)	1.36 (-0.60, 3.32)	-0.33 (-2.80, 2.14)
Physical activity	0.18 (-0.36, 0.72)	0.38 (-0.31, 1.07)	0.28 (-0.64, 1.20)	-0.01 (-1.23, 1.21)	0.07 (-1.61, 1.74)	-0.46 (-2.71, 1.79)

* Models were initially adjusted for age, sex, ethnic, education, marital status, medical insurance, family history of CVD, smoking status, drinking status, and physical activity, and subsequently refitted with the marginal structural Cox model using inverse probability weights based on Bayesian additive regression trees.

Abbreviation

RERI: relative excess risks due to interaction; CI, confidence interval; NDVI: Normalized Difference Vegetation Index; CVD: cardiovascular disease; IHD: ischemic heart disease; MI: myocardial infarction.

indicator representing urban development(Chen and Nordhaus, 2011; Zhang and Seto, 2011), our results suggested that in more urbanized areas, the protective effect of increasing green space against CVD mortality might be more pronounced. Therefore, our study from China reinforces evidence to clarify the protective effect of residential greenness on CVD.

The potential mechanisms underlying the relationship deserve discussion. First, greenness could lead to better immune function because the plants encountered by people are filled with various micro-organisms(Rook, 2013). Immune function could affect cardiovascular health through certain mechanisms such as inflammation, which may damage blood vessels and result in conditions including atherosclerosis and hypertension (Frostegård, 2013). Second, residential greenness is associated with reduced oxidative stress through the activation of the sympathetic nervous system and hypothalamus-pituitary axis. This provides

a restorative and calming effect that has been linked to lower stress levels, improved psychological well-being, and contributes to better cardiovascular health(Yeager et al., 2018; Zhuet al., 2023). A meta-analysis of randomized controlled trials (RCTs) revealed that exposure to green spaces, in comparison to non-green spaces, was associated with a reduction in adverse emotions, specifically fatigue, with an effect size of -0.84 (95 % CI: -1.15 to -0.54). Moreover, it was linked to decreased physiological markers, such as heart rate levels, with an effect size of 0.60 (95 % CI: -0.90 to -0.31)(Songet al., 2022). It is also possible that areas with substantial greenness, such as parks or yards, replace potential sources of pollution that might otherwise have been present in those locations(Browning et al., 2022). Other possible mechanisms may include higher angiogenic capacity, temperature regulation, sleep improvement, circadian alignment, and social interactions and community cohesion(Billingset al., 2020; Jameset al., 2015).

The association between greenness and CVD mortality could be influenced by demographics. In a cohort study involving U.S. women, the association was not observed to be significant (James et al., 2016b), which could potentially be attributed to sex differences in perceptions and usage of residential greenness (Richardson and Mitchell, 2010). However, we did not detect statistically significant difference by sex in our Chinese population, indicating that greenness impacts women and men equally. Particularly, we found a negative additive interaction for NDVI and age on CVD mortality, indicating that the public health consequences of an intervention on residential greenness would be larger for participants who are young. A longitudinal cohort study among the elderly aged above 80 in China showed a strong protective association for contemporaneous greenness and mortality. Individuals in the highest quartile of NDVI had a 27 % decreased mortality than those in the lowest quartile within a radial buffer of 250 m (HR 0.73, 95 % CI 0.70–0.76) (Jiet et al., 2019). The older adults are more susceptible to the effects of environmental hazards, while residential greenness can protect them from air pollution- and heat-related cardiovascular stress in their daily life (Achebak et al., 2019; Changet et al., 2022; Silveira et al., 2021). Consequently, promoting access to green spaces and creating age-friendly environments may offer potential benefits for the cardiovascular health of older adults in the context of urbanization and population aging. Furthermore, we found marital status may modify the causal association between residential greenness and CVD mortality. Similarly, a national cohort study from Canada supported the effect modification by personal marital status on urban greenness and mortality, where a higher protective effect of greenness was observed on mortality among people who were married. The reasons behind these findings may stem from the voluntary choice of unmarried individuals with comparatively lower socioeconomic, psychosocial statuses, and unhealthy lifestyles to marry, as well as from the unequal availability of natural and societal resources among different subgroups of unmarried individuals (Leunget et al., 2022).

In addition, we examined the effect modification by lifestyle factors, including smoking, drinking, and physical activity. Non-smokers and non-drinkers, who do not experience the detrimental effects of smoking or drinking on their cardiovascular system, may have a healthier baseline cardiovascular status, making them more responsive to the beneficial effects of greenness. Previous research has underscored physical activity as an effect modifier in the links between greenness and mortality. For instance, in the U.S. Nurses' Health Study cohort, NDVI-mortality associations were most pronounced among highly active women (James et al., 2016a). Similarly, another cohort study reported a significantly negative association between greenness and mortality exclusively among highly active individuals (Coleman et al., 2022). Recognizing the stronger protective effect of greenness against CVD mortality among individuals with healthier lifestyles highlights the potential benefits of integrating nature-based and behavioral interventions into public health efforts.

5. Limitations

This study is one of the few to use various causal inference approaches by controlling confounding or other sources of bias to investigate the association between residential greenness and CVD mortality, offering robust evidence on that residential greenness might be related to lower CVD mortality, especially for developing countries with the accelerated urbanization and tremendous burden from CVD. Other strengths include its prospective cohort design, large sample size, standardized diagnosis, and long follow-up duration. However, several limitations should be addressed. First, NDVI does not capture the type of greenness (e.g., park or tree cover), access to green spaces, or safety of nearby green spaces. Also, this analysis is subject to the issues related to the modifiable areal unit problem (Nouriet et al., 2017). Second, causal inference models are typically built on the assumption of no unmeasured confounders, which can be challenging to definitively rule out. Some

confounders, such as diet factors, and cardiovascular comorbidities were not included in this present study. Moreover, in this large cohort study, questionnaire data were only collected at baseline, which did not account for potential changes during the follow-up period. Third, we were not able to identify movers, although this issue is likely to be minimized in our study. We included community residents who signed health service contracts for physical checkups at local healthcare centers. They were generally permanent residents identified through official residential records and enrolled in China's basic public health service project. Last, the impacts of climate change, as well as indoor and ambient air pollution, are yet to be fully explored.

6. Conclusion

In conclusion, our large-scale prospective cohort study, combined with state-of-the-art causal inference techniques, has revealed potential causal links between increased residential greenness exposure and a reduced risk of CVD mortality in South China. Older adults, people who were married, and individuals having healthier lifestyles (particularly non-smokers and non-drinkers) were more likely to benefit from greenness. Our study has important public health implications that improving access to greenness, promoting healthier lifestyles, and addressing environmental factors can have a positive impact on cardiovascular health and contribute to healthier communities overall.

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CRedit authorship contribution statement

Xiaowen Wang: Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Yuqin Zhang:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Benmarhnia Tarik:** Writing – review & editing, Methodology. **Kai Zhang:** . **Shao Lin:** Writing – review & editing, Methodology. **Xinlei Deng:** Writing – review & editing, Methodology. **Haogao Gu:** Writing – review & editing. **Wenjing Wu:** Writing – review & editing, Data curation. **Xiao Lin:** Writing – review & editing. **Zhicheng Du:** Writing – review & editing. **Ying Wang:** Writing – review & editing. **Yanji Qu:** Writing – review & editing. **Ziqiang Lin:** Writing – review & editing. **Man Zhang:** Writing – review & editing. **Yongqing Sun:** Writing – review & editing. **Guang-hui Dong:** Writing – review & editing, Methodology. **Yongyue Wei:** Writing – review & editing, Supervision, Methodology. **Wangjian Zhang:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Yuantaohao:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

The authors do not have permission to share data. The NDVI dataset is publicly available from the Land Processing Distributed Active Archive Center (<https://lpdaac.usgs.gov>). The ChinaHighPM2.5 dataset is open access and freely available to all users from <https://weijing-rs.github.io/product.html>. The cohort data are available from the corresponding authors upon reasonable request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2024.108894>.

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