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Association of Long-Term Exposure to $PM_{2.5}$ Constituents and Green Space With Arthritis and Rheumatoid Arthritis

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Key Points:

- $PM_{2.5}$ constituents and green space are associated with the incidence of arthritis
- $PM_{2.5}$ exposure and reduced greenness had a synergistic effect on arthritis
- The risk of arthritis was higher in urban participants than in rural participants

Supporting Information:

Supporting Information may be found in the online version of this article.

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Abstract There is limited evidence regarding the effects of long-term exposure to $PM_{2.5}$ constituents on the risk of arthritis and rheumatoid arthritis, and the interaction between $PM_{2.5}$ and green space remains unclear. This study examined the relationship between long-term exposure to $PM_{2.5}$ constituents and the risk of arthritis and rheumatoid arthritis, with the exposure period extending from recruitment until self-reported outcomes, death, loss to follow-up, or end of follow-up. Additionally, the study assessed whether there was an interactive effect between $PM_{2.5}$ and green space on these risks. We gathered cohort data on 18,649 individuals aged ≥45 years. We applied generalized linear mixed-effects models to estimate the effects of $PM_{2.5}$ constituents, NDVI, and their interaction on arthritis and rheumatoid arthritis. The quantile g-computation and weighted quantile sum regression model were applied to estimate the combined effect of $PM_{2.5}$ constituents. Our results showed that exposure to single and mixed $PM_{2.5}$ constituents adversely affected arthritis and rheumatoid arthritis, and was mainly attributed to the black carbon component. We observed "U" or "J" shaped exposure-response curves for the effects of $PM_{2.5}$, OM, NO_3^- and NH_4^+ exposure on the development of arthritis/rheumatoid arthritis. Additionally, the odds ratio of arthritis for per interquartile range (IQR) increase in $PM_{2.5}$ was 1.209 (95% CI:1.198, 1.221), per 0.1-unit decrease in NDVI was 1.091 (95% CI:1.033, 1.151), and the interaction term was 1.005 (95% CI:1.002, 1.007). These findings flesh out the existing evidence for $PM_{2.5}$ constituents, NDVI and arthritis, rheumatoid arthritis, but the underlying mechanisms still require further exploration.

Plain Language Summary This study aims to explore the correlation between long-term exposure to $PM_{2.5}$ constituents and the incidence of arthritis and rheumatoid arthritis, as well as to evaluate whether there is a synergistic effect of $PM_{2.5}$ and green spaces on the risk of these conditions. The generalized linear mixed-effects model was utilized to analyze the impact of $PM_{2.5}$ constituents, NDVI, and their interactions on arthritis and rheumatoid arthritis. The joint effects of $PM_{2.5}$ constituents were assessed using quantile g-computation and weighted quantile sum regression model. Our results indicated that both individual and mixed exposures to $PM_{2.5}$ constituents have adverse effects on arthritis and rheumatoid arthritis, primarily attributed to the black carbon component. Additionally, the odds ratio of arthritis for per interquartile range (IQR) increase in $PM_{2.5}$ was 1.209 (95% CI:1.198, 1.221), per 0.1-unit decrease in NDVI was 1.091 (95% CI:1.033, 1.151), and the interaction term was 1.005 (95% CI:1.002, 1.007).

1. Introduction

Arthritis is a prevalent chronic disease in middle-aged and elderly people. It is characterized by joint pain, limited mobility, and joint conformity, and can cause permanent joint changes and kidney diseases (Lin et al., 2022). There are more than 100 million arthritis patients in China, of which the two most common types, rheumatoid arthritis and osteoarthritis, affect more than 16.5 million and 50 million patients, respectively (GBD, 2023). Globally, the age-standardized prevalence of rheumatoid arthritis increased by 7.4% between 1990 and 2017 and the prevalence of osteoarthritis increased by 113.25% between 1990 and 2019 (Finckh et al., 2022; Long et al., 2022). Previous studies have shown that the rising incidence of arthritis and rheumatoid arthritis is related to ambient air pollution, in addition to genetic factors and unhealthy lifestyles (Liu et al., 2021; McInnes et al., 2016).

Particulate matter inhalation has been reported to induce oxidative stress, activate the inflammatory response of the human immune system and accelerate the process of the arthritis and rheumatoid arthritis (Di et al., 2020; Zhang et al., 2023). Studies have shown that particulate matter exposure may be closely related to the occurrence of rheumatoid arthritis (Kim et al., 2024; Moore et al., 2024). For example, studies in Italy, Canada, United Kingdom and United States suggested that long-term exposure to $PM_{2.5}$ was linked to an increased risk of developing arthritis and rheumatoid arthritis (Adami et al., 2022; Alex et al., 2020; Zhang et al., 2023; Zhao et al., 2020). However, most of above studies were carried out in developed and low-pollution countries. Besides, $PM_{2.5}$ is a mixture composed of multiple components, mainly including black carbon (BC), organic matter (OM), nitrate (NO_3^-), sulfate (SO_4^{2-}) and ammonium ion (NH_4^+) (Zhang, Yin, et al., 2022). It remains unclear if some $PM_{2.5}$ components have higher impacts on the risk of arthritis and rheumatoid arthritis (Liu, Luo, et al., 2022).

Simultaneously, there is another gap in the link between green space exposure with arthritis and rheumatoid arthritis. Green space has been found to have health benefits potentially by promoting physical activity (Richardson et al., 2013) and social contact (de Vries et al., 2013) and reducing exposure to environmental hazards (Nieuwenhuijsen et al., 2017) such as air pollutants (Ji et al., 2020). Numerous studies have shown that green space is associated with reduced morbidity and mortality of various outcomes, including nonalcoholic fatty liver disease (Liu et al., 2023), osteoporosis (Tan et al., 2024b), and inflammatory bowel disease (Zhang, Chen, et al., 2022). However, no prospective studies have yet explored the impact of green space exposure on the risk of developing arthritis and rheumatoid arthritis. Additionally, green space could influence the relationship between air pollutants and health outcomes. This may be related to the ability of vegetation to filter air pollutants. Epidemiological studies showed that $PM_{2.5}$ and green space interactively affect the occurrence of type 2 diabetes (Yang et al., 2023), metabolic syndrome (Liu, Yan, et al., 2022) and non-accidental mortality (Crouse et al., 2019). Nevertheless, it remains unclear if $PM_{2.5}$ and green space interactively affect the risk of arthritis and rheumatoid arthritis.

In the present study, we pooled data from the China Family Panel Study (CFPS) and the China Health and Retirement Longitudinal Study (CHARLS), aiming to examine the associations of $PM_{2.5}$ and its constituents, and the interaction between $PM_{2.5}$ and green space with the risk of arthritis and rheumatoid arthritis in middle-aged and elderly people from 184 counties (districts) in 28 Chinese provinces.

2. Methods

2.1. Data Sources

The data for this study was obtained from two high quality publicly available databases, namely, CHARLS (http://charls.pku.edu.cn/en) and CFPS (https://www.isss.pku.edu.cn/cfps/). CHARLS is a longitudinal survey conducted by the National Institute of Development Studies, Peking University, which focuses on people aged 45 years and above. Similarly, as a national survey tracking sociodemographic patterns in China, the CFPS used a stratified multistage sampling strategy with households as the minimum sampling unit to obtain a nationally representative sample. In this study, we included data from four waves of CHARLS (2011, 2013, 2015, and 2018) and three waves of CFPS (2010, 2014, and 2018). Notably, only arthritis without specific classification was recorded as an endpoint in the CHARLS longitudinal follow-up, whereas only rheumatoid arthritis was recorded in the CFPS follow-up. Therefore, we acquired and cleaned the original data according to the following excluded criteria: (a) participants with arthritis ($n = 5{,}691$) or rheumatoid arthritis ($n = 518$) in the baseline survey; (b) missing key characteristic information (CHARLS: $n = 247$, CFPS: $n = 203$); (c) without follow-up outcomes (CHARLS: $n = 3{,}092$, CFPS: $n = 6{,}114$). Finally, we included 8,126 and 10,523 participants who were 45 years of age or older at baseline from the CHARLS and CFPS cohorts with at least one follow-up survey, respectively (Figure S1 in Supporting Information S1).

In this study, our annual average concentrations of $PM_{2.5}$ and its five constituents (BC, OM, NO_3^-, SO_4^{2-}, and NH_4^+) were mainly derived from the V4.CH.02 product (https://sites.wustl.edu/acag/datasets/surface-pm2-5/), which was developed by the Dalhousie University Atmospheric Composition Analysis Group (van Donkelaar et al., 2016). This product predicts grid estimates at $0.01° \times 0.01°$ spatial resolution by fully incorporating satellite-based aerosol optical depth observations using a nested GEOS-Chem chemical transport model and a geographically weighted regression. Predicted $PM_{2.5}$ estimates showed a high consistency with measurements in globally distributed ground sites ($R^2 = 0.81$; $\beta = 0.90$). In China, the annual average concentration of $PM_{2.5}$, including all chemical components, also exhibited good consistency with surface observations, having a crossvalidation R^2 that ranged from 0.75 to 0.83 (Shi et al., 2021). However, it is worth noting that the V4.CH.02 product only covers exposure data up to 2017. Therefore, the exposure data for 2018 were obtained from the China Air Pollution Tracker data set (TAP, http://tapdata.org.cn/, accessed 31 March 2023. Text S1 in Supporting Information S1). In this study, since we only had access to the city level of participants, participants from the same city were matched with the same annual average $PM_{2.5}$ and constituent concentrations. Exposure estimates were converted from 0.01° × 0.01° spatial resolution to city-level scales by averaging the grid estimates of administrative polygons containing cities. Subsequently, we obtained the concentrations of $PM_{2.5}$ and its constituent by using the address translation tool to obtain the latitude and longitude of each city based on the city address at the baseline survey. We calculated mean $PM_{2.5}$ and constituent levels from recruitment until self-reported outcomes, death, loss to follow-up, or end of follow-up as the primary long-term exposures (Li et al., 2023). Furthermore, we also identified exposures of 1-, 2-, and 3- years average $PM_{2.5}$ and constituent and utilized them in the sensitivity analysis (Zhang et al., 2019).

Green space in residential areas was measured with the Normalized Difference Vegetation Index (NDVI). We obtained NDVI values from Moderate Resolution Imaging Spectroradiometer for Spectroscopy (MODIS) Terra NDVI product (https://modis.gsfc.nasa.gov/data/dataprod/mod13.php) and NDVI values range from −1 to 1 (Yang et al., 2021). Larger NDVI values indicate denser green vegetation, and negative values are usually considered blue space or water. We extracted the latitude and longitude of the cities where the participants resided. NDVI values for the corresponding coordinates were calculated, and green space levels were assigned to each participant. In this study, we used the NDVI-1,000 m as a measure of the degree of greenness.

2.2. Outcome Measurement

Arthritis and rheumatoid arthritis patients in our study were defined as those who responded "Yes" to the question "Are you diagnosed by doctor with arthritis or rheumatoid arthritis?." At each follow-up survey, investigators asked participants about their disease to track follow-up results.

2.3. Covariates

We chose a comprehensive range of covariates, including age, sex (male, female), education (primary school and below, secondary school and above), marital status (married, cohabiting, divorced, widowed, single), BMI (≤30, >30 kg/m^2), smoking (yes, no), alcohol consumption (yes, no), physical exercise (yes, no), napping time (0 min, 0–30 min, 30–60 min, >60 min), urbanicity (urban, rural), hypertension (yes, no), diabetes (yes, no), heart disease (yes, no), kidney disease (yes, no), asthma (yes, no), household fuel use (clean fuels, solid fuels, others). Coal, crop residues, or wood are classified as "solid fuels", while natural gas, biogas, and liquefied petroleum gas are classified as "clean fuels." The information mentioned above was obtained by uniformly trained investigators using a standard questionnaire (Liu et al., 2021).

2.4. Statistical Analysis

2.4.1. Descriptive Analysis

Continuous variables were described by means and standard deviations (SDs), and categorical variables were demonstrated using the expression of frequencies and proportions. Baseline characteristics of patients and nonpatients were compared using Student's *t*-test, Mann-Whitney U *t*-tests and Chi-square test for normally, skewed distributed, and categorical variables, respectively.

2.4.2. Association Analysis of $PM_{2.5}$ Constituents With Arthritis and Rheumatoid Arthritis

We used generalized linear mixed models (GLMM) with a random city intercept to evaluate the associations of $PM_{2.5}$ and its five constituents with arthritis and rheumatoid arthritis, with adjustment for all the covariates described above. Given that constituent concentrations are highly correlated with total $PM_{2.5}$ mass, we further considered calculating residuals that are uncorrelated with $PM_{2.5}$ levels and representing changes in constituent levels independent of $PM_{2.5}$ by establishing a linear mixed model with constituent concentrations as the dependent variable and $PM_{2.5}$ levels as the independent variable. Finally, two different models were adopted to investigate the association between $PM_{2.5}$ component exposure and arthritis and rheumatoid arthritis. Specifically, in model 1, we adjusted for covariates such as age, sex, education level, marital status, BMI, alcohol and

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smoking habits, physical exercise, nap duration, city, medical history, and household fuel use; in model 2, we further adjusted for residuals based on model 1. Besides, we estimated odds ratios (OR) and 95% confidence intervals (CIs) relating arthritis and rheumatoid arthritis per interquartile range (IQR) increase in $PM_{2.5}$ and its constituents after average exposure. Then, to further explore the dose-response relationship of $PM_{2.5}$ and its constituents with arthritis and rheumatoid arthritis a three-node constrained cubic spline function was used.

2.4.3. Association Analysis of Mixed Exposure of $PM_{2.5}$ Constituents With Arthritis and Rheumatoid Arthritis

Given the high correlation between $PM_{2.5}$ and its constituents, it is likely that individuals are exposed to all constituents simultaneously in real-life settings. Consequently, the quantile g-computation (qg-computation) and the weighted quantile sum (WQS) regression model were employed to assess the combined effect of $PM_{2.5}$ constituents and to quantify the weight of each $PM_{2.5}$ constituent. The qg-computation and WQS models have been extensively applied in environmental epidemiology to assess the effects of exposure to multiple environmental contaminants on specific health outcomes (Guo et al., 2022). The WQS model constructs a weighted index to evaluate the combined effect of $PM_{2.5}$ components' mixed exposure and to determine the individual contribution of each component to this overall effect. The equation for the model is provided below:

$$g(\mu) = \beta_0 + \beta_1 \left(\sum_{i=0}^{c} \omega_i q_i \right) + z' \varphi$$

$$\text{WQS} = \sum_{i=1}^{c} \overline{\omega_i} q_i$$

In the model, β_0 represents the intercept; β_1 refer to the overall effect of the environmental mixture; ω_i stands for the weight of each component in the environmental mixture; $z' \varphi$ denotes the product of the covariate matrix and the covariate coefficients; c corresponds to the number of exposure variables; q_i represents different quartiles. In this study, we developed the WQS index utilizing quartiles of $PM_{2.5}$ components, employing 40% of the data set for model training and allocating the remaining 60% for validation purposes. However, it is crucial to acknowledge that the impact of each component within the mixture on the outcome, as assessed by the WQS regression model, was constrained to a uniform direction. To address the limitation of directional homogeneity, an analysis utilizing qg-computation was implemented to further explore the effects of $PM_{2.5}$ components on outcomes. Qg-computation provides an estimate of the effect of incrementally increasing all exposures by a quantile amount. Like WQS, qg-computation assigns fixed weights during the estimation process, however, qg-computation does not necessitate that all components exhibit associations with the outcome risk in the same direction. The sum of positive and negative weights equals 2. Detailed information regarding both models are available in our previously published article (He et al., 2024).

2.4.4. Analysis of Green Spaces Modification Effect

First, we constructed a product term for $PM_{2.5}$ concentration and green space level to calculate an interaction term to estimate the multiplicative joint effect of NDVI and $PM_{2.5}$ exposure. Then, we stratified the analyses by quartile values of NDVI values and $PM_{2.5}$ concentrations. Specifically, $PM_{2.5}$ concentrations and NDVI values were classified according to the cut-off values for the lowest (≤25%) and highest (>75%) quartiles. Subsequently, we analyzed the combined effect of another pollutant (NDVI/$PM_{2.5}$) in different subgroups for a given exposure ($PM_{2.5}$/NDVI) concentration ≤25%, 25%–75% and >75%. Additionally, considering some potential modifiers that can alter the effect of NDVI and $PM_{2.5}$ exposure, stratified analyzes were applied to assess the modifying effects of covariates such as sex, age, BMI and urbanicity on the association of NDVI, $PM_{2.5}$ and its constituents with arthritis/rheumatoid arthritis.

2.4.5. Sensitivity Analysis

To test the reliability of our results, we did some sensitivity analyses. Firstly, we repeated the analyses of $PM_{2.5}$ and its constituents in relation to arthritis and rheumatoid arthritis employing exposures for 1-, 2-, and 3-year prior to outcome, death, loss to follow-up, or the end of follow-up. Secondly, the study area, which was divided into eastern, western, central, and northeastern regions according to the economic level, was included in the model as covariates to assess the heterogeneity of different cities. Thirdly, a logistic regression model was established with arthritis and rheumatoid arthritis as the dependent variable and long-term $PM_{2.5}$ and its constituents exposure as the independent variable. Fourthly, since other chronic diseases may have a certain confounding effect on the progression of arthritis, we excluded participates with chronic diseases at baseline. Finally, we further adjusted for meteorological factor including mean temperature in the model. All statistical tests were bidirectional with a *P* value less than 0.05 deemed statistically significant. The data analyses process was implemented by *R* software (Version 4.3.0).

3. Results

There was a total of 2,582 and 421 participants with arthritis and rheumatoid arthritis during follow-up, with mean ages of 60.36 ± 10.29 years and 58.76 ± 9.70 years, respectively (Table 1). The map of distribution the concentration of $PM_{2.5}$ in each province of China and the geographical distribution of the participants are depicted in Figure 1. The mean values of $PM_{2.5}$, BC, OM, NO_3^-, NH_4^+, SO_4^{2-} and NDVI, were 56.82, 2.84, 13.99, 12.16, 8.32, 10.85 and 0.426 μg/m^3 for the average exposure during the entire follow-up period in CHARLS study (Table S1 in Supporting Information S1). Similarly, the mean values of $PM_{2.5}$, OM, NO_3^-, SO_4^{2-}, NH_4^+, BC, and NDVI during the entire follow-up period in CFPS were also described in Table S1 of Supporting Information S1.

3.1. Single Effect of $PM_{2.5}$ Constituents on Arthritis and Rheumatoid Arthritis

After adjusting for all covariates, the risks of arthritis and rheumatoid arthritis for each IQR increase in $PM_{2.5}$ exposure were 1.209 (95% CI: 1.198, 1.221) and 1.220 (95% CI: 1.199, 1.240) (Table S2 in Supporting Information S1). The associations between each IQR increases of $PM_{2.5}$ constituents and the prevalence of arthritis and rheumatoid arthritis using two models are shown in Figure 2. An IQR increase in BC, OM, NO_3^-, SO_4^{2-}, and NH_4^+ was associated with an OR for arthritis of 2.256 (95% CI: 2.110, 2.412), 1.570 (95% CI: 1.526, 1.616), 1.466 (95% CI: 1.421, 1.512), 1.980 (95% CI: 1.903, 2.061), and 2.168 (95% CI: 2.060, 2.283) in model 2, respectively. Similarly, for the five $PM_{2.5}$ constituents, each IQR increment in BC, NO_3^-, SO_4^{2-}, and NH_4^+ dramatically correlated with an increased risk of incidence of rheumatoid arthritis.

We observed "U" or "J" shaped exposure-response curves for the effects of $PM_{2.5}$, OM, NO_3^- and NH_4^+ exposure on the development of arthritis and rheumatoid arthritis. And the risk of arthritis and rheumatoid arthritis increased monotonically with BC concentration (Figures S2 and S3 in Supporting Information S1).

3.2. Combined Effects of Mixed Exposure to $PM_{2.5}$ Constituents on Arthritis and Rheumatoid Arthritis

We used the WQS model to find that the risk of developing arthritis and rheumatoid arthritis from mixed exposure to $PM_{2.5}$ constituents was 1.450 (95% CI: 1.370, 1.540) and 1.450 (95% CI: 1.280, 1.650) respectively. The results of the qg-computation model were similar to the WQS regression model. The mixed exposure of $PM_{2.5}$ constituents could increase the risk of arthritis and rheumatoid arthritis, and the effect values were 1.300 (95% CI: 1.239, 1.363) and 1.236 (95% CI: 1.115, 1.370), respectively (Figure 3). And among the positive direction, BC (index weight: 0.483 and 0.527) predominated in the relationship between arthritis and rheumatoid arthritis (Figure S4 in Supporting Information S1).

3.3. Interaction Effect of $PM_{2.5}$ and Green Space on Arthritis and Rheumatoid Arthritis

We found that each 0.1-unit decrease in NDVI, the risks of developing arthritis and rheumatoid arthritis were 1.091 (95% CI: 1.033, 1.151) and 1.011 (95% CI: 0.926, 1.105), respectively (Table S2 in Supporting Information S1). The results indicate that interaction of $PM_{2.5}$ and NDVI on the incidence of arthritis ($OR_{\text{interaction term}} = 1.005$, 95% CI: 1.002, 1.007; $P = 0.001$) and rheumatoid arthritis ($OR_{\text{interaction term}} = 1.010$, 95% CI: 1.006, 1.014; $P < 0.001$) was statistically significant (Table S2 in Supporting Information S1). Additionally, we compared the effects of $PM_{2.5}$ exposure on arthritis and rheumatoid arthritis within different greenness strata, and we found a monotonic trend of decreasing $PM_{2.5}$ effects (Figures 4c and 4d). Specifically, the risk of arthritis per 10 μg/m^3 increase in $PM_{2.5}$ was 1.611 (95% CI: 1.497, 1.735), 1.193 (95% CI: 1.148, 1.241), and 1.177 (95% CI: 1.110, 1.249), respectively, when stratified by NDVI values for the lowest fourth (≤25%), 25%–75% centile, and highest fourth (>75%), respectively. Furthermore, we stratified $PM_{2.5}$ concentrations into low, medium and high tertiles and

Table 1
Baseline Characteristics of the Study Participants

Variables	China health and retirement longitudinal study (CHARLS) Total (*N* = 8,126)	No-arthritis (*N* = 5,544)	Arthritis (*N* = 2,582)	*P*-value	The China family panel studies (CFPS) Total (*N* = 10,523)	No-RA (*N* = 10,102)	RA (*N* = 421)	*P*-value
Age (years)[a]	58.35 ± 9.58	57.41 ± 9.07	60.36 ± 10.29	<0.001	55.86 ± 8.13	55.74 ± 8.04	58.76 ± 9.70	<0.001
Age (years)								
45–65	6,128(75.41%)	4,390(79.18%)	1,738(67.31%)	<0.001	8,902(84.60%)	8,586(85.02%)	316(75.06%)	<0.001
≥65	1,998(24.59%)	1,154(20.82%)	844(32.69%)		1,621(15.40%)	1,516(15.01%)	105(24.94%)	
Sex								
Male	4,114(50.63%)	2,851(51.42%)	1,263(48.92%)	0.038	5,257(49.96%)	5,113(50.61%)	144(34.20%)	<0.001
Female	4,012(49.37%)	2,693(48.58%)	1,319(51.08%)		5,266(50.04%)	4,989(49.39%)	277(65.80%)	
Marital status								
Married/cohabitating	7,233(89.01%)	5,003(90.24%)	2,230(86.37%)	<0.001	9,646(91.67%)	9,269(91.75%)	377(89.55%)	0.383
Divorce	74(0.91%)	47(0.85%)	27(1.05%)		128(1.22%)	122(1.21%)	6(1.46%)	
Widowed	755(9.29%)	457(8.24%)	298(11.54%)		668(6.35%)	633(6.27%)	35(8.31%)	
Unmarried	64(0.78%)	37(0.67%)	27(1.05%)		81(0.77%)	78(0.77%)	3(0.71%)	
Education								
Primary school or below	5,282(65.00%)	3,440(62.05%)	1,842(71.34%)	<0.001	6,084(57.82%)	5,814(57.55%)	270(64.13%)	0.009
Secondary school and above	2,844(35.00%)	2,104(37.95%)	740(28.66%)		4,439(42.18%)	4,288(42.45%)	151(35.87%)	
BMI (kg/m^2)								
≤30	7,711(94.89%)	5,266(94.99%)	2,445	0.616	9,613(91.35%)	9,287(91.93%)	326(77.43%)	<0.001
>30	415(5.11%)	278(5.01%)	137		910(8.65%)	815(8.07%)	95(22.57%)	
Urbanicity								
Urban	3,067(37.74%)	2,102(37.92%)	965(37.37%)	0.657	4,393(41.75%)	4,243(42.00%)	150(35.63%)	0.011
Rural	5,059(62.26%)	3,442(62.08%)	1,617(62.63%)		6,130(58.25%)	5,859(58.00%)	271(64.37%)	
Smoking								
Yes	3,357(41.31%)	2,311(41.68%)	1,046(40.51%)	0.329	3,559(33.82%)	6,645(65.78%)	319(75.77%)	<0.001
No	4,769(58.69%)	3,233(58.32%)	1,536(59.49%)		6,964(66.18%)	3,457(34.22%)	102(24.23%)	
Drinking								
Yes	2,814(34.63%)	2,001(36.09%)	813(31.49%)	<0.001	2,027(19.26%)	8,136(80.54%)	360(85.51%)	0.013
No	5,312(65.37%)	3,543(63.91%)	1,769(68.51%)		8,496(80.74%)	1,966(19.46%)	61(14.49%)	
Physical								
Yes	3,555(43.75%)	2,424(43.72%)	1,131(43.80%)	0.965	2,986(71.62%)	7,229(71.56%)	308(73.16%)	0.511
No	4,571(56.25%)	3,120(56.28%)	1,451(56.20%)		7,537(28.38%)	2,873(28.44%)	113(26.84%)	
Household air pollution from cooking								
Clean fuel	3,826(47.08%)	2,680(48.34%)	1,146(44.38%)	0.004	5,510(52.36%)	5,319(52.65%)	191(45.37%)	<0.001
Solid fuel	4,252(52.33%)	2,832(51.08%)	1,420(55.00%)		4,906(46.62%)	4,687(46.40%)	219(52.02%)	
Others	48(0.59%)	32(0.58%)	16(0.62%)		107(1.02%)	96(0.95%)	11(2.61%)	
Napping time (Minutes)								
0	3,566(43.88%)	2,439(43.99%)	1,127(43.65%)	0.036	5,151(48.95%)	4,937(48.87%)	214(50.83%)	0.712
0–30	681(8.38%)	499(9.00%)	232(8.99%)		242(2.30%)	234(2.32%)	8(1.90%)	
30–60	2,512(30.91%)	1,756(31.67%)	756(29.28%)		3,401(32.32%)	3,274(32.41%)	127(30.17%)	
>60	1,367(16.83%)	900(16.24%)	467(18.08%)		1,729(16.43%0	1,657(16.40%)	72(17.10%)	

Note. BMI, body mass index; RA, rheumatoid arthritis. The sum of the percentages in the table may not be equal to 1, as we have rounded the results to two decimal places. [a]Stand for the continuous variable.

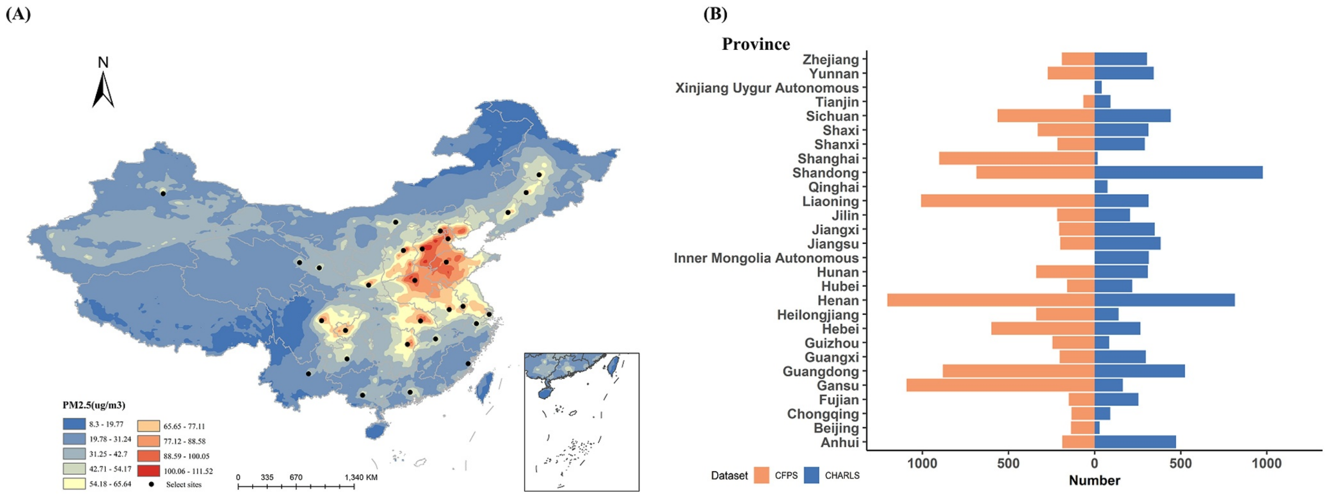

Figure 1. Distribution map of $PM_{2.5}$ concentration in each province of China during the study period (a) and the geographical distribution of 18,649 middle-aged and elderly people in 28 provinces of China from two cohorts.

discovered that for every 0.1 unit decrease in NDVI at $PM_{2.5}$ concentrations in the high tertile, an increased risk of arthritis and rheumatoid arthritis was observed (Figures 4a and 4b).

3.4. Stratified Analysis of Sex, Age, BMI and Urbanicity

Subgroup analysis by urbanicity showed that $PM_{2.5}$ was associated with higher risk of incident arthritis and rheumatoid arthritis in participants who lived in urban areas ($P < 0.001$, Figure 5). Tables S3–S7 in Supporting Information S1 describes the ORs of $PM_{2.5}$ constituents exposure with arthritis and rheumatoid arthritis in different subgroups. The associations between BC concentration per increase in IQR and arthritis as well as rheumatoid arthritis were stronger among urban participants ($OR_{arthritis}$ = 2.794, 95% CI: 2.482, 3.144; $OR_{rheumatoid\ arthritis}$ = 3.816, 95% CI: 2.960, 4.920) than that among rural participants ($OR_{arthritis}$ = 2.044, 95% CI: 1.883, 2.218; $OR_{rheumatoid\ arthritis}$ = 2.009, 95% CI: 1.661, 2.429), with a statistically significant effect ($P < 0.001$).

3.5. Sensitivity Analysis

Firstly, we repeated the analyses of $PM_{2.5}$ and its constituents in relation to arthritis and rheumatoid arthritis employing exposures for 1-, 2-, and 3-year prior to outcome, death, loss to follow-up, or the end of follow-up, and found that the results were robust in direction and magnitude (Table S8 in Supporting Information S1). Secondly, we included region as a covariate in the model, the effect estimates for arthritis and rheumatoid arthritis changed without statistical significance (Table S9 in Supporting Information S1). Thirdly, we restricted the subjects to participants without chronic diseases at the beginning of follow-up, some differences between groups were observed, but did not affect the overall results (Table S10 in Supporting Information S1). Fourthly we used logistics regression to analyze the association between $PM_{2.5}$ and its components exposure and arthritis and rheumatoid arthritis, and the findings were consistent with the results of our main analysis (Table S11 in Supporting Information S1). Finally, we further adjusted for meteorological factors including temperature in the model, and the results were not materially altered (Table S12 in Supporting Information S1).

4. Discussion

In our investigation of two national retrospective population-based cohort studies, we observed significant effect of $PM_{2.5}$ and its constitution on the incidence of arthritis and rheumatoid arthritis. Mixed effects analyses indicated that the adverse effects of $PM_{2.5}$ constituents exposure in this study were mainly attributable to the BC component. Additionally, there was a synergistic effect between $PM_{2.5}$ exposure and green space reduction on arthritis/rheumatoid arthritis effects.

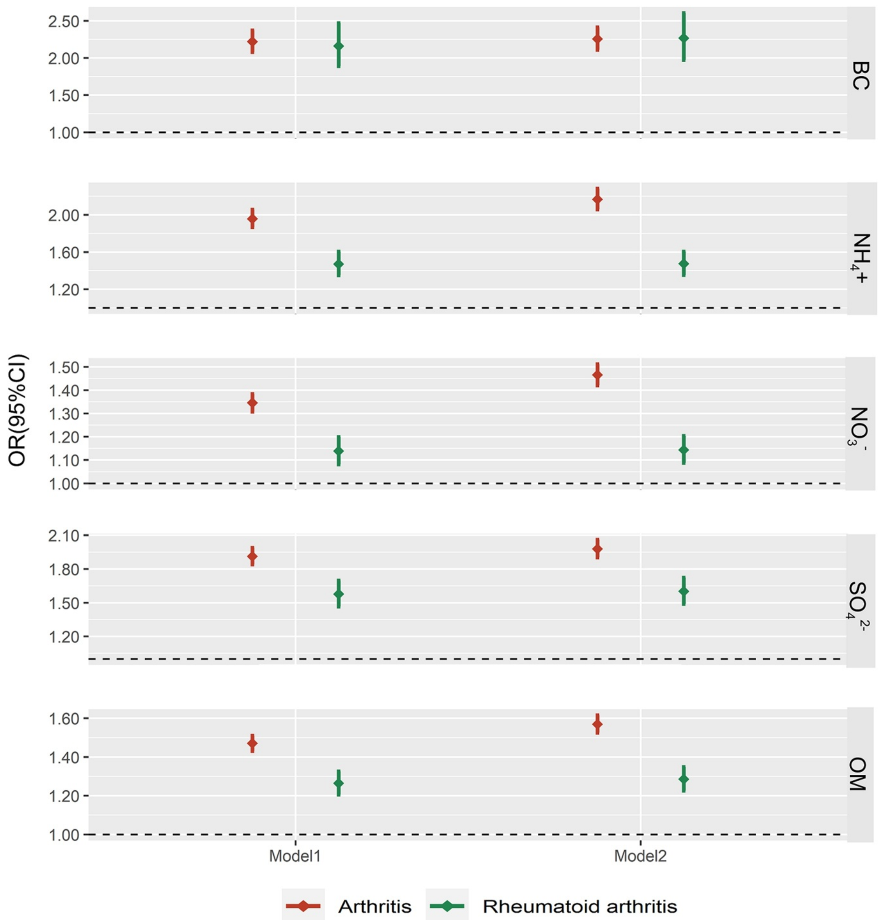

Figure 2. Odds ratios (with 95% CIs) for arthritis/rheumatoid arthritis associated with per IQR increase in exposure to $PM_{2.5}$ constituents. Abbreviations: OR, Odds ratios; CI, confidence interval; IQR, interquartile range; BC, black carbon; OM, organic matter; NO_3^-, nitrate; NH_4^+, ammonium; SO_4^{2-}, sulfate; Model 1 included single constituent concentration; Model 2 included single constituent residual calculated by constructing a linear regression model with constituent concentration as the dependent variable and $PM_{2.5}$ as the independent variable. All models were adjusted for age, sex, BMI, education, smoking status, drinking status, marital status, urbanicity, physical hypertension, diabetes, heart, kidney disease, asthma and napping time.

4.1. Comparison With Previous Studies

In line with our results, earlier studies from Canada, the United States, and Verona have shown that $PM_{2.5}$ exposure is a hazardous factor for arthritis and rheumatoid arthritis (Adami et al., 2021; De Roos et al., 2014; Hart et al., 2013). Notably, there are inconsistencies with the results of some studies (Di et al., 2020). Such differences could be explained by differences in study area, follow-up time and exposure levels. Besides, previous studies used fixed monitoring site data rather than more accurate remote sensing data to assess individual exposure, which may also introduce some information bias and affect the reliability of causal inference.

In this multi-city study, we found that the $PM_{2.5}$ constituents were positively associated with the risk of developing arthritis and rheumatoid arthritis, with BC accounting for the greatest hazard contribution. Although similar results have not been found, there is still evidence to support the adverse effects of BC exposure. An epidemiological study showed that constituent of $PM_{2.5}$ can increase the risk of developing osteoarthritis, and BC appears to be the most important constituent in the association between $PM_{2.5}$ and osteoarthritis-related outcomes (Wang et al., 2024). A systematic review summarizing 35 existing studies found that BC and OM were significantly associated with cardiovascular and respiratory health outcomes (Achilleos et al., 2017).

We also found that exposure to lower green space was associated with higher odds of arthritis and rheumatoid arthritis, and low green space and high $PM_{2.5}$ interactively impacted on arthritis and rheumatoid arthritis.

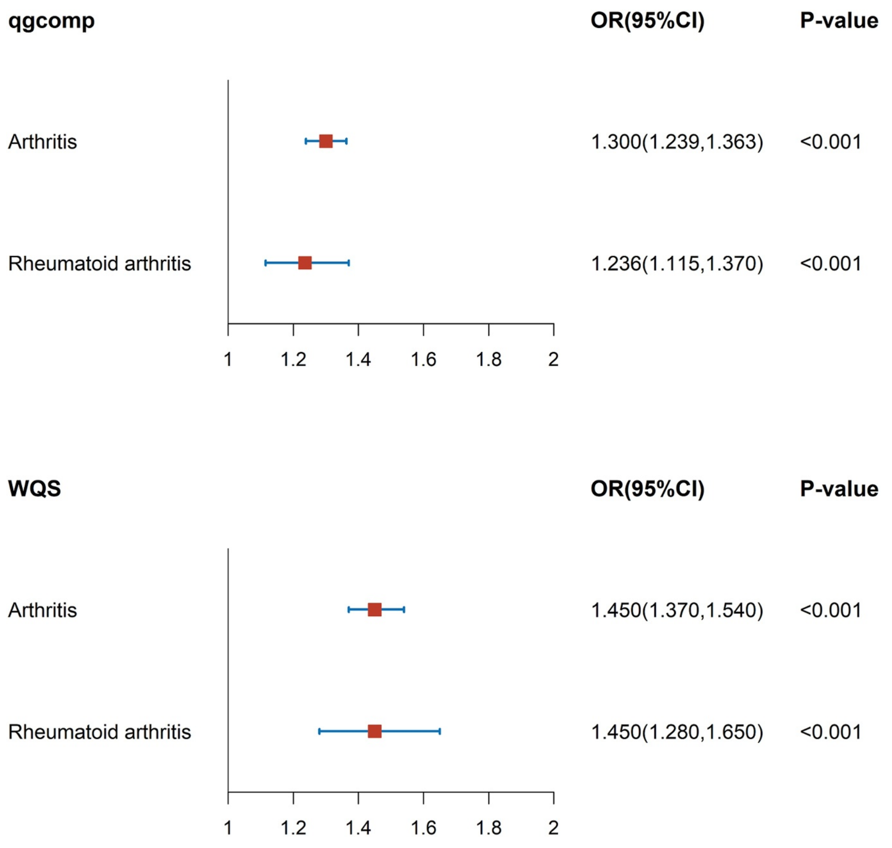

Figure 3. Association of $PM_{2.5}$ constituents with arthritis/rheumatoid arthritis based on WQS and qg-computation regression models.

Although there are no studies on green space, arthritis and rheumatoid arthritis at present, studies have confirmed that green space exposure is strongly associated with various diseases (Jimenez et al., 2022; Tan et al., 2024a). A cohort study suggested an 8% increase in mortality risk for every 0.1-unit reduction in NDVI (Ji et al., 2020). Yang et al. discovered that higher levels of residential green space reduced the risk of developing type 2 diabetes, and that air pollution played a major role in this association (Yang et al., 2023).

4.2. Potential Mechanisms

Although exact mechanisms by which $PM_{2.5}$ and its components affect arthritis/rheumatoid arthritis have not been elucidated to date, there are still some biological mechanisms that seem plausible. On the one hand, inhalation of ambient air particulates matter triggers the activation of transcription factors and nuclear factors by inducing excessive oxidation of airway epithelium, which ultimately leads to the increase of serum CRP levels and the secretion of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1) (Bayram et al., 2001; Liu et al., 2019). On the other hand, inhalation of particulate matter induces the formation of inducible bronchus associated lymphoid tissue (iBALT), which is associated with citrullination of proteins that trigger the development of rheumatoid arthritis (Moyron-Quiroz et al., 2004).

Currently, BC is mainly produced by incomplete combustion of fossil fuels or biomass and is thought to contribute the most to the impact of the $PM_{2.5}$ mass. Due to the adsorption characteristics of BC aerosol, its surface can adsorb other pollutants, such as polycyclic aromatic hydrocarbons, heavy metals, and so on. People can catch absorbed toxic substances into the body by breathing, which can cause inflammation of the immune system (Bongaerts et al., 2022). It has been demonstrated that BC may be related to mediating DNA methylation, promoting oxidative stress, vasoconstriction, systemic inflammation, and elevated blood pressure (Hvidtfeldt et al., 2019, 2021). Additionally, exposure to BC can lead to synovial inflammation, articular degeneration, and impaired osteoblast differentiation (Ma et al., 2018; Ren et al., 2019).

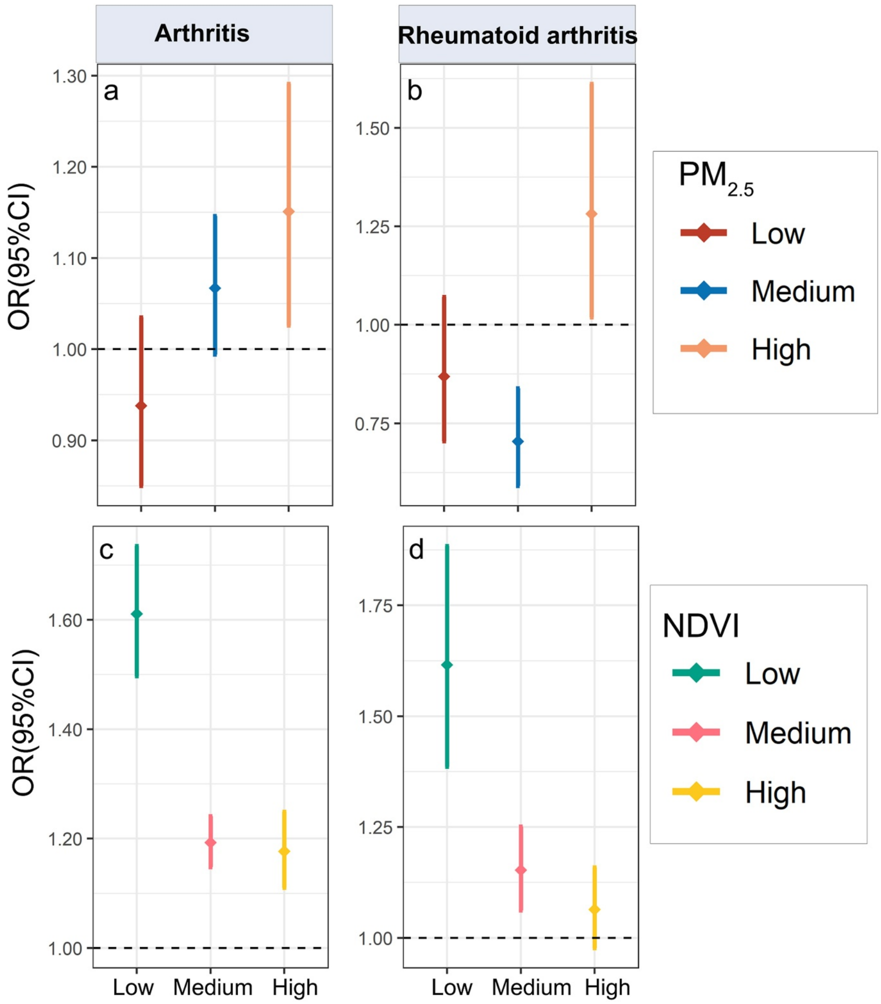

Figure 4. Effect of NDVI ($PM_{2.5}$) alteration on arthritis/rheumatoid arthritis at different levels of $PM_{2.5}$ (NDVI). Panels (4a and 4b) represents the effect of each 0.1-unit reduction in NDVI on arthritis/rheumatoid arthritis at different $PM_{2.5}$ concentrations; panels (4c and 4d) represents the effect of each 10 μg/m^3 increase in $PM_{2.5}$ on arthritis/rheumatoid arthritis at different NDVI levels. All models were adjusted for age, sex, BMI, education, smoking status, drinking status, marital status, urbanicity, physical hypertension, diabetes, heart, kidney disease, asthma and napping time.

Green space can offer protection from hazardous environmental exposures, including heatwaves and air pollution (Yuchi et al., 2020). Specifically, vegetation can retain fine dust particles and influence the deposition and dispersion of particulate matter. Studies have shown that particulate matter is susceptible to impact and retention on moist, rough or charged surfaces (Beckett et al., 1998). Therefore, the surface of vegetation leaves is well suited for the deposition of particulate matter due to its wetness and roughness. From an aerodynamic point of view, green space and vegetation can filter air pollutants and there may also be in vivo biological interactions (Ji et al., 2020). In this light, we encourage the government taking more public health protection strategies, including the construction or restoration of natural green space, to offset the harm caused by air pollutants.

4.3. Strength and Limitations

This study is the first to investigate the association of long-term exposure to ambient $PM_{2.5}$ constituents and green space with related arthritis and rheumatoid arthritis in two large longitudinally designed cohort studies, which have important implications for the increasing social burden of aging and the health of the elderly. This study also has some limitations. Firstly, since participants' residential addresses were inaccessible, exposure was assigned at the city level rather than in individual assessments. Therefore, misclassification bias was unavoidable in our study. Secondly, we have not considered the confounding effects of gaseous pollutants such as nitrogen dioxide,

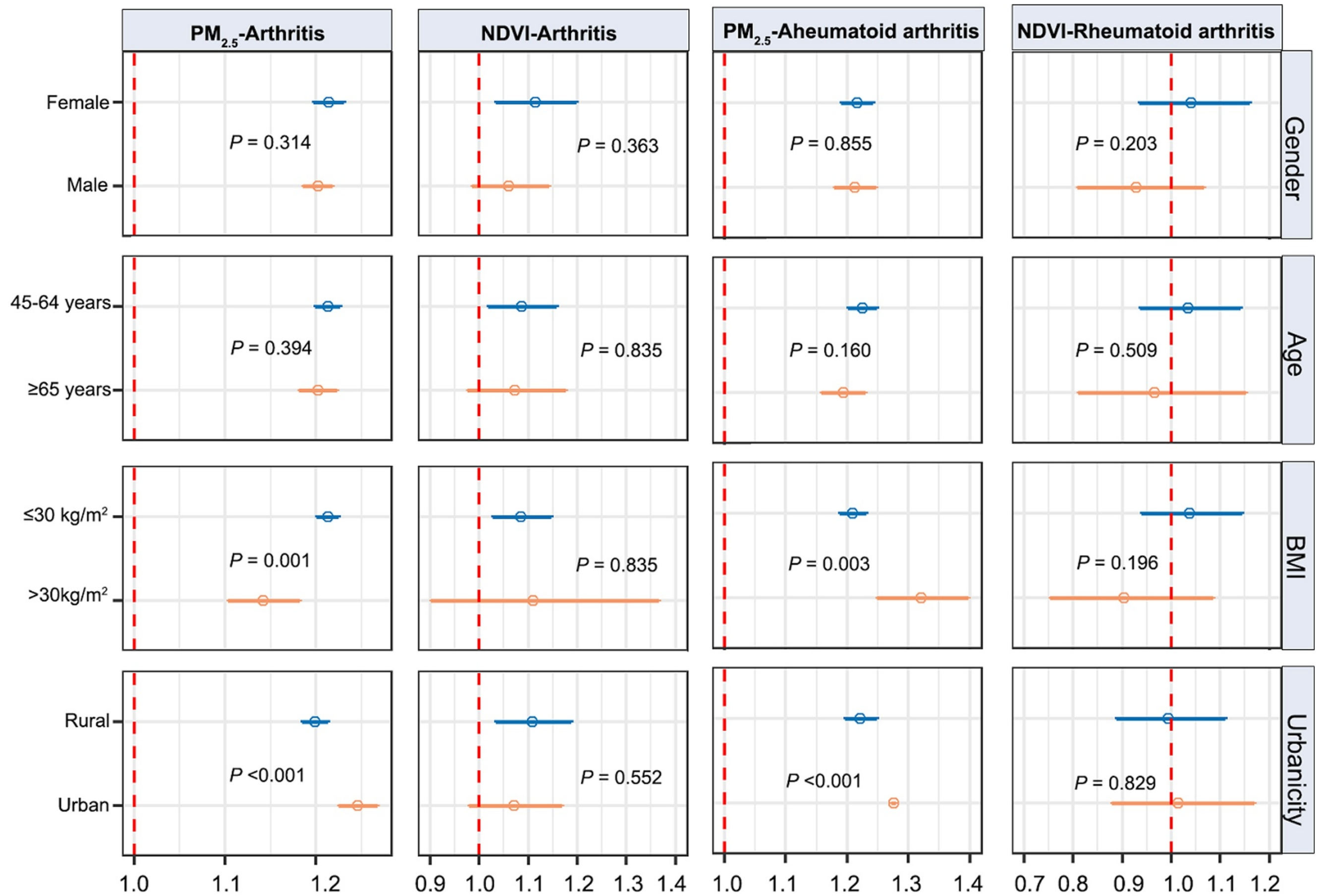

Figure 5. Subgroup analyses of odds ratios (with 95% CIs) of arthritis/arthritis associated with a IQR increase in green space and $PM_{2.5}$ exposure. All models were adjusted for age, sex, BMI, education, smoking status, drinking status, marital status, urbanicity, physical hypertension, diabetes, heart, kidney disease, asthma and napping time.

ozone, and sulfur dioxide because fully validated exposure data on gaseous pollutants are not available in the mainland of china. Secondly, due to data availability, we were unable to control for confounding effects of humidity and precipitation in the model. Thirdly, due to the lack of specific disease typing of arthritis, we were unable to confirm the relationship between exposure and different arthritis subtypes in more detail.

5. Conclusion

Exposure to $PM_{2.5}$ constituents (e.g., black carbon) is associated with a higher risk of arthritis and rheumatoid arthritis. Green space could alleviate the risk of arthritis and rheumatoid arthritis associated with $PM_{2.5}$ exposure. The study findings suggest that increasing vegetation cover area and targeting specific particulate matter components could be useful in decreasing the risk of arthritis and rheumatoid arthritis.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

All data are publicly available and stated in the manuscript.

1. [Dataset] Data on the rheumatoid arthritis is publicly available at Zhao et al. (2015).
2. [Dataset] Data on the arthritis is publicly available at Institute of Social Science Survey, Peking University. (2015).

3. [Dataset] Data of $PM_{2.5}$ and its components from the V4.CH.02 product is available for download at https://sites.wustl.edu/acag/datasets/surface-pm2-5/.
4. [Dataset] Data of NDVI from Moderate Resolution Imaging Spectroradiometer for Spectroscopy (MODIS) Terra NDVI product is available at Didan, K. (2021).

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References

Achilleos, S., Kioumourtzoglou, M. A., Wu, C. D., Schwartz, J. D., Koutrakis, P., & Papatheodorou, S. I. (2017). Acute effects of fine particulate matter constituents on mortality: A systematic review and meta-regression analysis. *Environment International*, *109*, 89–100. https://doi.org/10.1016/j.envint.2017.09.010

Adami, G., Pontalti, M., Cattani, G., Rossini, M., Viapiana, O., Orsolini, G., et al. (2022). Association between long-term exposure to air pollution and immune-mediated diseases: A population-based cohort study. *RMD Open*, *8*(1), e002055. https://doi.org/10.1136/rmdopen-2021-002055

Adami, G., Viapiana, O., Rossini, M., Orsolini, G., Bertoldo, E., Giollo, A., et al. (2021). Association between environmental air pollution and rheumatoid arthritis flares. *Rheumatology*, *60*(10), 4591–4597. https://doi.org/10.1093/rheumatology/keab049

Alex, A. M., Kunkel, G., Sayles, H., Flautero Arcos, J. D., Mikuls, T. R., & Kerr, G. S. (2020). Exposure to ambient air pollution and autoantibody status in rheumatoid arthritis. *Clinical Rheumatology*, *39*(3), 761–768. https://doi.org/10.1007/s10067-019-04813-w

Bayram, H., Sapsford, R. J., Abdelaziz, M. M., & Khair, O. A. (2001). Effect of ozone and nitrogen dioxide on the release of proinflammatory mediators from bronchial epithelial cells of Nonatopic Nonasthmatic subjects and atopic asthmatic patients in vitro. *The Journal of Allergy and Clinical Immunology*, *107*(2), 287–294. https://doi.org/10.1067/mai.2001.111141

Beckett, K. P., Freer-Smith, P. H., & Taylor, G. (1998). Urban woodlands: Their role in reducing the effects of particulate pollution. *Environmental Pollution*, *99*(3), 347–360. https://doi.org/10.1016/s0269-7491(98)00016-5

Bongaerts, E., Lecante, L. L., Bové, H., Roeffaers, M. B. J., Ameloot, M., Fowler, P. A., & Nawrot, T. S. (2022). Maternal exposure to ambient black carbon particles and their presence in maternal and fetal circulation and organs: An analysis of two independent population-based observational studies. *The Lancet Planetary Health*, *6*(10), e804–e811. https://doi.org/10.1016/s2542-5196(22)00200-5

Crouse, D. L., Pinault, L., Balram, A., Brauer, M., Burnett, R. T., Martin, R. V., et al. (2019). Complex relationships between greenness, air pollution, and mortality in a population-based Canadian cohort. *Environment International*, *128*, 292–300. https://doi.org/10.1016/j.envint.2019.04.047

De Roos, A. J., Koehoorn, M., Tamburic, L., Davies, H. W., & Brauer, M. (2014). Proximity to traffic, ambient air pollution, and community noise in relation to incident rheumatoid Arthritis. *Environmental Health Perspectives*, *122*(10), 1075–1080. https://doi.org/10.1289/ehp.1307413

de Vries, S., van Dillen, S. M., Groenewegen, P. P., & Spreeuwenberg, P. (2013). Streetscape greenery and health: Stress, social cohesion and physical activity as mediators. *Social Science & Medicine*, *94*, 26–33. https://doi.org/10.1016/j.socscimed.2013.06.030

Di, D., Zhang, L., Wu, X., & Leng, R. (2020). Long-term exposure to outdoor air pollution and the risk of development of rheumatoid arthritis: A systematic review and meta-analysis. *Seminars in Arthritis and Rheumatism*, *50*(2), 266–275. https://doi.org/10.1016/j.semarthrit.2019.10.005

Didan, K. (2021). MODIS/Aqua vegetation indices 16-Day L3 global 1km SIN grid V061 [Dataset]. *NASA EOSDIS Land Processes Distributed Active Archive Center*. https://doi.org/10.5067/MODIS/MYD13A2.061

Finckh, A., Gilbert, B., Hodkinson, B., Bae, S. C., Thomas, R., Deane, K. D., et al. (2022). Global epidemiology of rheumatoid arthritis. *Nature Reviews Rheumatology*, *18*, 591–602. https://doi.org/10.1038/s41584-022-00827-y

GBD. (2023). Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: A systematic analysis for the global burden of disease study 2021. *Lancet Rheumatol*, *5*(9), e508–e522. https://doi.org/10.1016/s2665-9913(23)00163-7

Guo, X., Li, N., Wang, H., Su, W., Song, Q., Liang, Q., et al. (2022). Combined exposure to multiple metals on cardiovascular disease in NHANES under five statistical models. *Environmental Research*, *215*, 114435. https://doi.org/10.1016/j.envres.2022.114435

Hart, J. E., Källberg, H., Laden, F., Costenbader, K. H., Yanosky, J. D., Klareskog, L., et al. (2013). Ambient air pollution exposures and risk of rheumatoid arthritis. *Arthritis Care & Research*, *65*(7), 1190–1196. https://doi.org/10.1002/acr.21975

He, Y. S., Cao, F., Musonye, H. A., Xu, Y. Q., Gao, Z. X., Ge, M., et al. (2024). Serum albumin mediates the associations between heavy metals and two novel systemic inflammation indexes among U.S. adults. *Ecotoxicology and Environmental Safety*, *270*, 115863. https://doi.org/10.1016/j.ecoenv.2023.115863

Hvidtfeldt, U. A., Geels, C., Sørensen, M., Ketzel, M., Khan, J., Tjønneland, A., et al. (2019). Long-term residential exposure to PM(2.5) constituents and mortality in a Danish cohort. *Environment International*, *133*, 105268. https://doi.org/10.1016/j.envint.2019.105268

Hvidtfeldt, U. A., Severi, G., Andersen, Z. J., Atkinson, R., Bauwelinck, M., Bellander, T., et al. (2021). Long-term low-level ambient air pollution exposure and risk of lung cancer—a pooled analysis of 7 European cohorts. *Environment International*, *146*, 106249. https://doi.org/10.1016/j.envint.2020.106249

Institute of Social Science Survey, Peking University. (2015). *China Family Panel Studies (CFPS)*. Peking University Open Research Data Platform. V43. https://doi.org/10.18170/DVN/45LCSO

Ji, J. S., Zhu, A., Lv, Y., & Shi, X. (2020). Interaction between residential greenness and air pollution mortality: Analysis of the Chinese longitudinal healthy longevity survey. *The Lancet Planetary Health*, *4*(3), e107–e115. https://doi.org/10.1016/s2542-5196(20)30027-9

Jimenez, M. P., Elliott, E. G., DeVille, N. V., Laden, F., Hart, J. E., Weuve, J., et al. (2022). Residential green space and cognitive function in a large cohort of Middle-Aged women. *JAMA Network Open*, *5*(4), e229306. https://doi.org/10.1001/jamanetworkopen.2022.9306

Kim, S. H., Kim, S. Y., Yoon, H. Y., & Song, J. W. (2024). PM(10) increases mortality risk in rheumatoid arthritis-associated interstitial lung disease. *RMD Open*, *10*(1), e003680. https://doi.org/10.1136/rmdopen-2023-003680

Li, X., Xie, J., Xu, J., Deng, L., Cao, G., Huang, S., et al. (2023). Long-term exposure to ambient PM(2.5) and age-related cataracts among Chinese middle-aged and older adults: Evidence from two national cohort studies. *Environmental Science & Technology*, *57*(32), 11792–11802. https://doi.org/10.1021/acs.est.3c02646

Lin, H. C., Hung, P. H., Hsieh, Y. Y., Lai, T. J., Hsu, H. T., Chung, M. C., & Chung, C. J. (2022). Long-term exposure to air pollutants and increased risk of chronic kidney disease in a community-based population using a fuzzy logic inference model. *Clinical Kidney Journal*, *15*(10), 1872–1880. https://doi.org/10.1093/ckj/sfac114

Liu, L., Luo, S., Zhang, Y., Yang, Z., Zhou, P., Mo, S., & Zhang, Y. (2022). Longitudinal impacts of PM(2.5) constituents on adult mortality in China. *Environmental Science & Technology*, *56*(11), 7224–7233. https://doi.org/10.1021/acs.est.1c04152

Liu, L., Yan, L. L., Lv, Y., Zhang, Y., Li, T., Huang, C., et al. (2022). Air pollution, residential greenness, and metabolic dysfunction biomarkers: Analyses in the Chinese longitudinal healthy longevity survey. *BMC Public Health*, *22*(1), 885. https://doi.org/10.1186/s12889-022-13126-8

Liu, M., Yang, S., Ye, Z., Zhang, Y., He, P., Zhou, C., et al. (2023). Residential green and blue spaces with nonalcoholic fatty liver disease incidence: Mediating effect of air pollutants. *Ecotoxicology and Environmental Safety*, *264*, 115436. https://doi.org/10.1016/j.ecoenv.2023.115436

Liu, Q., Gu, X., Deng, F., Mu, L., Baccarelli, A. A., Guo, X., & Wu, S. (2019). Ambient particulate air pollution and circulating C-reactive protein level: A systematic review and meta-analysis. *International Journal of Hygiene and Environmental Health*, *222*(5), 756–764. https://doi.org/10.1016/j.ijheh.2019.05.005

Liu, Y. H., Lu, Y. K., Liu, X. T., Li, Y. L., Hu, L. K., Gao, H. Y., et al. (2021). Association of household solid fuel use and long-term exposure to PM(2.5) with arthritis in middle-aged and older population in China: A cohort study. *Ecotoxicology and Environmental Safety*, *230*, 113104. https://doi.org/10.1016/j.ecoenv.2021.113104

Long, H., Liu, Q., Yin, H., Wang, K., Diao, N., Zhang, Y., et al. (2022). Prevalence trends of site-specific osteoarthritis from 1990 to 2019: Findings from the global burden of disease study 2019. *Arthritis & Rheumatology*, *74*(7), 1172–1183. https://doi.org/10.1002/art.42089

Ma, J., Guo, A., Wang, S., Man, S., Zhang, Y., Liu, S., & Liu, Y. (2018). From the lung to the knee joint: Toxicity evaluation of carbon black nanoparticles on macrophages and chondrocytes. *Journal of Hazardous Materials*, *353*, 329–339. https://doi.org/10.1016/j.jhazmat.2018.04.025

McInnes, I. B., Buckley, C. D., & Isaacs, J. D. (2016). Cytokines in rheumatoid arthritis—Shaping the immunological landscape. *Nature Reviews Rheumatology*, *12*(1), 63–68. https://doi.org/10.1038/nrrheum.2015.171

Moore, J. M., Norris, J. M., & Clark, M. L. (2024). Exposure to air pollutants and rheumatoid arthritis biomarkers: A scoping review. *Seminars in Arthritis and Rheumatism*, *65*, 152365. https://doi.org/10.1016/j.semarthrit.2024.152365

Moyron-Quiroz, J. E., Rangel-Moreno, J., Kusser, K., Hartson, L., Sprague, F., Goodrich, S., et al. (2004). Role of inducible Bronchus Associated Lymphoid Tissue (iBALT) in respiratory immunity. *Nature Medicine*, *10*(9), 927–934. https://doi.org/10.1038/nm1091

Nieuwenhuijsen, M. J., Khreis, H., Triguero-Mas, M., Gascon, M., & Dadvand, P. (2017). Fifty shades of green: Pathway to healthy urban living. *Epidemiology*, *28*(1), 63–71. https://doi.org/10.1097/ede.0000000000000549

Ren, Q., Wu, Y., Ma, J., Shan, Q., Liu, S., & Liu, Y. (2019). Carbon black-induced detrimental effect on osteoblasts at low concentrations: Remarkably compromised differentiation without significant cytotoxicity. *Ecotoxicology and Environmental Safety*, *178*, 211–220. https://doi.org/10.1016/j.ecoenv.2019.04.029

Richardson, E. A., Pearce, J., Mitchell, R., & Kingham, S. (2013). Role of physical activity in the relationship between urban green space and health. *Public Health*, *127*(4), 318–324. https://doi.org/10.1016/j.puhe.2013.01.004

Shi, W., Liu, C., Annesi-Maesano, I., Norback, D., Deng, Q., Huang, C., et al. (2021). Ambient PM(2.5) and its chemical constituents on lifetime-ever pneumonia in Chinese children: A multi-center study. *Environment International*, *146*, 106176. https://doi.org/10.1016/j.envint.2020.106176

Tan, T., Tang, L., Guo, X., Li, T., Tian, Y., & Ouyang, Z. (2024a). Associations of residential greenness with bone mineral density and osteoporosis: The modifying effect of genetic susceptibility. *Annals of the Rheumatic Diseases*, *83*(5), 669–676. https://doi.org/10.1136/ard-2023-224941

Tan, T., Tang, L., Guo, X., Li, T., Tian, Y., & Ouyang, Z. (2024b). Associations of residential greenness with bone mineral density and osteoporosis: The modifying effect of genetic susceptibility. *Annals of the Rheumatic Diseases*, *83*(5), 669–676. https://doi.org/10.1136/ard-2023-224941

van Donkelaar, A., Martin, R. V., Brauer, M., Hsu, N. C., Kahn, R. A., Levy, R. C., et al. (2016). Global estimates of fine particulate matter using a combined geophysical-statistical method with information from satellites, models, and monitors. *Environmental Science & Technology*, *50*(7), 3762–3772. https://doi.org/10.1021/acs.est.5b05833

Wang, P., Duan, F., Lv, Y., Man, S., Liu, S., & Liu, Y. (2024). Long- and intermediate-term ambient particulate pollution is associated with increased osteoarthritis risk: A population-based prospective analysis. *Environmental Science & Technology*, *58*(22), 9536–9547. https://doi.org/10.1021/acs.est.3c10893

Yang, T., Gu, T., Xu, Z., He, T., Li, G., & Huang, J. (2023). Associations of residential green space with incident type 2 diabetes and the role of air pollution: A prospective analysis in UK biobank. *Science of the Total Environment*, *866*, 161396. https://doi.org/10.1016/j.scitotenv.2023.161396

Yang, Z., Xu, R., Wang, Q., Fan, Z., Wang, Y., Liu, T., et al. (2021). Association of exposure to residential greenness with semen quality: A retrospective longitudinal study of sperm donation volunteers in Guangdong province, China. *Ecotoxicology and Environmental Safety*, *220*, 112396. https://doi.org/10.1016/j.ecoenv.2021.112396

Yuchi, W., Sbihi, H., Davies, H., Tamburic, L., & Brauer, M. (2020). Road proximity, air pollution, noise, green space and neurologic disease incidence: A population-based cohort study. *Environmental Health*, *19*(1), 8. https://doi.org/10.1186/s12940-020-0565-4

Zhang, J., Fang, X. Y., Wu, J., Fan, Y. G., Leng, R. X., Liu, B., et al. (2023). Association of combined exposure to ambient air pollutants, genetic risk, and incident rheumatoid arthritis: A prospective cohort study in the UK Biobank. *Environmental Health Perspectives*, *131*(3), 37008. https://doi.org/10.1289/ehp10710

Zhang, Y., Yin, Z., Zhou, P., Zhang, L., Zhao, Z., Norbäck, D., et al. (2022). Early-life exposure to PM(2.5) constituents and childhood asthma and wheezing: Findings from China, Children, Homes, Health study. *Environment International*, *165*, 107297. https://doi.org/10.1016/j.envint.2022.107297

Zhang, Z., Chen, L., Qian, Z. M., Li, H., Cai, M., Wang, X., et al. (2022). Residential green and blue space associated with lower risk of adult-onset inflammatory bowel disease: Findings from a large prospective cohort study. *Environment International*, *160*, 107084. https://doi.org/10.1016/j.envint.2022.107084

Zhang, Z., Dong, B., Li, S., Chen, G., Yang, Z., Dong, Y., et al. (2019). Particulate matter air pollution and blood glucose in children and adolescents: A cross-sectional study in China. *Science of the Total Environment*, *691*, 868–873. https://doi.org/10.1016/j.scitotenv.2019.07.179

Zhao, N., Smargiassi, A., Hatzopoulou, M., Colmegna, I., Hudson, M., Fritzler, M. J., et al. (2020). Long-term exposure to a mixture of industrial SO_2, NO_2, and $PM_{2.5}$ and anti-citrullinated protein antibody positivity. *Environmental Health*, *19*(1), 86. https://doi.org/10.1186/s12940-020-00637-3

Zhao, Y. H., Lin, Y. F., Strauss, J., & Park, A. (2015). *China health and retirement longitudinal study (2008 pilot survey)*. Peking University Open Research Data Platform. V1. https://doi.org/10.18170/DVN/SXKEWK