Do Exposures to Green Space Reduce the Risk of Hypertension?

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Research

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Abstract

Background: Few epidemiological research examined the effects of greenness on cardiovascular diseases in developing countries. We aimed to explore the relationships between green space and hypertension and blood pressure in China.

Methods: This cross-sectional study recruited 39, 259 adults from five counties in central China. Blood pressure measurements were performed according to a standardized protocol. Normalized difference vegetation index (NDVI) and enhanced vegetation index (EVI) was used to assess the exposure to greenness. We used mixed linear models to test greenspace-cardiovascular disease outcome pathways.

Results: Higher green space was related to decreased hypertension prevalence and blood pressure. After fully adjusting the covariates, each interquartile range increase in $NDVI_{500m}$ and EVI_{500m} were related to an 8% decrease in odds of hypertension. The changes in SBP and DBP (95% CI) were - 0.88 mm Hg (- 1.17, - 0.58) and - 0.64 mm Hg (- 0.82, - 0.46) for NDVI, and - 0.79 mm Hg (- 1.14, - 0.45) and - 0.67 mm Hg (- 0.87, - 0.46) for EVI, respectively. Subgroup analyses showed that the effects of green space were more pronounced in males, smokers, and drinkers.

Conclusions: The effects of green space may reduce the risk of hypertension. Also, behavioral factors may affect this potential pathway.

1 Introduction

Hypertension is the major cause of cardiovascular disease [1]. In China, hypertension prevalence was 23.2% and hypertension standardized treatment rate (aged 35 to 75 years) was only 22.9%, reflecting inadequate control of hypertension [2, 3]. From the perspective of public health, community-level behavioral interventions with hypertension control are more effective than individual-level interventions [4]. Thus, exploration of the associations of possible population interventions with hypertension in China is crucial for national public health policy.

Residing in green space with a high level of air quality potentially leads to increasing frequency of physical activity and decreasing level of stress, which can further improve cardiovascular outcomes [5, 6]. Growing epidemiological studies investigated the relationships between green space and blood pressure in recent years. EM Bijnens, TS Nawrot, RJ Loos, M Gielen, R Vlietinck, C Derom and MP Zeegers [7] indicated that higher greenspace was related to lower night SBP. Similarly, X Xiao, BY Yang, LW Hu, I Markevych, MS Bloom, SC Dharmage, B Jalaludin, LD Knibbs, J Heinrich, L Morawska, et al. [8] concluded that higher green space was related to lower hypertension prevalence. However, there have also been inconsistent findings showing no significant association of greenness with hypertension [9–11]. More disadvantaged populations are already at greater risk of hypertension, thus investigating the relationships between green space and blood pressure is a pressing need for possible interventions. A study of 249, 405 participants in the United States observed negative associations of green space with hypertension in lower-income neighborhoods (OR = 0.86, 95% CI: 0.83, 0.89) but positive associations in

higher-income neighborhoods (OR = 1.05, 95% CI: 1.02, 1.08) [12]. However, epidemiological research examing the relationships between green space and blood pressure remained limited in developing countries [13, 14].

This study aimed to examine greenspace-cardiovascular disease outcome pathways and effect modifiers in the relationships.

2 Methods

2.1 Study population

Our study included the participants from the Rural Cohort Study in China (ChiCTR-OOC-15006699). We have published a detailed profile elsewhere [15]. Briefly, this study recruited participants using multi-stage random cluster sampling (The flowchart of participant recruitment was shown in Fig. 1). All participants lived in five rural counties (Xinxiang, Suiping, Yuzhou, Yima, and Tongxu) in central China (Fig. 2). Overall, we obtained baseline survey data of 39, 259 participants. 165 participants were excluded due to missing the outcome variables. Finally, we included 39,094 participants in the analyses. Before the survey and physical examination, the study population has signed informed consent forms. The study was approved by the Ethics Committee of Zhengzhou University. The study was reported according to the guideline (The checklist of guidelines was shown in Table S1).

2.2 Outcome variables

We used electronic sphygmomanometers to measure blood pressure and calibrated it before each measurement according to a standardized protocol [16]. After participants rest for five minutes, we conducted blood pressure measurements. Before the physical examination, smoking, drinking, and engaging in physical activity were not allowed for at least half an hour. Talking was not allowed during the blood pressure measurement. The study population was diagnosed with hypertension if they had taken antihypertensive medicine or they had been diagnosed with hypertension by a professional clinician or SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg [17].

2.3 Greenness exposure assessment

Individual exposure to green space was estimated using NDVI and EVI. NDVI was widely used for historical and climate applications [18] and EVI could minimize canopy-soil variations and improved sensitivity over dense vegetation conditions [19, 20]. Therefore, the two vegetation indices could effectively characterize vegetation states and processes, which have been frequently used worldwide. We downloaded the vegetation index database of MODIS (MOD13A1). They were calculated from reflectance in red, near-infrared, and blue wavebands. High densities of green space showed higher vegetation index values [21]. The three-year average NDVI and EVI (500-m buffer) were used in the main analyses.

2.4 Air pollution assessment

Individual exposure to particulate matter with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$) was estimated using the spatiotemporal models at a 0.1° × 0.1° spatial resolution. We had described the model elsewhere [22]. Briefly, we obtained air pollutant monitoring station data from the China Meteorological Administration. MODIS Collection 6 provided aerosol optical depth data. The spatiotemporal models showed high predictive accuracy and the 10-fold cross-validation R^2 for annual $PM_{2.5}$ was 86% [23].

2.5 Covariates

Baseline data included demographic, socioeconomic, behavioral, and health status covariates. Socioeconomic covariates included district (Xinxiang, Suiping, Yuzhou, Yima, and Tongxu), educational level (low, medium, high), marital status (married vs. unmarried), and income (< = 500 yuan/month, 500–1000 yuan/month, >= 1000 yuan/month). Behavioral factors included smoking, drinking, diet, and exercising. Information on diet and exercising was obtained from the standard questionnaire [24, 25]. Health status covariates included family history of hypertension.

2.6 Statistical analysis

The mixed linear models were employed to investigate the relationships between green space and hypertension and blood pressure. Model one was not adjusted for covariates. Model two was adjusted for demographic, socioeconomic, behavioral, and health status factors, and body mass index. Based on Model two, Model three additionally adjusted for $PM_{2.5}$. Survey sites were adjusted as a random effect in the three models [26]. To test potential modifications in the associations, we performed interaction analyses. If the *P*-value for interaction term < 0.05, the effect modifications were considered to be statistically significant.

Several sensitivity analyses were conducted: (1) We explored the associations of green space with hypertension and blood pressure (1000-m buffer). (2) To examine individual exposure to green space, we investigated the relationships using $NDVI_{500m}$ for different years. (3) The people who had taken anti-hypertensive medicines and all hypertensive patients were excluded to eliminate the causal effect of hypertension on blood pressure. All the analyses were performed using R 4.0.2.

3 Results

This study included 39, 094 participants and 60.6% (n = 23, 677) were females (Table 1). Table S2 showed detailed information in five counties. Among 39, 094 participants, 19.1% (n = 7458) were smokers, 18.0% (n = 7053) were drinkers, 19.1% (n = 7461) had a high-fat diet, and 32.3% (n = 12, 614) reported a low level of physical activity. The three-year average NDVI and EVI (500-buffer) were 0.48 and 0.34 units, respectively (Table 2). The distributions of vegetation indices stratified by region were shown in Table S3. Among the 12, 763 hypertensive patients, 61.3% of them were self-reported, 38.7% were diagnosed by physicians. The prevalence of hypertension was 32.6% and 6, 267 patients had taken antihypertensive drugs within two weeks before the survey.

Table 1
Characteristics of participants.

Characteristics	All	Hypertension	Non-hypertension
N	39094	12763	26331
Age (n, %)			
< 65	28817 (73.7)	7844 (61.5)	20973 (79.7)
≥65	10277 (26.3)	4917 (38.5)	5358 (20.3)
Sex (n, %)			
Male	15417 (39.4)	5094 (39.9)	10323 (39.2)
Female	23677 (60.6)	7669 (60.1)	16008 (60.8)
Educational level (n, %)			
Low	17482 (44.7)	6793 (53.2)	10689 (40.6)
Medium	15592 (39.9)	4395 (34.4)	11197 (42.5)
High	6020 (15.4)	1575 (12.3)	4445 (16.9)
Marital status (n, %)			
Married	35105 (89.8)	11121 (87.1)	23984 (91.1)
Unmarried	3989 (10.2)	1642 (12.9)	2347 (8.9)
Income (n, %)			
<=500 yuan/month	13944 (35.7)	5045 (39.5)	8899 (33.8)
500–1000 yuan/month	12850 (32.9)	4200 (32.9)	8650 (32.9)
>=1000 yuan/month	12300 (31.4)	3518 (27.6)	8782 (33.4)
Smoking (n, %)			
Never	28462 (72.8)	9353 (73.3)	19109 (72.6)
Former	1819 (4.7)	1333 (10.4)	1841 (7.0)
Current	7458 (19.1)	2077 (16.3)	5381 (20.4)
Drinking (n, %)			
Never	30222 (77.3)	9765 (76.5)	20457 (77.7)
Former	1819 (4.7)	709 (5.6)	1110 (4.2)
Current	7053 (18.0)	2289 (17.9)	4764 (18.1)
High-fat diet (n, %)			

Characteristics	All	Hypertension	Non-hypertension
No	31633 (80.9)	10754 (84.3)	20879 (79.3)
Yes	7461 (19.1)	2009 (15.7)	5452 (20.7)
Exercising (n, %)			
Low	12614 (32.3)	4783 (37.5)	7831 (29.7)
Medium	14768 (37.8)	4377 (34.3)	10391 (39.5)
High	11712 (29.9)	3603 (28.2)	8109 (30.8)
Family history of hypertension (n, %)			
No	31530 (80.7)	9248 (72.5)	22282 (84.6)
Yes	7564 (19.3)	3515 (27.5)	4049 (15.4)

Table 2
Distributions of vegetation indices.

Vegetation index	Mean	Min	Quantiles			Max	Interquartile range
			Q25	Q50	Q75		
$NDVI_{500m}$	0.48	0.15	0.45	0.50	0.53	0.59	0.08
$NDVI_{1000m}$	0.49	0.18	0.45	0.52	0.54	0.61	0.09
EVI_{500m}	0.34	0.10	0.31	0.35	0.39	0.44	0.09
EVI_{1000m}	0.34	0.10	0.30	0.36	0.39	0.44	0.09

Abbreviations: NDVI, the normalized difference vegetation index; EVI, the enhanced vegetation index.

Table 3 showed the relationships between green space and hypertension and blood pressure. In model one, each 0.08 units increment in NDVI was related to an 11% decrease in odds of hypertension, and a decrease of 1.18 and 1.08 mmHg in SBP and DBP, respectively. In model three, each 0.08 units increase in NDVI was related to an 8% decrease in odds of hypertension, and reductions in SBP of 0.88 and DBP of 0.64 mmHg, respectively.

Table 3
The relationships between green space and hypertension and blood pressure.

Vegetation index	Hypertension		Systolic blood pressure		Diastolic blood pressure	
	Odds ratio (95% CIs)	*P*	Changes in mmHg (95% CIs)	*P*	Changes in mmHg (95% CIs)	*P*
$NDVI_{500m}$						
Model 1[a]	0.89 (0.86, 0.92)	< 0.001	− 1.18 (− 1.49, − 0.87)	< 0.001	− 1.08 (− 1.26, − 0.90)	< 0.001
Model 2[b]	0.91 (0.87, 0.94)	< 0.001	− 0.93 (− 1.21, − 0.66)	< 0.001	− 0.79 (− 0.96, − 0.63)	< 0.001
Model 3[c]	0.92 (0.88, 0.95)	< 0.001	− 0.88 (− 1.17, − 0.58)	< 0.001	− 0.64 (− 0.82, − 0.46)	< 0.001
EVI_{500m}						
Model 1[a]	0.89 (0.85, 0.92)	< 0.001	− 1.07 (− 1.41, − 0.72)	< 0.001	− 1.11 (− 1.32, − 0.91)	< 0.001
Model 2[b]	0.91 (0.87, 0.95)	< 0.001	− 0.88 (− 1.18, − 0.57)	< 0.001	− 0.86 (− 1.04, − 0.67)	< 0.001
Model 3[c]	0.92 (0.88, 0.96)	< 0.001	− 0.79 (− 1.14, − 0.45)	< 0.001	− 0.67 (− 0.87, − 0.46)	< 0.001

Abbreviations: NDVI, the normalized difference vegetation index; CI, confidence interval; EVI, the enhanced vegetation index.

Note: Interquartile range for three-year average $NDVI_{500m}$ and EVI_{500m} were 0.08 and 0.09 units.

[a] Model 1: no adjustment for other covariates.

[b] Model 2: Demographic, socioeconomic, behavioral, health status factors, and body mass index were adjusted.

[c] Model 3: Demographic, socioeconomic, behavioral, health status factors, body mass index, and $PM_{2.5}$ were adjusted.

We then conducted the subgroup analyses to examine the interaction effects of potential modifiers (Fig. 3). Table S4 and Table S5 showed detailed information. The effects of green space were more pronounced in males, smokers, and drinkers ($P_{interaction} < 0.05$). For instance, each interquartile range (IQR) increment in NDVI was related to a 13% decrease in odds of hypertension in males, whereas 5% in females ($P_{interaction} = 0.005$), and it was also associated with a reduction of 1.30 mmHg in SBP in males, whereas 0.63 mmHg in females ($P_{interaction} = 0.002$). Besides, no significant effect modification was found in covariates including high-fat diet, physical activity, and Body mass index.

In sensitivity analyses, using the NDVI and EVI (1000-m buffer) showed similar results (Table S6), and using $NDVI_{500m}$ values from different years was generally consistent with using the values of three-year

average (Table S7). Changes in SBP and DBP remained similar when we excluded the people who had taken anti-hypertensive medicines (Table S8). After excluding all hypertensive patients, the relationships between green space and blood pressure were attenuated but remained significant, with an IQR (0.09 units) increase in $NDVI_{500m}$ related to 0.40 and 0.32 mmHg decrease in SBP and DBP, respectively.

4 Discussion

It was one of few studies exploring the relationships between green space and hypertension and blood pressure in developing countries. The effects of green space may reduce the risk of hypertension. Besides, sex, smoking, and drinking could further modify the associations. The studies of associations between green space and blood pressure are still in the initial stage and lack of systematic studies in developing countries. Given increasing environmental pollution accompanied by the accelerated urbanization process and high prevalence of hypertension in China as well as other developing countries, our findings may be particularly important for public health.

Some studies reported similar results [6, 8, 13, 27–30]. Our study showed that an IQR (0.08 units) increment in $NDVI_{500m}$ was significantly associated with an 8% decrease in odds of hypertension. A study conducted in the urban area of the United States including 249, 405 indicated that a 0.1-units increase in $NDVI_{1000m}$ was related to a 7% decrease in odds of hypertension [12]. Additionally, AM Dzhambov, I Markevych and P Lercher [18] reported that each IQR (0.16 units) increase in $NDVI_{500m}$ was related to a 36% decrease in odds of hypertension based on a study of 555 adults in an Alpine valley of Austria. However, some studies showed inconsistent findings. A study including 3,063 women in Germany reported null associations [11]. A meta-analysis of 4 studies reported no significant association of greenness with hypertension incidence [31]. Differences in characteristics of participants, study setting, greenness exposure assessment, statistical models, and adjustment for covariates may explain the inconsistency.

We found that higher green space was related to lower blood pressure. Our findings were in line with a cross-sectional study of 3,150 in India [14] showing an interquartile range increase in $NDVI_{250m}$ related to a decrease in SBP of 4.3 mmHg and a decrease in DBP of 1.2 mmHg, respectively. However, several previous studies showed inconsistent results [7, 8, 18, 21]. BY Yang, I Markevych, MS Bloom, J Heinrich, Y Guo, L Morawska, SC Dharmage, LD Knibbs, B Jalaludin, P Jalava, et al. [27] reported that higher green space was related to lower SBP, whereas a null association was found between $NDVI_{500m}$ and DBP. A study including 427 newborns in Belgium reported that an IQR (20.3%) increment in green space (5000 m buffer) was related to decrease in DBP of 1.2 mm Hg (95% CI: − 2.4, − 0.0), whereas no association was found for SBP (− 1.2 mm Hg, 95% CI: − 2.5, 0.1) [32]. LD Bloemsma, U Gehring, JO Klompmaker, G Hoek, NAH Janssen, E Lebret, B Brunekreef and AH Wijga [10] conducted a study of 1,505 children, which found that green space was not significantly related to changes in blood pressure. The study participants listed above (e.g., adults, newborns, and children) have different characteristics, lifestyles, living, and working

environments that may modify the effects of greenness. Thus, the relationships between green space and blood pressure remained unclear.

Residing in green space may improve cardiovascular disease outcomes [6]. The mechanisms underlying the association may be explained by immunological and psychological pathways [6, 33, 34]. Specifically, people residing in green space are exposed to more diverse microbes beneficial to the host immune system (improving immune regulation) and less noise and air pollution (reducing inflammatory response), are more likely to increase physical activity (strengthening immune and nervous system), promote the exchange of microbiota (increase social interactions), and promote metabolism (sunlight helps in the synthesis of vitamin D) [33]. Higher green space may benefit mental health such as depression [35, 36].

The subgroup analyses indicated that the effects of green space were more pronounced in males, smokers, and drinkers. The results of sex modification in previous studies have been inconsistent. X Jia, Y Yu, W Xia, S Masri, M Sami, Z Hu, Z Yu and J Wu [13] suggested that green space was related to lower hypertension prevalence for males (OR = 0.18, 95% CI: 0.09, 0.27) and for females (OR = 0.78, 95% CI: 0.48, 0.99). However, BY Yang, I Markevych, MS Bloom, J Heinrich, Y Guo, L Morawska, SC Dharmage, LD Knibbs, B Jalaludin, P Jalava, et al. [27] reported that 0.17 units increase in $NDVI_{500m}$ was related to lower hypertension prevalence for females, whereas a null association was found for males. Inconsistent results may due to them that women have a higher frequency of using green space in China, for example, square dancing was the most popular exercise among them [27]. AM Dzhambov, I Markevych and P Lercher [18] concluded that there was no evidence of significant interactions between sex and greenness-hypertension pathway. There has been limited evidence of how behavioral factors affect the relationships between green space and hypertension and blood pressure. Existing evidence showed that green space could provide diverse microbes, some of which are important inducers of the immunoregulatory pathways, and activation of the immune regulatory system consequently reduced chronic inflammation [33]. C Menni, C Lin, M Cecelja, M Mangino, ML Matey-Hernandez, L Keehn, RP Mohney, CJ Steves, TD Spector, C-F Kuo, et al. [37] indicated the significant relationships between gut microbial diversity and lower arterial stiffness. Smoking and drinking could trigger inflammatory response, oxidative stress, and metabolic disorders, which further affect systemic vascular resistance [38, 39]. Thus, the effects of green space on inflammatory response and immune system could be more pronounced in smokers and drinkers than normal people.

Several limitations existed in this study. First, as an inherent drawback of cross-sectional design, causal associations should be treated with caution. Second, demographic covariates, socioeconomic covariates, and health behavior covariates were collected using the questionnaire, which may introduce recall bias. Third, some potential confounders including traffic noise, the walkability of a community, psychological status, and indoor greenness exposure were not adjusted in the model because of data unavailability [8, 18].

5 Conclusion

In summary, our study suggested that the effects of green space may reduce the risk of hypertension. Furthermore, the effects of greenness were more pronounced in males, smokers, and drinkers. Given the limitations of the cross-sectional study, prospective studies are warranted in the future.

Abbreviations

NDVI: Normalized Difference Vegetation Index; $PM_{2.5}$: Particulate matter with aerodynamic diameter ≤ 2.5 μm; SBP: Systolic blood pressure; BMI: Body mass index; MODIS: Moderate Resolution Imaging Spectroradiometer; DBP: Diastolic blood pressure; EVI: Enhanced Vegetation Index.

Declarations

Authors' contributions

JJ and GC: Analysis, Drafting the manuscript. BL, YL, YG, and SL: Design, Methodology, Funding acquisition. CW and HX: Data acquisition, Editing the manuscript, Funding acquisition.

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Ethics approval and consent to participate

Before the survey and physical examination, the study population has signed informed consent forms. This work was approved by the Ethics Committee of Zhengzhou University.

Competing interests

We declare no competing interests.

Availability of data and materials

The data can be obtained from the corresponding author due to reasonable grounds.

Consent for publication

Not applicable.

References

1. The International Consortium for Blood Pressure Genome: **Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk**. *Nature* 2011, **478**(7367):103-109.
2. Wang Z, Chen Z, Zhang L, Wang X, Hao G, Zhang Z, Shao L, Tian Y, Dong Y, Zheng C *et al*: **Status of Hypertension in China**. *Circulation* 2018, **137**(22):2344-2356.
3. Lu J, Lu Y, Wang X, Li X, Linderman GC, Wu C, Cheng X, Mu L, Zhang H, Liu J *et al*: **Prevalence, awareness, treatment, and control of hypertension in China: data from 1·7 million adults in a population-based screening study (China PEACE Million Persons Project)**. *The Lancet* 2017, **390**(10112):2549-2558.
4. Leong DP, Joseph PG, McKee M, Anand SS, Teo KK, Schwalm J-D, Yusuf S: **Reducing the Global Burden of Cardiovascular Disease, Part 2**. *Circulation Research* 2017, **121**(6):695-710.
5. Markevych I, Schoierer J, Hartig T, Chudnovsky A, Hystad P, Dzhambov AM, de Vries S, Triguero-Mas M, Brauer M, Nieuwenhuijsen MJ *et al*: **Exploring pathways linking greenspace to health: Theoretical and methodological guidance**. *Environ Res* 2017, **158**:301-317.
6. James P, Banay RF, Hart JE, Laden F: **A Review of the Health Benefits of Greenness**. *Curr Epidemiol Rep* 2015, **2**(2):131-142.
7. Bijnens EM, Nawrot TS, Loos RJ, Gielen M, Vlietinck R, Derom C, Zeegers MP: **Blood pressure in young adulthood and residential greenness in the early-life environment of twins**. *Environ Health* 2017, **16**(1):53.
8. Xiao X, Yang BY, Hu LW, Markevych I, Bloom MS, Dharmage SC, Jalaludin B, Knibbs LD, Heinrich J, Morawska L *et al*: **Greenness around schools associated with lower risk of hypertension among children: Findings from the Seven Northeastern Cities Study in China**. *Environ Pollut* 2020, **256**:113422.
9. Moreira TCL, Polizel JL, Santos IdS, Silva Filho DF, Bensenor I, Lotufo PA, Mauad T: **Green Spaces, Land Cover, Street Trees and Hypertension in the Megacity of São Paulo**. *International Journal of Environmental Research and Public Health* 2020, **17**(3).
10. Bloemsma LD, Gehring U, Klompmaker JO, Hoek G, Janssen NAH, Lebret E, Brunekreef B, Wijga AH: **Green space, air pollution, traffic noise and cardiometabolic health in adolescents: The PIAMA birth cohort**. *Environ Int* 2019, **131**:104991.

11. Jendrossek M, Standl M, Koletzko S, Lehmann I, Bauer CP, Schikowski T, von Berg A, Berdel D, Heinrich J, Markevych I: **Residential Air Pollution, Road Traffic, Greenness and Maternal Hypertension: Results from GINIplus and LISAplus**. *Int J Occup Environ Med* 2017, **8**(3):131-142.
12. Brown SC, Lombard J, Wang K, Byrne MM, Toro M, Plater-Zyberk E, Feaster DJ, Kardys J, Nardi MI, Perez-Gomez G *et al*: **Neighborhood Greenness and Chronic Health Conditions in Medicare Beneficiaries**. *American Journal of Preventive Medicine* 2016, **51**(1):78-89.
13. Jia X, Yu Y, Xia W, Masri S, Sami M, Hu Z, Yu Z, Wu J: **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**. *Environmental Research* 2018, **167**:175-183.
14. Lane KJ, Stokes EC, Seto KC, Thanikachalam S, Thanikachalam M, Bell ML: **Associations between Greenness, Impervious Surface Area, and Nighttime Lights on Biomarkers of Vascular Aging in Chennai, India**. *Environ Health Perspect* 2017, **125**(8):087003.
15. Liu X, Mao Z, Li Y, Wu W, Zhang X, Huo W, Yu S, Shen L, Li L, Tu R *et al*: **Cohort Profile: The Henan Rural Cohort: a prospective study of chronic non-communicable diseases**. *Int J Epidemiol* 2019, **48**(6):1756-1756j.
16. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, Jones DW, Kurtz T, Sheps SG, Roccella EJ: **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.
17. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, Ferguson TB, Ford E, Furie K, Gillespie C *et al*: **Heart Disease and Stroke Statistics—2010 Update**. *Circulation* 2010, **121**(7).
18. Dzhambov AM, Markevych I, Lercher P: **Greenspace seems protective of both high and low blood pressure among residents of an Alpine valley**. *Environ Int* 2018, **121**(Pt 1):443-452.
19. Brando PM, Goetz SJ, Baccini A, Nepstad DC, Beck PSA, Christman MC: **Seasonal and interannual variability of climate and vegetation indices across the Amazon**. *Proceedings of the National Academy of Sciences* 2010, **107**(33):14685.
20. de Keijzer C, Tonne C, Sabia S, Basagaña X, Valentín A, Singh-Manoux A, Antó JM, Alonso J, Nieuwenhuijsen MJ, Sunyer J *et al*: **Green and blue spaces and physical functioning in older adults: Longitudinal analyses of the Whitehall II study**. *Environ Int* 2019, **122**:346-356.
21. Markevych I, Thiering E, Fuertes E, Sugiri D, Berdel D, Koletzko S, von Berg A, Bauer C-P, Heinrich J: **A cross-sectional analysis of the effects of residential greenness on blood pressure in 10-year old children: results from the GINIplus and LISAplus studies**. *BMC Public Health* 2014, **14**:477.
22. Chen G, Li S, Knibbs LD, Hamm NAS, Cao W, Li T, Guo J, Ren H, Abramson MJ, Guo Y: **A machine learning method to estimate PM2.5 concentrations across China with remote sensing, meteorological and land use information**. *Sci Total Environ* 2018, **636**:52-60.
23. Liu F, Guo Y, Liu Y, Chen G, Wang Y, Xue X, Liu S, Huo W, Mao Z, Hou Y *et al*: **Associations of long-term exposure to PM1, PM2.5, NO2 with type 2 diabetes mellitus prevalence and fasting blood glucose**

levels in Chinese rural populations. *Environ Int* 2019, **133**(Pt B):105213.

24. Yang YX, Wang XL, Leong PM, Zhang HM, Yang XG, Kong LZ, Zhai FY, Cheng YY, Guo JS, Su YX: **New Chinese dietary guidelines: healthy eating patterns and food-based dietary recommendations**. *Asia Pac J Clin Nutr* 2018, **27**(4):908-913.
25. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF *et al*: **International physical activity questionnaire: 12-country reliability and validity**. *Med Sci Sports Exerc* 2003, **35**(8):1381-1395.
26. Li N, Chen G, Liu F, Mao S, Liu Y, Liu S, Mao Z, Lu Y, Wang C, Guo Y *et al*: **Associations between long-term exposure to air pollution and blood pressure and effect modifications by behavioral factors**. *Environmental Research* 2020, **182**.
27. Yang BY, Markevych I, Bloom MS, Heinrich J, Guo Y, Morawska L, Dharmage SC, Knibbs LD, Jalaludin B, Jalava P *et al*: **Community greenness, blood pressure, and hypertension in urban dwellers: The 33 Communities Chinese Health Study**. *Environ Int* 2019, **126**:727-734.
28. Groenewegen PP, Zock JP, Spreeuwenberg P, Helbich M, Hoek G, Ruijsbroek A, Strak M, Verheij R, Volker B, Waverijn G *et al*: **Neighbourhood social and physical environment and general practitioner assessed morbidity**. *Health Place* 2018, **49**:68-84.
29. Vienneau D, de Hoogh K, Faeh D, Kaufmann M, Wunderli JM, Roosli M, Group SNCS: **More than clean air and tranquillity: Residential green is independently associated with decreasing mortality**. *Environ Int* 2017, **108**:176-184.
30. de Keijzer C, Basagana X, Tonne C, Valentin A, Alonso J, Anto JM, Nieuwenhuijsen MJ, Kivimaki M, Singh-Manoux A, Sunyer J *et al*: **Long-term exposure to greenspace and metabolic syndrome: A Whitehall II study**. *Environ Pollut* 2019, **255**(Pt 2):113231.
31. 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.
32. Madhloum N, Nawrot TS, Gyselaers W, Roels HA, Bijnens E, Vanpoucke C, Lefebvre W, Janssen BG, Cox B: **Neonatal blood pressure in association with prenatal air pollution exposure, traffic, and land use indicators: An ENVIRONAGE birth cohort study**. *Environ Int* 2019, **130**:104853.
33. Rook GA: **Regulation of the immune system by biodiversity from the natural environment: an ecosystem service essential to health**. *Proc Natl Acad Sci U S A* 2013, **110**(46):18360-18367.
34. Grinde B, Patil GG: **Biophilia: does visual contact with nature impact on health and well-being?** *Int J Environ Res Public Health* 2009, **6**(9):2332-2343.
35. Liao J, Yang S, Xia W, Peng A, Zhao J, Li Y, Zhang Y, Qian Z, Vaughn MG, Schootman M *et al*: **Associations of exposure to green space with problem behaviours in preschool-aged children**. *Int J Epidemiol* 2019.
36. Banay RF, James P, Hart JE, Kubzansky LD, Spiegelman D, Okereke OI, Spengler JD, Laden F: **Greenness and Depression Incidence among Older Women**. *Environmental Health Perspectives* 2019, **127**(2).

37. Menni C, Lin C, Cecelja M, Mangino M, Matey-Hernandez ML, Keehn L, Mohney RP, Steves CJ, Spector TD, Kuo C-F *et al*: **Gut microbial diversity is associated with lower arterial stiffness in women**. *Eur Heart J* 2018, **39**(25):2390-2397.
38. Lifton RP, Gharavi AG, Geller DS: **Molecular mechanisms of human hypertension**. *Cell* 2001, **104**(4):545-556.
39. Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, Mente A, Yusuf S: **Reducing the Global Burden of Cardiovascular Disease, Part 1: The Epidemiology and Risk Factors**. *Circ Res* 2017, **121**(6):677-694.

Figures

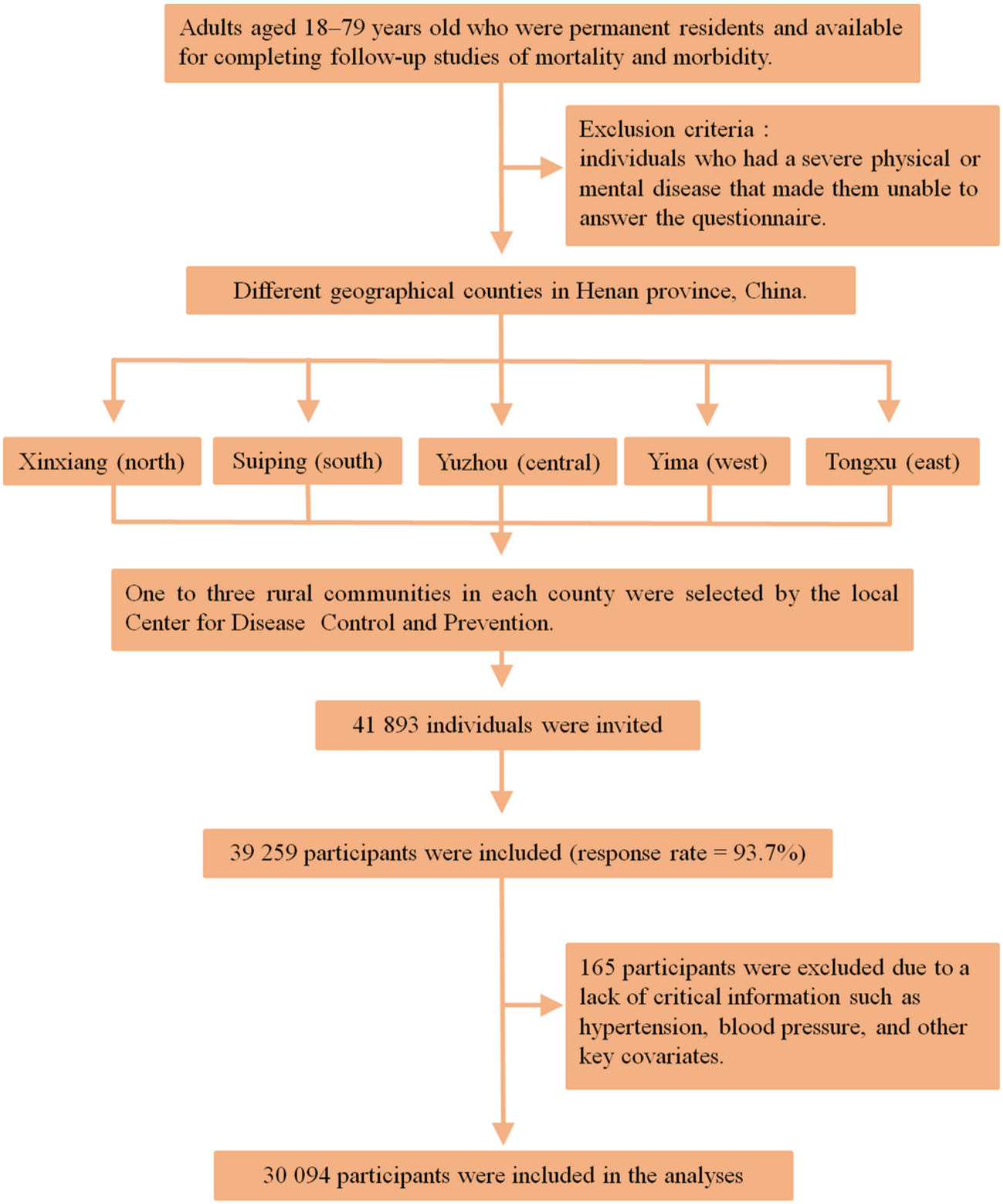

Figure 1

The flowchart of participant recruitment.

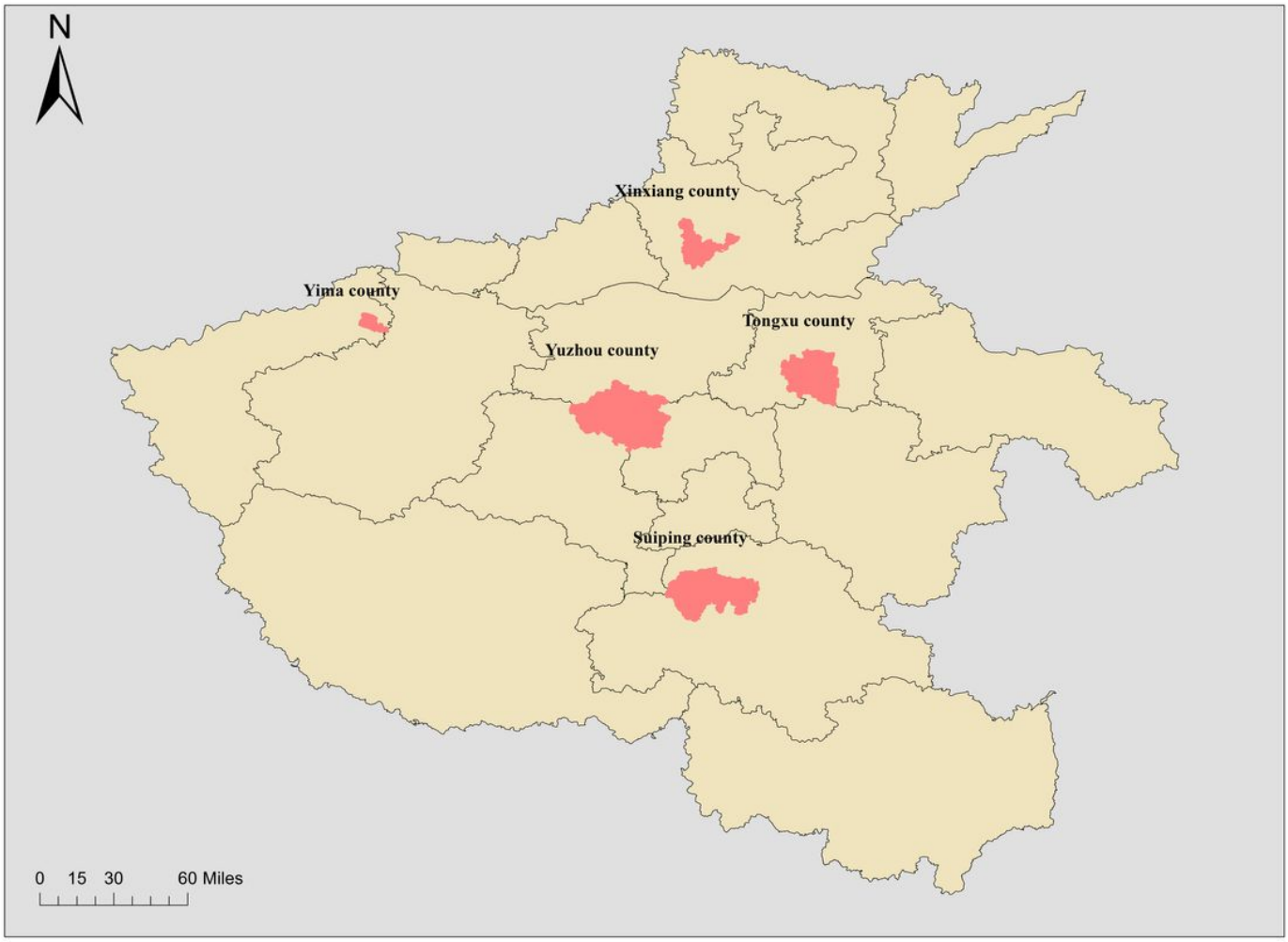

Figure 2

The locations of study areas on the map of Henan province. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

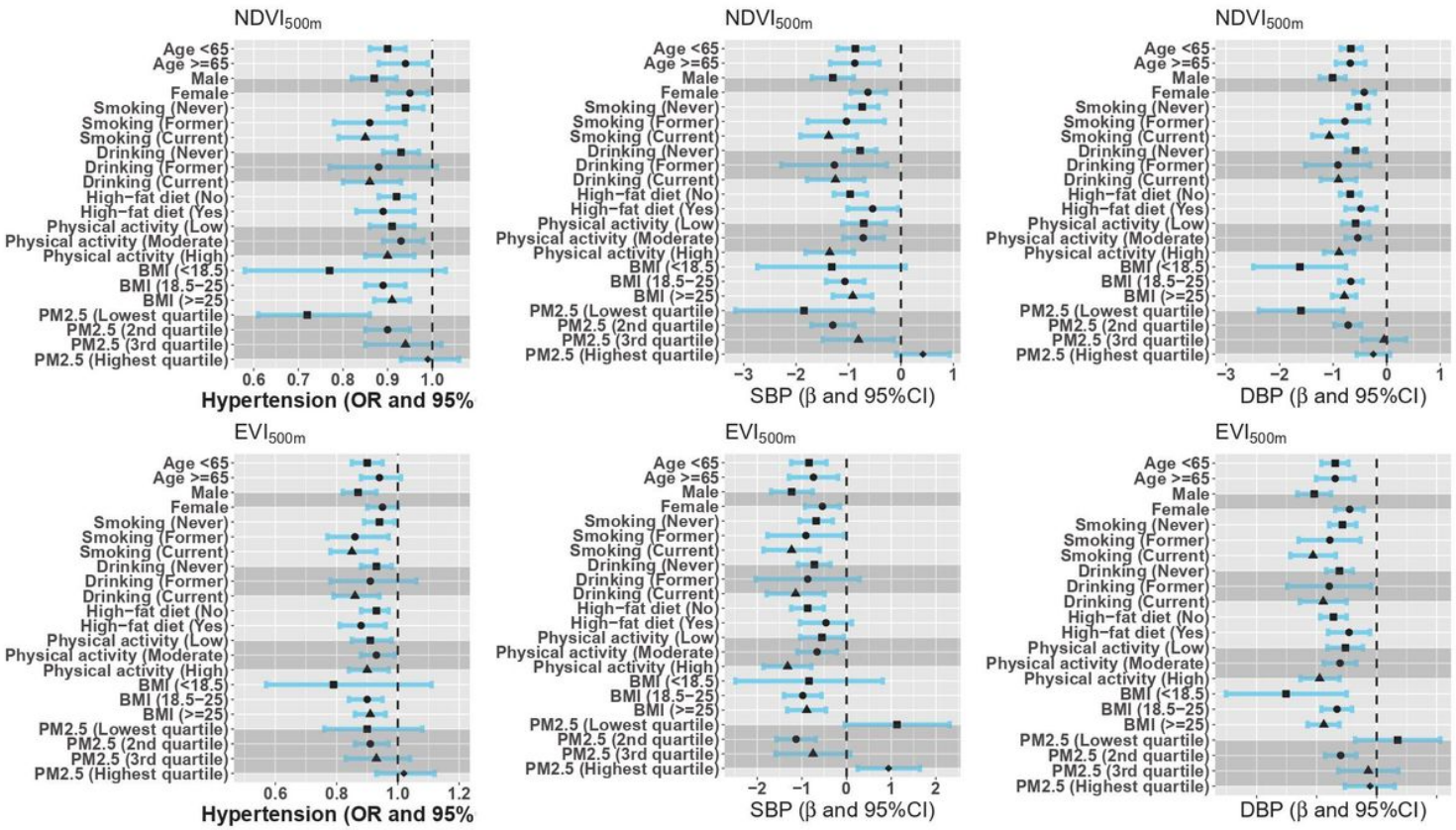

Figure 3

Interaction effect analyses in the green space-cardiovascular disease outcome pathways. Abbreviations: NDVI, the normalized difference vegetation index; EVI, the enhanced vegetation index; SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval; IQR, interquartile range. Note: In the interaction effect analyses, the first group of each subgroup was the reference group. Age, sex, socioeconomic, behavioral, health status covariates, body mass index, and air pollutant were adjusted.

Supplementary Files

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- SupplementalMaterials1211.docx