



Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpolResidential greenness and blood lipids in urban-dwelling adults: The 33 Communities Chinese Health Study[☆]

Bo-Yi Yang^{a,1}, Iana Markevych^{b,c,1}, Joachim Heinrich^{b,d}, Michael S. Bloom^e, Zhengmin Qian^f, Sarah Dee Geiger^g, Michael Vaughn^h, Shan Liuⁱ, Yuming Guo^j, Shyamali C. Dharmage^{k,l}, Bin Jalaludin^{m,n,o,p}, Luke D. Knibbs^q, Da Chen^r, Pasi Jalava^s, Shao Lin^e, Steve Hung-Lam Yim^{t,u,v}, Kang-Kang Liu^a, Xiao-Wen Zeng^a, Li-Wen Hu^a, Guang-Hui Dong^{a,*}

^a Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Occupational and Environmental Health, School of Public Health, Sun Yat-sen University, Guangzhou, 510080, China

^b Institute and Clinic for Occupational, Social and Environmental Medicine, University Hospital, LMU Munich, Ziemssenstraße 1, 80336, Munich, Germany

^c Institute of Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Ingolstädter Landstraße 1, 85764, Neuherberg, Germany

^d Comprehensive Pneumology Center Munich, German Center for Lung Research, Ziemssenstraße 1, 80336, Munich, Germany

^e Department of Environmental Health Sciences and Epidemiology and Biostatistics, University at Albany, State University of New York, Rensselaer, NY, 12144, USA

^f Department of Epidemiology and Biostatistics, College for Public Health & Social Justice, Saint Louis University, Saint Louis, 63104, USA

^g School of Nursing and Health Studies, Northern Illinois University, DeKalb, 60115, USA

^h School of Social Work, College for Public Health & Social Justice, Saint Louis University, Saint Louis, 63103, USA

ⁱ NHC Key Laboratory of Food Safety Risk Assessment, China National Center for Food Safety Risk Assessment 7 Panjiayuan Nanli, Room 312, Beijing, 100021, China

^j Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, 3004, Australia

^k Allergy and Lung Health Unit, Centre for Epidemiology and Biostatistics, School of Population & Global Health, The University of Melbourne, Melbourne, VIC, 3010, Australia

^l Murdoch Children Research Institute, Melbourne, VIC, 3010 Australia

^m Centre for Air Quality and Health Research and Evaluation, Glebe, NSW, 2037, Australia

ⁿ Population Health, South Western Sydney Local Health District, Liverpool, NSW, 2170, Australia

^o Ingham Institute for Applied Medical Research, Liverpool, NSW, 2170, Australia

^p School of Public Health and Community Medicine, The University of New South Wales, Kensington, NSW, 2052, Australia

^q School of Public Health, The University of Queensland, Herston, Queensland, 4006, Australia

^r School of Environment, Guangzhou Key Laboratory of Environmental Exposure and Health and Guangdong Key Laboratory of Environmental Pollution and Health, Jinan University, Guangzhou, 510632, China

^s Department of Environmental and Biological Sciences, University of Eastern Finland, Kuopio, FI 70211, Finland

^t Department of Geography and Resource Management, The Chinese University of Hong Kong, Hong Kong, Shatin, N.T, Hong Kong, China

^u Stanley Ho Big Data Decision Analytics Research Centre, The Chinese University of Hong Kong, Shatin, N.T, Hong Kong, China

^v Institute of Environment, Energy and Sustainability, The Chinese University of Hong Kong, Shatin, N.T, Hong Kong, China

ARTICLE INFO

Article history:

Received 25 October 2018

Received in revised form

29 March 2019

ABSTRACT

While exposure to places with higher greenness shows health benefits, evidence is scarce on its lipidemic effects. We assessed the associations between residential greenness and blood lipids and effect mediations by air pollution, physical activity, and adiposity in China. Our study included 15,477 adults

Abbreviations: AOD, aerosol optical depth; BMI, body mass index; CI, confidence interval; GDP, gross domestic products; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile ranges; LDL-C, low-density lipoprotein cholesterol; NDVI, normalized difference vegetation index; NO₂, nitrogen dioxide; OR, odds ratio; PM_{2.5}, particles <2.5 μm in aerodynamic diameter; SAVI, soil adjusted vegetation index; SD, standard deviations; TC, total cholesterol; TG, triglycerides; WHO, World Health Organization; 33CCHS, the 33 Communities Chinese Health Study.

[☆] This paper has been recommended for acceptance by Dr. Payam Dadvand.

* Corresponding author. Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, 74 Zhongshan 2nd Road, Yuexiu District, Guangzhou, 510080, China.

E-mail address: donggh5@mail.sysu.edu.cn (G.-H. Dong).

¹ The two authors contributed equally to this work.

<https://doi.org/10.1016/j.envpol.2019.03.128>

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Accepted 31 March 2019
Available online 4 April 2019

Keywords:
Greenness
Dyslipidemia
Blood lipids
Mediation
Cross-sectional study

from the population-based 33 Communities Chinese Health Study, conducted between April and December 2009, in Northeastern China. We measured total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Residential greenness was estimated using two satellite-derived vegetation indices – the Normalized Difference Vegetation Index (NDVI) and the Soil Adjusted Vegetation Index (SAVI). We used both nitrogen dioxide (NO₂) and particles $\leq 2.5 \mu\text{m}$ in aerodynamic diameter (PM_{2.5}) as proxies of outdoor air pollution. Associations were assessed using linear mixed effects regression models and logistic mixed effects regression models, and mediation analyses were also performed. Living in higher greenness areas was consistently associated with lower TC, TG, and LDL-C levels and higher HDL-C levels (e.g., change in TC, TG, LDL-C, and HDL-C per 0.1-unit increase in NDVI_{500-m} was -1.52% , -3.05% , -1.91% , and 0.52% , respectively). Similar results were obtained for the corresponding dyslipidemias. These associations were generally stronger in women and older adults. While educational levels showed effect modifications, the effect pattern was inconsistent. Both outdoor air pollution and body mass index mediated 9.1–62.3% and 5.6–40.1% of the associations for greenness and blood lipids, respectively, however, physical activity did not. Our results suggest beneficial associations between residing in places with higher greenness and blood lipid levels, especially in women and the elder individuals. The associations were partly mediated by lower air pollution and adiposity.

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1. Introduction

Our planet has gone through a process of rapid urbanization during the past 60 years. Over 50% of the world's population now lives in urban areas (United Nations, 2015). As the world's most populous country, China has also urbanized rapidly in recent several decades (Guan et al., 2018). From 1978 to 2015, China's urbanization level increased from 18% to 56%, and the growth is expected to continue in the future (Guan et al., 2018; United Nations, 2015). Urbanization poses a major challenge in providing adequate access to areas with higher levels of vegetation (i.e., "greenness") (Nieuwenhuijsen et al., 2017), for which many health benefits have been demonstrated (Markevych et al., 2017). For instance, several studies have suggested reduced cardiovascular mortality (Gascon et al., 2016) and morbidity (Maas et al., 2009; Pereira et al., 2012; Tamosiunas et al., 2014; Yitshak-Sade et al., 2017) for populations living in higher levels of greenness areas.

Abnormalities in blood lipids (i.e., dyslipidemias) are major risk factors for cardiovascular disease (Catapano et al., 2016). The dyslipidemias prevalence is high and is growing worldwide, especially in developing countries such as China (Cahalin et al., 2014; Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults, 2016). However, epidemiological evidence to characterize the relationships between blood lipids and greenness is limited. We were aware of only four relevant studies and the results were mixed (Brown et al., 2016; Kim et al., 2016; Markevych et al., 2016a,b; Paquet et al., 2014). While two of the studies reported significant associations (Brown et al., 2016; Kim et al., 2016), the remaining two did not detect an association (Markevych et al., 2016a; Paquet et al., 2014). Furthermore, these four published studies were all from developed countries, and no such study was performed in a developing country like China.

The mechanisms through which greenness may affect cardiovascular health in general and lipid metabolism in particular are yet to be investigated. Vegetation may reduce exposure to ambient air pollution (Hirabayashi and Nowak, 2016), heat (Bowler et al., 2010), and noise (Dzhambov and Dimitrova, 2014), as well as reduce adiposity (Markevych et al., 2017), which might be beneficial to lipid metabolism (Cai et al., 2017; Vangelova and Deyanov, 2007). Living near greenspaces could also increase physical activity levels (Lachowycz and Jones, 2011), which is a well-documented protective factor for dyslipidemias (Lin et al., 2015). Furthermore, green-space is usually an enriched microbial environment, which may improve lipid metabolism (Rook, 2013).

Therefore, we hypothesized that higher residential greenness levels would enhance lipid metabolism via reduced exposure to air pollution and adiposity and increased physical activity. Accordingly, we explored the associations between residential greenness and blood lipids in Chinese adults. As a secondary aim, we examined whether these presumed associations were mediated by residential air pollution exposure, physical activity, and adiposity. To fulfill these study aims, we analyzed data from the 33 Communities Chinese Health Study (33CCHS), a large population-based investigation with detailed data on blood lipids levels (i.e., total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)), objective measurements of greenness indicators (Normalized Difference Vegetation index (NDVI) and Soil Adjusted Vegetation Index (SAVI)), air pollutant concentrations, physical activity, and adiposity.

2. Methods

2.1. Study locations

The present analysis was based on the 33CCHS investigation (Yang et al., 2018a and 2018b), which was carried out from April to December 2009 in Liaoning Province. This province, located between 118°53' and 125°46' E and 38°43' and 43°26' N, is one of the most important industrial areas in Northeastern China (Fig. 1). It has approximately 44 million residents, 64% of whom are urban dwellers. Industrial processes, traffic, and use of household solid fuels are the major sources of pollutant emissions in Liaoning province, and air pollution is often severe (Song et al., 2017). The prevalence of cardiovascular disease, and its metabolic risk markers (such as dyslipidemias), are often reported to be high in this area (Gu et al., 2005).

2.2. Design and study populations

The detailed design of the 33CCHS has been published before (Yang et al., 2018a and 2018b). As shown in Fig. 2, we applied a four-stage cluster random sampling strategy to select participants. First, we selected three cities (Shenyang, Anshan, and Jinzhou) from 14 cities in Liaoning province. There are 11 administrative districts in the three cities (five in Shenyang and three each in Anshan and Jinzhou). Second, in each of these 11 districts, we selected three communities, generating a total of 33 communities (each

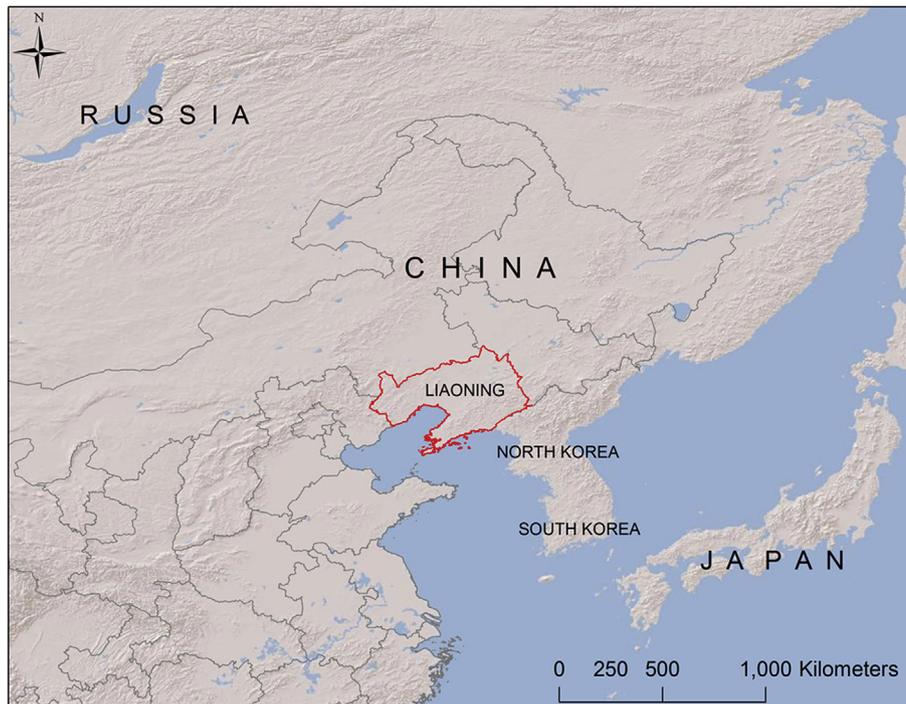


Fig. 1. Location of study area (Liaoning province) on the map of China.

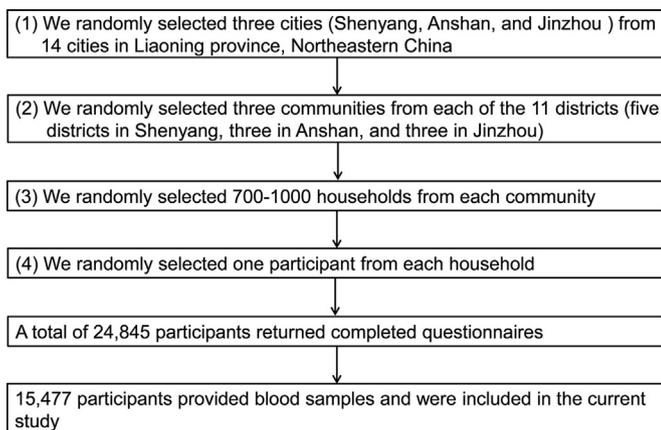


Fig. 2. Sampling process for the 33 Communities Chinese Health Study.

approximately 0.25–0.64 km² and with a population of 4200–6000). Third, we then randomly selected 700–1000 households from each of the 33 communities. Lastly, we randomly selected one adult from each household. We excluded the following people from the study: people who resided at the current address for less than five years; women who were in pregnancy, and those who had severe pre-existing disease (e.g. terminal cancers) who could not complete a questionnaire.

Based on the sampling frame, a total of 28,830 participants (aged 18–74 years) were invited to take part in the study. Of those, 24,845 participants returned questionnaires (response rate = 86.2%). We further excluded 9368 individuals from the study because they refused to provide a blood sample. Thus, the final sample size of 15,477 participants (62.3%) was included in the data analysis.

The Human Studies Committee of Sun Yat-Sen University approved the study protocols. All participants provided written informed consent before data collection.

2.3. Blood lipids and dyslipidemias

Peripheral venous blood samples were drawn after an overnight fast. The levels of TC, TG, LDL-C, and HDL-C were measured on a Hitachi Autoanalyzer (Type 7170A; Hitachi Ltd.; Tokyo, Japan). We defined hypercholesterolemia as TC \geq 240 mg/dL; hypertriglyceridemia as TG \geq 200 mg/dL; hypoalphalipoproteinemia as HDL-C \leq 40 mg/dL; and hyperbetalipoproteinemia as LDL-C \geq 160 mg/dL (Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults, 2016).

2.4. Residential greenness

We defined the residential greenness using satellite-based vegetation indices –NDVI (Tucher, 1979) and SAVI (Huete, 1988). SAVI and NDVI indices were both calculated according to the difference of surface reflectance over absorbance in two vegetation-informative light bands. For SAVI, a correction factor was additionally added to suppress soil pixels. NDVI and SAVI values range from –1 to +1, with –1 indicating water areas and +1 representing fully vegetated areas. To calculate the two indices, we used cloud-free Landsat 5 Thematic Mapper satellite images at a spatial resolution of 30 m \times 30 m (<http://earthexplorer.usgs.gov>) (August 2010). We captured maximum vegetation contrasts across the 33 study communities by selecting images taken in the summer. We used 2010 data because it was the year closest to the health data collection (2009). NDVI and SAVI were abstracted as means in 100, 500, and 1000 m circular buffers around each of the study communities. In the current analyses, we focused on the 500 m buffer taking into account the progress from the recently published studies (Markevych et al., 2014; Markevych et al., 2016a,b; Davdand et al., 2014a,b) while other buffer are also reported. We conducted the calculations using ArcGIS 10.4 (ESRI, Redlands, CA, USA).

2.5. Air pollution

Daily concentrations of particles $\leq 2.5 \mu\text{m}$ in aerodynamic diameter ($\text{PM}_{2.5}$) were estimated by spatiotemporal modelling, using $\text{PM}_{2.5}$ data from ground monitoring stations, satellite-based observations of aerosol optical depth (AOD), meteorologic data, and land use information, which has been described previously (Yang et al., 2018a and 2018b). Details are provided in the supplement ($\text{PM}_{2.5}$ assessment). Nitrogen dioxide (NO_2) data were obtained from the nearest ground monitoring station, located within approximately 1 km from study participants' home addresses. A description of the NO_2 assessment has been previously published (Yang et al., 2018a, 2018b), and is summarized in the supplement (NO_2 assessment). In the current study, we used three year (2006–2008) annual average measurements of NO_2 and $\text{PM}_{2.5}$ as proxies for long-term exposure air pollution exposure.

2.6. Covariates and mediators

The following covariates were considered and collected using the standardized questionnaires: age (years), sex (male vs female), ethnicity (Han vs "others"), household income (≤ 5000 Yuan; 5001–10,000 Yuan; 10,001–30,000 Yuan; $\geq 30,000$ Yuan), highest level of educational attainment (none; primary school; middle school; >junior college), tobacco smoking (smoker vs non-smoker), alcohol consumption ("drinker" (consumed at least two alcoholic drinks per week for males and one alcoholic drink per week for females) vs "non-drinker" (never drinks or stop drinking for more than six months)), exercise (running, walking, dancing, swimming, or playing ball games, etc.) regularly (yes (more than 180 min per week) vs no (less than 180 min per week)), intake of sugar-sweetened soft drinks (≤ 1 day per week; 2–4 days per week; ≥ 5 days per week), low calorie or low fat diet (yes (occasionally, frequently, or everyday) vs no (never or almost never)), and family history of dyslipidemia (yes vs no). Body mass index (BMI; kg/m^2) was calculated using height and body weight measurements. Gross domestic product (GDP) levels in each district were obtained from the three cities' Statistical Yearbooks. We then built a directed acyclic graph (DAG, Fig. S1) with the help of DAGitty v1.0 software (www.dagitty.net) and retained age, sex, ethnicity, education levels, household income, and area-level GDP as potential confounders in the main models. Also, according to the DAG, physical activity, air pollution, and BMI were selected as potential mediators (Fig. S1).

2.7. Statistical analysis

Means \pm standard deviations (SD), medians and interquartile ranges, or frequencies were obtained from descriptive analyses. Spearman's rank correlation test was applied to examine the relationship between exposure measurements. We used Student's *t*-test to evaluate associations between NDVI and covariates as appropriate.

The linearity of the associations between greenness measures and blood lipid levels were graphically tested through the smoothing curves and statistically tested using restricted cubic spline functions. In the main analysis, we hypothesized a linear relationship between greenness levels and blood lipids levels. We natural log-transformed the levels of TC, TG, HDL-C, and LDL-C to normalize the distribution before regression analysis and used $100 \times [\exp(\beta) - 1]$ to express the associations as percent change in outcome per 0.1-unit change in NDVI and SAVI. We used generalized linear mixed models with logic link to assess associations between greenness and dyslipidemias (Yang et al., 2018a and

2018b) (also see the supplement: description of Generalized Linear Mixed Models). The results are presented as odds ratios (OR) and their corresponding 95% confidence intervals (CI) per 0.1-unit higher NDVI and SAVI. Two levels of covariate adjustments were used: (1) crude models (no adjustment); and (2) adjusted models (adjusted for age, sex, ethnicity, education levels, income level, and area level GDP, which were selected using DAG).

Several sensitivity analyses were also performed by evaluating the impact of different residential buffer sizes (i.e., 100-m and 1000-m buffers), excluding participants taking lipid lowering medications, and excluding participants who had cardiovascular disease or diabetes mellitus. In addition, we investigated the associations between greenness and use of lipid-lowering drugs, and repeated the analyses after merging participants with dyslipidemias (i.e., dyslipidemias according to examined blood lipid levels, including hypercholesterolemia and hypertriglyceridemia) with those who took lipid-lowering drugs. Furthermore, we estimated non-linear relationships between greenness and blood lipids, by categorizing $\text{NDVI}_{500\text{-m}}$ levels into quartiles.

As associations between greenness and blood lipids may be different among sub-populations, we conducted stratified and interaction analyses (by adding a cross-product term into the regression model) to explore potential effect modification by age (≥ 45 years vs < 45 years, based on the average age of the study participants), sex (male vs female), and education levels (< 9 years vs ≥ 9 years, referring to none/primary school/middle school vs \geq junior college).

Furthermore, we performed mediation analyses to quantify the contribution of air pollution, physical activity, and BMI as mediators of the association between residential greenness and blood lipids. We estimated proportions of the mediated effect following Baron and Kenny's method for causal mediation (Baron and Kenny, 1986). We compared the exposure effect estimates from the full model with the exposure effect estimate obtained from the mediation model. Standard errors were estimated by bootstrapping (5000 simulations).

The statistical analyses were performed in SAS 9.2 (SAS Institute, Inc. Cary, NC) and R software (version 3.4.3, R foundation for Statistical Computing, Vienna, Austria). A two-tailed *p* value < 0.05 indicated significant levels.

3. Results

3.1. Descriptive statistics

Participants included in this analysis were similar to the participants in the overall 33CCHS, in terms of sociodemographic and lifestyle variables (Table S1). The participants were 45 years of age on average and 53% were males (Table 1). Most participants possessed middle school or higher educational levels (85%) and belonged to the middle-to-high income group (80%, annual family income per year $> 10,000$ Yuan). Prevalence rates of dyslipidemias ranged from 8.6% for hyperbetaipoproteinemia to 22.6% for hypertriglyceridemia.

3.2. Greenness exposure

Greenness levels differed substantially across the 33 study communities (e.g. $\text{NDVI}_{500\text{-m}}$ ranged from 0.184 to 0.802). NDVI and SAVI were highly and positively correlated (Spearman's correlation coefficients of around 0.98 within the same buffer size, Table S2). However, their correlations of NDVI and SAVI with $\text{PM}_{2.5}$ and NO_2 were low (Spearman's correlation coefficients ≤ 0.43).

Table 1
Characteristics of study participants from the 33 Communities Chinese Health Study (n = 15,477).

Characteristic	Value (mean ± SD, n(%), or median (Q1, Q3))
Demographic & Lifestyle Factors	
Age (years)	44.97 ± 13.45
Sex	
Males	8156 (52.7%)
Females	7321 (47.3%)
Ethnicity	
Han	14,554 (94.0%)
Other	923 (6.0%)
Education	
Junior college or higher	3579 (23.1%)
Middle school	9554 (61.7%)
Primary school	1863 (12.0%)
No school	481 (3.1%)
Annual family income	
≤5000 Yuan	1167 (7.5%)
5001–10,000 Yuan	1977 (12.8%)
10,001–30,000 Yuan	7869 (50.8%)
≥30,000 Yuan	4464 (28.8%)
Regular exercise	
No	10,545 (68.1%)
Yes	4932 (31.9%)
Body mass index	
≤25 kg/m ²	9220 (59.6%)
26–30 kg/m ²	5418 (35.0%)
≥30 kg/m ²	839 (5.4%)
Lipid Levels	
TC (mg/dL)	179.92 (155.98, 205.41)
TG (mg/dL)	118.58 (81.42, 176.99)
HDL-C (mg/dL)	50.97 (43.63, 60.61)
LDL-C (mg/dL)	98.60 (75.67, 122.31)
Hypercholesterolemia	1717 (11.1%)
Hypertriglyceridemia	3494 (22.6%)
Hypoalphalipoproteinemia	2836 (18.3%)
Hyperbetalipoproteinemia	1333 (8.6%)
Greenness & Air Pollutant Levels	
NDVI _{100-m}	0.255 (0.227, 0.393)
NDVI _{500-m}	0.291 (0.232, 0.398)
NDVI _{1000-m}	0.305 (0.254, 0.404)
SAVI _{100-m}	0.143 (0.119, 0.214)
SAVI _{500-m}	0.158 (0.129, 0.235)
SAVI _{1000-m}	0.167 (0.140, 0.240)
PM _{2.5} (μg/m ³)	73.00 (71.00, 97.00)
NO ₂ (μg/m ³)	33.00 (31.00, 40.00)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NO₂, nitrogen dioxide; NDVI, normalized difference vegetation index; PM_{2.5}, particle with aerodynamic diameter ≤2.5 μm; SAVI, soil adjusted vegetation index; SD, standard deviation; TC, total cholesterol; TG, triglycerides.

3.3. Main analyses

In the main model, a 0.1-unit increase in NDVI_{500-m} was significantly associated with 1.52%, 3.05%, and 1.91% lower TC, TG, and LDL-C levels, respectively, and a 0.52% higher HDL-C level (Table 2).

Table 2
Associations for residential greenness (per 0.1 higher NDVI_{500-m} and SAVI_{500-m}) with blood lipid levels.

Model	% changes (95% CI)			
	TC	TG	HDL-C	LDL-C
NDVI _{500-m}				
Crude	-1.51 (-1.78, -1.24)	-5.89 (-6.68, -5.11)	1.47 (1.16, 1.80)	-1.31 (-1.84, -0.78)
Adjusted ^a	-1.52 (-1.80, -1.22)	-3.05 (-3.82, -2.28)	0.52 (0.20, 0.85)	-1.91 (-2.44, -1.38)
SAVI _{500-m}				
Crude	-2.45 (-2.89, -2.01)	-9.35 (-10.66, -8.06)	2.40 (1.89, 2.91)	-2.18 (-3.05, -1.34)
Adjusted ^a	-2.38 (-2.85, -1.92)	-4.63 (-5.83, -3.41)	0.73 (0.21, 1.26)	-2.96 (-3.80, -2.11)

Abbreviations: CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NDVI, normalized difference vegetation index; SAVI, soil adjusted vegetation index; TC, total cholesterol; TG, triglycerides.

^a Adjusted for age, sex, ethnicity, education level, household income, and district-level gross domestic product.

Similar results were obtained for dyslipidemias (Fig. 3). Higher NDVI_{500-m} levels were associated with lower odds of hypercholesterolemia, hypertriglyceridemia, and hyperbetalipoproteinemia, and no association was detected for hypoalphalipoproteinemia.

The significance of the associations between SAVI_{500-m} and blood lipid metrics was the same as those with NDVI_{500-m}.

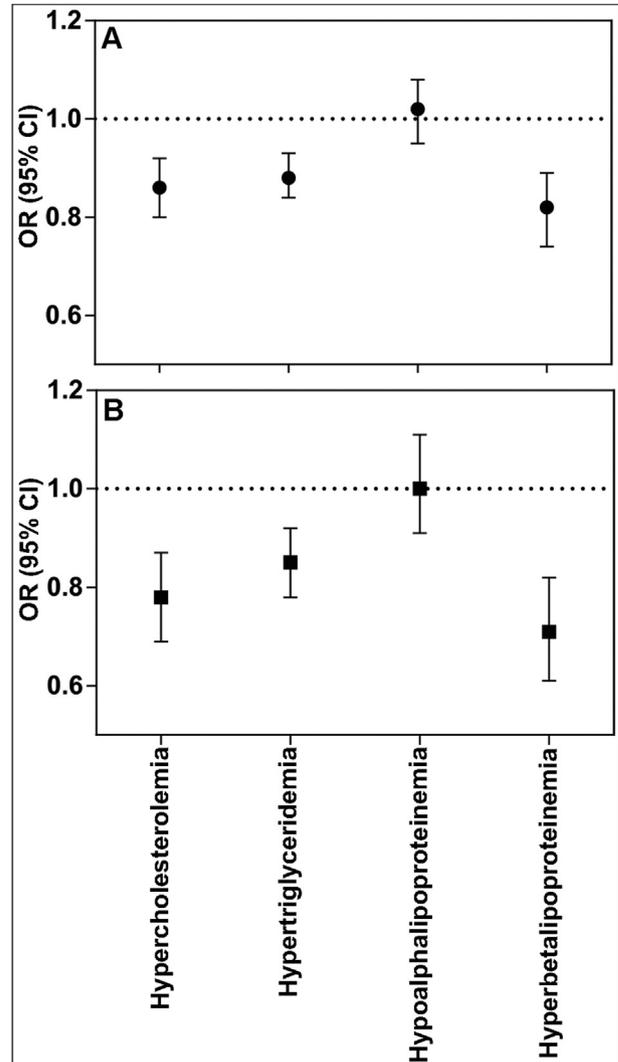


Fig. 3. Associations for 0.1-unit higher NDVI-500m (panel A) and SAVI-500m (panel B) with dyslipidemias.

CI, confidence interval; NDVI, normalized difference vegetation index; OR, odds ratio; SAVI, soil adjusted vegetation index.

However, the magnitudes of the associations for SAVI_{500-m} were consistently greater than those for NDVI_{500-m} (Table 2 and Fig.3). This could be due to the lower background SAVI_{500-m} levels compared to NDVI_{500-m}.

3.4. Sensitivity analyses

The direction and significance of the associations based on NDVI and SAVI with the 100-m and 1000-m buffers were consistent with those of the main analysis (500-m buffer) (Tables S3–S6). After excluding participants who were taking lipids lowering drugs (Table S7) or those with cardiovascular disease and/or diabetes (Table S8), the results remained similar to those from the main analyses. Higher greenness levels were also associated with lower odds of using lipid-lowering medications, but the associations did not reach statistical significance (Table S9). The results were similar when we combined the participants taking lipid-lowering medications with those who had dyslipidemias diagnosed based on blood lipids levels (Table S9). The association for NDVI_{500-m} and HDL-C was non-linear (P value for non-linear was 0.002) (Fig. S2), we thus further estimated the associations between categorical (i.e., quartile) NDVI_{500-m} and HDL-C levels. Compared to the participants in the first quartile of NDVI_{500-m} levels, those in the second, third, and fourth had significant increases in HDL-C levels; however, the P value for trend was not significant (P = 0.819) (Table S10).

3.5. Stratified analyses

In subgroup analyses by age, associations of greenness (i.e., NDVI_{500-m} and SAVI_{500-m}) with TC, TG, and HDL-C were stronger in

participants aged ≥45 years than in participants <45 years (all p values for interactions were less than 0.05) (Fig. 4; Table S11). When the analyses were stratified by sex, stronger associations between greenness (i.e., NDVI_{500-m} and SAVI_{500-m}) and TC and LDL-C were observed in females compared to males (all P values for interactions were less than 0.05) (S11). In stratified analyses by education level, the pattern of the effects was mixed; while associations of NDVI_{500-m} with TC and LDL-C were stronger in participants with lower education level, its association with HDL-C was stronger in those who were more highly educated (S11).

3.5. Mediation analyses

As shown in Table 3, PM_{2.5} mediated only small to moderate parts of the NDVI_{500-m} associations with TC (9.1%) and LDL-C levels (28.6%) but large proportions of the associations with HDL-C (62.3%). NO₂ mediated the associations of greenness with TG (10.7%) and HDL-C (18.1%) levels. BMI significantly mediated 5.6–40.1% of all the associations between greenness and lipid levels, although physical activity did not mediate any of the associations (data not shown). We found similar mediation results for the associations between greenness and the prevalence of dyslipidemias (Table S12).

4. Discussion

4.1. Key findings

This large cross-sectional study is the first attempt to estimate associations for residential exposure to residential greenness with blood lipids in China. We found that residing in areas with higher

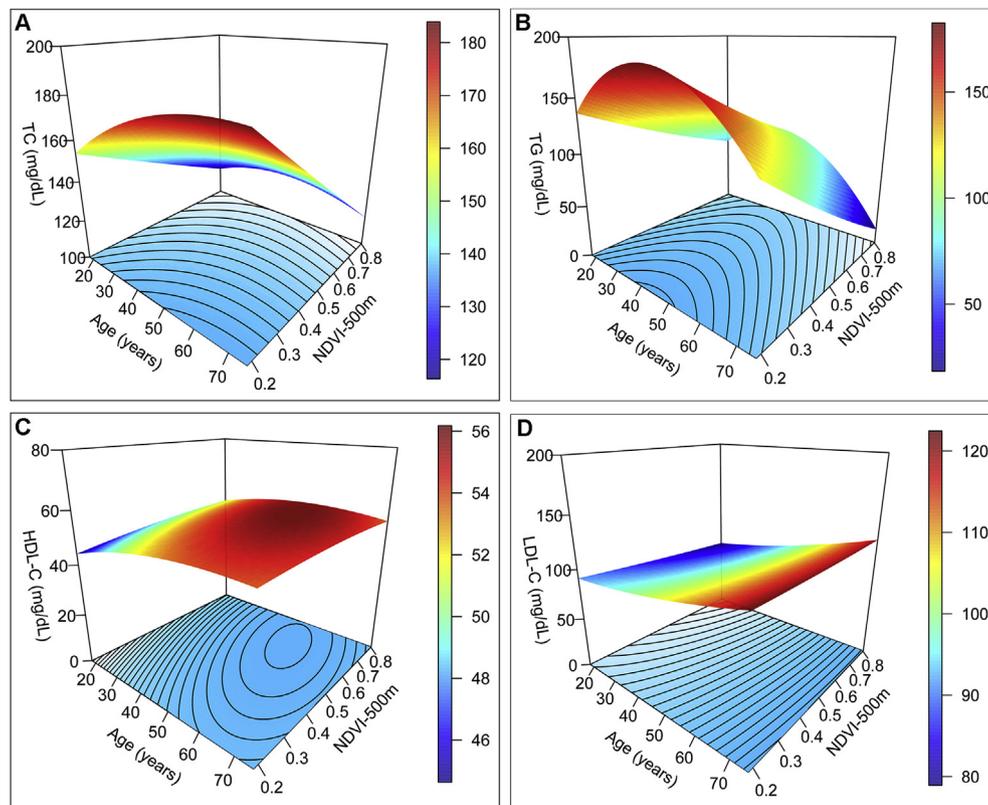


Fig. 4. The 3D response surface and 2D contour plots showing the interactive effects of age and greenness (NDVI-500m) on blood lipid levels. Panel A for total cholesterol (TC), panel B for triglycerides (TG), panel C for high-density lipoprotein cholesterol (HDL-C), and panel D for low-density lipoprotein cholesterol (LDL-C). CI, confidence interval; NDVI, normalized difference vegetation index.

Table 3
Mediation of associations between residential NDVI_{500-m} and blood lipids by air pollutants.

Outcome	Mediator	Proportion mediated (%)	P-value
TC	PM _{2.5}	9.1	<0.0001
	NO ₂	2.0	0.120
	BMI	13.9	<0.0001
TG	PM _{2.5}	0.01	0.600
	NO ₂	10.7	<0.0001
	BMI	33.2	<0.0001
HDL-C	PM _{2.5}	62.3	0.012
	NO ₂	18.1	<0.0001
	BMI	40.1	<0.0001
LDL-C	PM _{2.5}	28.6	<0.0001
	NO ₂	0.07	0.570
	BMI	5.6	<0.0001

Note: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NO₂, nitrogen dioxide; NDVI, normalized difference vegetation index; PM_{2.5}, particle with aerodynamic diameter $\leq 2.5 \mu\text{m}$; TC, total cholesterol; TG, triglycerides.

levels of greenness was consistently associated with lower levels of TC, TG, and LDL-C and higher HDL-C levels. These associations were modified by sex, age, and education level. Moreover, we found that lower air pollution and BMI, but not physical activity, partially mediated the associations.

4.2. Comparison with other published studies

These results support our *a priori* hypothesis that residential greenness may exert beneficial effects on lipid metabolism via lowering TC, TG, and LDL-C levels as well as increasing HDL-C levels. Our findings partially agree with those from a retrospective cohort study of 249,405 older Americans (≥ 65 years), which found that higher levels of greenness (measured by NDVI), was associated with lower rates of hyperlipidemia (Brown et al., 2016). Similarly, Kim et al. (2016) found that a higher density of nearby parks and green areas was associated with lower odds of hyperlipidemia. However, a prospective cohort study of 3205 Australian adults did not detect association between public open space greenness and incident dyslipidemia (Paquet et al., 2014), which might be due to very low greenness levels in the study area. Similarly, Markevych and colleagues (Markevych et al., 2016a) found no statistically significant associations for greenness, as measured by NDVI, with levels of TC, TG, HDL-C, and LDL-C in 1552 German children. The authors noted that the null results might be attributed to: (1) a young “lipids-healthy” population; and (2) a mix of fasting and non-fasting blood samples that biased the results towards the null hypothesis (Markevych et al., 2016a). Our findings may support their first speculation (Markevych et al., 2016a), as we found weaker associations for greenness with TC, TG, and LDL-C among younger study participants (<45 years), although stronger associations for older study participants (≥ 45 years). In contrast to these four previously published studies (Brown et al., 2016; Markevych et al., 2016a,b; Paquet et al., 2014), we collected fasting blood samples for all participants and objectively measured a comprehensive panel of four lipid biomarkers. In addition, we employed DAG to select a minimum set of confounders and built a parsimonious model to obtain more precise estimates.

We also identified stronger associations for residential greenness and blood lipids in females than in males. Several previous epidemiological studies also explored the impact of sex on associations between greenness and other health outcomes in adults, but the evidence is mixed (Astell-Burt et al., 2014; Markevych et al., 2014; van den Berg et al., 2016). Nevertheless, our current findings are not entirely unexpected as Chinese women may spend

more time using greenspaces than Chinese men. For example, square dancing is a popular physical activity among Chinese adults, which is usually practiced in nearby parks nearby and mostly by women (Gao et al., 2016). Women may also spend more time closer to home than men, and thus take greater advantage of local greenspaces (Björk et al., 2016). The impact of education was inconsistent as a modifier of associations between greenness and lipids. We found stronger associations of greenness with TC, TG, and LDL-C in participants with lower education levels. Several similar studies documented that the beneficial effects of greenness on other health outcomes were strongest for those with low socioeconomic status, which tends to be strongly correlated to education level (van den Berg et al., 2016; Dadvand et al., 2014a,b). One explanation for the effect may be that people with lower education generally have a poorer health status and live in more polluted areas with less greenspace than those with higher education, and so they may be more likely to benefit from greenspace use (Su et al., 2011). In addition, it is possible that participant with lower education levels mostly work outdoor and therefore used more greenspace than the educated ones, who mostly worked indoors. However, we adjusted for confounding by education level in the regression models and so the impact was likely to have been modest. Yet, we also found opposite trend for HDL-C, in that stronger associations were observed in the participants with higher education levels. It is tempting to speculate that individuals with higher education might live in closer proximity to higher quality greenspaces or be more likely to utilize greenspaces than those with lower education, leading to the difference (Table S13). However, without more detailed information about the type and use of greenspace we were unable to directly assess this possibility. Future studies with more detailed greenspace exposure information are needed for a more definitive explanation.

4.3. Potential underlying mechanisms

Prior evidence suggests that greener areas was associated with lower levels of air pollution (Hirabayashi and Nowak, 2016). Our study also found that greenness was negatively correlated with air pollutant levels. Additionally, mounting evidence demonstrates associations for higher air pollution levels with an increased risk of dyslipidemias (Cai et al., 2017; Bell et al., 2017). Thus, it is plausible to speculate that lower ambient air pollution associated with higher greenness could underlay our observed greenness-lipids associations. Our mediation analysis suggested that air pollutants partially mediated the association between residential greenness and blood lipids. Exposure to greenspace could reduce adiposity, which is a leading risk factor for dyslipidemia (Sarkar, 2017). Thus, BMI may mediate the associations between greenness and dyslipidemias, and our current results support this hypothesis. In addition, closer proximity to greenspaces, such as parks, has been correlated with increased physical activity (Lachowycz and Jones, 2011), a well-documented protective factor for lipid metabolism (Lin et al., 2015). However, our results did not change after including physical activity in the models, and we also did not detect mediation by this factor. Therefore, our findings do not support this mechanism. There are also some other potential mechanisms. Additional potential mechanisms have been postulated to explain greenness-lipids associations, including psychological and physiological stress alleviation, buffering noise and heat effects (Markevych et al., 2017), and microbial enrichment (Rook, 2013). Unfortunately, the absence of such data precludes us from exploring other potential mechanisms. Future studies are therefore needed to add mechanistic evidence on the association between greenness and lipids.

4.4. Implications for policy makers

Our study suggests a beneficial impact for residential greenness on lipid metabolism, and this association may at least partially result from lowering adiposity and air pollution, especially PM_{2.5}. Dyslipidemias are important metabolic risk factors for cardiovascular disease, and clinical trials have demonstrated that lipid-lowering drugs could greatly reduce the risk for major coronary events (Fulcher et al., 2015). Our results show that if NDVI_{500-m} increases by 0.1-unit, then levels of TC and TG would decrease by 1–3%. Our findings, therefore, may have important public health implications for policy makers when designing interventions, such as planning for open spaces around residential areas, to mitigate the growing prevalence of dyslipidemias and to lower the incidence of cardiovascular disease worldwide.

4.5. Strengths and limitations

The current study has several strengths. First, our analysis has a large sample size and the response rate was high. Second, we investigated in the role of air pollution, physical activity, and adiposity as intervening variables that may be involved in intermediate pathways by which greenness exerts beneficial effects on lipid metabolism. Third, we performed a series of sensitivity analyses that demonstrated the robustness of our results.

Our study also has important limitations. First, the cross-sectional design precludes us from inferring causality; reverse causality, in which those with higher lipid levels may be less likely to reside close to greenspace, cannot be ruled out. However, we adjusted for socioeconomic factors and so the likelihood is modest. Second, greenness exposure estimates were based on community centroids rather than on personal exposure, which might have introduced measurement errors in exposure assessment. However, these errors were likely to have been nondifferential with respect to serum lipids and so may have shifted the effect estimates towards null (Hutcheon et al., 2010). Third, all covariates, were collected using a questionnaire and so some participants may have been misclassified, potentially leading to exposure misclassification. Fourth, while the NDVI and SAVI provide information on general vegetation level, they are not informative about the type, context, and quality of greenspace, which prevents us from further investigating which specific aspects of greenspace are important in these associations. Finally, we conducted a large number of independent statistical tests, which increases the probability of false-positive results or chance findings. Multiple testing was not corrected, in order to maximize our ability to find modest effects. However, the observed associations in our study are generally consistent and robust, which speaks for their validity. Due to these limitations, our findings should be interpreted cautiously, and further replications in a longitudinal data set are warranted.

5. Conclusions

In conclusion, exposure to higher residential greenness was associated with a beneficial effect on lipid metabolism, and the associations were stronger in women and older participants. Ambient air pollution levels and adiposity mediated the association between greenness and lipids but only in part, suggesting that other mechanisms may underpin the association as well. Our results might be useful for policy makers for reducing cardiovascular disease burden through feasible and achievable targeted interventions such as increasing residential vegetation levels.

Declaration of interests

None

Funding

The research was funded by the National Natural Science Foundation of China (No.81703179; No.91543208; No.81803196; No.81673128); the National Key Research and Development Program of China (No.2016YFC0207000); the Fundamental Research Funds for the Central Universities (No.16ykzd02; No.17ykpy16); the Guangdong Province Natural Science Foundation (No.2016A030313342; 2017A050501062); and Science and Technology Program of Guangzhou (201807010032; 201803010054). YG was supported by the Career Development Fellowship of Australian National Health and Medical Research Council (No.APP1107107). The authors acknowledge the cooperation of participants in this study who have been very generous with their time and assistance.

Acknowledgements

The authors acknowledge the cooperation of participants in this study who have been very generous with their time and assistance.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envpol.2019.03.128>.

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