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Joint impacts of air pollution and healthy lifestyles on kidney function decline: insights from a nationwide cohort study

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ABSTRACT

Long-term exposure to ambient air pollution is a recognized environmental risk factor for chronic kidney disease (CKD), but its dynamic effects on kidney function remain incompletely understood. This nationwide longitudinal study included 5,306 participants from the China Health and Retirement Longitudinal Study (CHARLS) to examine associations between five major air pollutants (PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3) and kidney function decline, measured by the annual slope of estimated glomerular filtration rate (eGFR). Air pollutant exposures were assessed both as continuous variables and dichotomized by median levels. Higher exposure to PM_1, $PM_{2.5}$, PM_{10}, and NO_2 was consistently associated with faster eGFR decline. In fully adjusted models, each 1 μg/m^3 increase in $PM_{2.5}$ corresponded to a steeper decline in eGFR ($\beta = -0.02$; 95% CI: −0.03 to −0.02), while participants in high $PM_{2.5}$ areas had an annual decline of −0.51 mL/min/1.73 m^2 (95% CI: −0.72 to −0.31). O_3 showed a significant association only in binary models. Weighted quantile sum regression identified $PM_{2.5}$ and PM_1 as dominant contributors. A favorable lifestyle markedly mitigated pollution-related decline; under high PM_1 exposure, eGFR declined by −0.69 (95% CI: −1.06 to −0.33) in those with favorable lifestyles versus −2.20 (95% CI: −2.65 to −1.75) in those with unfavorable lifestyles. These findings were robust across multiple sensitivity analyses. These findings emphasize the adverse impact of long-term air pollution exposure on kidney function and suggest that healthy lifestyle behaviors may offer significant protective benefits.

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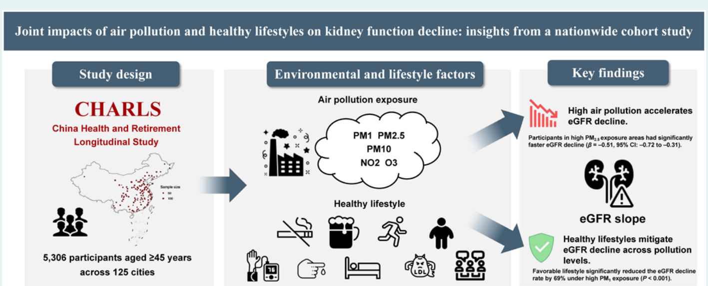
GRAPHICAL ABSTRACT



1. Introduction

Chronic kidney disease (CKD) is a progressive, irreversible condition that compromises kidney function and affects over 10% of the global population, impacting more than 800 million individuals [1]. It is among the leading causes of death worldwide. With an aging population and increasing life expectancy, the prevalence of CKD continues to grow [2]. This condition not only poses significant threats to individual health but also imposes substantial economic and resource burdens on global healthcare systems [3]. While traditional risk factors, such as diabetes and hypertension [4], have been

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extensively studied, the contribution of environmental risk factors to the onset and progression of CKD has received comparatively less attention [5].

Emerging evidence suggests that environmental pollutants, including fine particulate matter ($PM_{2.5}$, PM_{10}) and nitrogen oxides (NO_2), significantly elevate the risk of respiratory and cardiovascular diseases [6–8] and may also contribute to kidney function decline through mechanisms such as oxidative stress and chronic inflammation [9,10]. However, most existing research has focused on isolated health outcomes associated with air pollution, leaving the dynamic relationship between air pollution exposure and kidney function insufficiently explored.

The present study focuses on five key ambient air pollutants: PM_1, $PM_{2.5}$, PM_{10}, NO_2, and ozone (O_3). These pollutants originate from various anthropogenic activities, including fossil fuel combustion, industrial processes, vehicular emissions, and photochemical reactions. Their small aerodynamic diameters and chemical reactivity enable them to penetrate deep into the respiratory tract and enter systemic circulation, where they may exert widespread biological effects. Table 1 provides an overview of their definitions, principal sources, and known or potential health impacts.

Simultaneously, healthy lifestyles have gained growing attention for their protective roles in preventing and managing chronic diseases. Healthy behaviors, such as avoiding smoking, maintaining a balanced diet, engaging in regular physical activity, and sustaining a healthy weight, are known to improve cardiovascular and metabolic health and may also mitigate the adverse health effects of environmental risk factors [36–38]. Although previous studies have highlighted the protective effects of healthy lifestyles on various chronic conditions, limited research has explored whether these behaviors can offset the detrimental effects of air pollution on kidney function.

This study leverages nationally representative data from China and adopts a longitudinal design to investigate the association between long-term exposure to air pollution and kidney function decline, while assessing the potential modifying role of healthy lifestyle behaviors. By systematically analyzing both the individual and combined effects of five major air pollutants, this research aims to clarify the dynamic effects of air pollution on renal health and to explore whether healthy behaviors offer protective benefits. Findings from this study may inform targeted prevention strategies, support evidence-based environmental health policy, and guide population-level interventions to mitigate the burden of CKD.

Table 1. Characteristics, major sources, and known or potential health effects of selected ambient air pollutants included in this study.

Pollutant	Definition	Major sources	Known or potential health effects
PM_1	Particulate matter with aerodynamic diameter ≤1 µm	Ultrafine particles from combustion engines, industrial emissions, secondary aerosol formation [11,12]	Penetrates deep into alveoli; associated with systemic inflammation, cardiovascular and renal damage [13–16]
$PM_{2.5}$	Particulate matter with diameter ≤2.5 µm	Traffic emissions, coal and biomass burning, industrial combustion [17]	Linked to oxidative stress, atherosclerosis, lung function decline, and CKD progression [18–20]
PM_{10}	Particulate matter with diameter ≤10 µm	Road dust, construction, agricultural activities, fossil fuel combustion [21,22]	Causes airway irritation, asthma exacerbation, and potential renal impact [23–25]
NO_2	Reactive nitrogen oxide gas formed during high-temperature combustion	Vehicular emissions, power plants, gas stoves, and heaters [26]	Triggers respiratory inflammation, impairs vascular function, linked to CKD risk [27–29]
O_3	Secondary pollutant formed by photochemical reactions between NOx and VOCs in sunlight	Results from interaction of NOx and VOCs [30–32]	Induces oxidative stress, affects pulmonary and cardiovascular systems [33–35]

2. Materials and methods

2.1. Study population

This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS) [39]. Initiated by Peking University in 2011, CHARLS is a nationwide longitudinal study tracking the health and aging of Chinese adults aged 45 and older. The study employed a stratified multistage probability sampling method, covering 28 provinces in China and enrolling 17,708 participants. Participants underwent standardized interviews, physical examinations, and biomarker testing, providing comprehensive data on sociodemographic factors, lifestyles, and health metrics. Follow-ups were conducted biennially from the baseline survey onward. The CHARLS datasets can be downloaded at http://charls.pku.edu.cn/en. Ethical approval for this study was granted by the Biomedical Ethics Committee of Peking University (IRB00001052-11014 and IRB00001052-11015). All participants provided written informed consent before participation, in accordance with the ethical standards of the Declaration of Helsinki.

This study utilized CHARLS data collected across three waves: wave 1 (2011–2012), wave 2 (2013–2014), and wave 3 (2015–2016). However, only wave 1 and wave 3 included biomarker data necessary for calculating estimated glomerular filtration rate (eGFR). Inclusion criteria were: (1) age ≥45 years and (2) availability of complete data for calculating kidney function (creatinine and cystatin C). Exclusion criteria included: (1) missing community location data, (2) death or loss to follow-up, (3) age <45 years, (4) incomplete data on cystatin C or creatinine, and (5) community relocation during follow-up. Ultimately, 5306 participants met the criteria for analysis.

2.2. Environmental exposure measurement

Air pollution exposure data were sourced from the China High Air Pollution (CHAP) dataset (https://weijing-rs.github.io/product.html), recognized for its high resolution and reliability. The dataset integrates satellite remote sensing, artificial intelligence, ground observations, atmospheric reanalysis, and model simulations to capture the spatiotemporal heterogeneity of air pollution [40,41]. The pollutants analyzed included PM_1, $PM_{2.5}$, PM_{10}, and O_3 at a spatial resolution of 1 km × 1 km, and NO_2 at a resolution of 10 km × 10 km. Mean pollutant concentrations from the baseline to the final follow-up were calculated and matched with county-level geocodes corresponding to participants' residential addresses to estimate long-term exposure. Figure 1 displays the geographic distribution of participants alongside the average pollutant concentrations recorded from 2011 to 2016.

2.3. Healthy lifestyle measurement

A healthy lifestyle score was developed based on the American Heart Association's 'Life's Essential 8' framework and supporting studies [42,43]. This score included nine modifiable health risk factors: smoking, alcohol consumption, physical activity, BMI, lipids, blood glucose, blood pressure, sleep, and social participation. Smoking was scored as follows: 100 points for never smoking, 75 points for cessation ≥5 years, 50 points for cessation <5 years, and 0 points for current smokers. Alcohol consumption was deemed healthy if daily intake was ≤28 g for men or ≤14 g for women, receiving 100 points. Physical activity was assessed by calculating the total weekly time spent on moderate and vigorous exercise, with vigorous activity weighted double. Participants engaging in ≥150 min of activity per week received 100 points, with scores decreasing for lower levels of activity. BMI was scored as 100 for the ideal range (<25 kg/m^2), with lower scores assigned for deviations. Other health factors were similarly scored using established clinical thresholds. Missing data were imputed using the *mice* package (version 3.16.0). To compute the composite healthy lifestyle score, each indicator was weighted using standardized regression coefficients (β values) derived from generalized linear models (GLMs) evaluating their associations with eGFR slope changes [44]. Final scores were categorized into three groups: unhealthy (0–59), intermediate (60–79), and healthy (80–100).

2.4. Outcome assessment

The primary outcome of this study was the eGFR slope, defined as the annual rate of decline in eGFR, which served as a measure of changes in kidney function. In the main analysis, eGFR values were calculated using the CKD-EPI$_{cr\text{-}cys}$ equation [45]. The eGFR slope was calculated by taking the difference between eGFR measurements from wave 1 (2011–2012) and wave 3 (2015–2016), divided by the time interval in years between the two waves. This value reflects the annual rate of kidney function change over an approximate 4-year period.

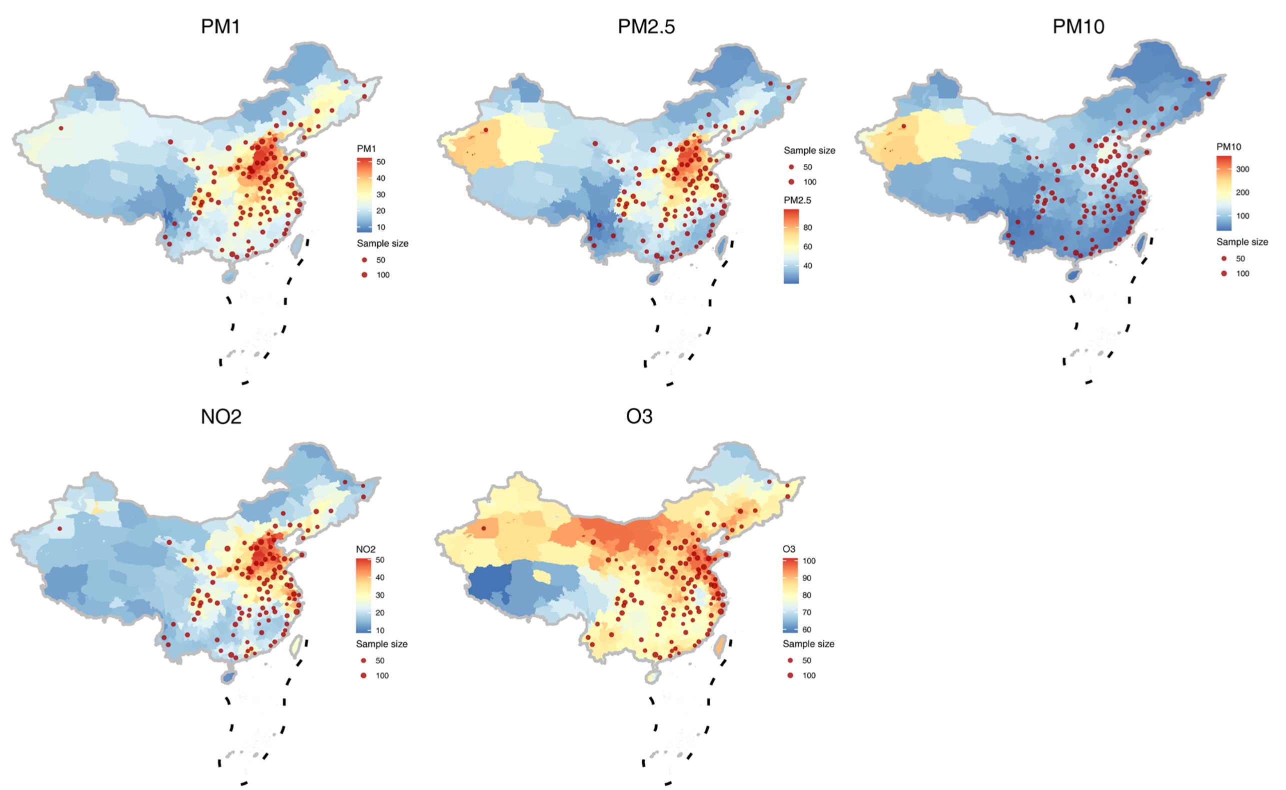

Figure 1. Spatial distribution of ambient air pollutants and study participants across China. Geographical distribution maps of ambient air pollutants and participant enrollment locations across China. NO_2: nitrogen dioxide; O_3: ozone; PM_1: particulate matter with an aerodynamic diameter less than 1 μm; $PM_{2.5}$: particulate matter with an aerodynamic diameter less than 2.5 μm; PM_{10}: particulate matter with an aerodynamic diameter < 10 μm.

2.5. Covariates

Covariates included sociodemographic characteristics (sex, age, education level, urban or rural residence, and region), lifestyle factors, and health-related variables [46]. Sociodemographic data were obtained through standardized interviews conducted by trained interviewers. Indoor air pollution exposure was assessed based on the type of heating and cooking fuels used (solid vs. clean fuels). Health-related variables were collected through blood tests and structured questionnaires. In addition to lifestyle-related biomarkers, blood urea nitrogen (BUN) and serum uric acid (UA) were incorporated as key health indicators. All covariates were gathered at baseline to ensure they accurately represented potential confounding effects throughout the study period.

2.6. Statistical analyses

To comprehensively assess the relationship between air pollution exposure and kidney function decline, we first analyzed air pollutant concentrations as continuous variables in the primary regression models. For interpretability and subgroup comparisons, particularly in stratified analyses involving lifestyle categories, we additionally categorized exposure levels into two groups using the median as a cutoff: *Q*1 (low exposure) and *Q*2 (high exposure). Descriptive statistics were used to analyze baseline characteristics across the overall population and lifestyle-specific groups. Generalized linear models with a Gaussian distribution and identity link function were employed to assess the associations between individual air pollutants and the continuous outcome variable – the annual eGFR slope. Stratified analyses assessed the effects of lifestyle categories (unfavorable, intermediate, favorable) and pollutant exposure subgroups (low, high) on eGFR decline rates, adjusting for potential confounders. These adjustments were made incrementally, with models including sociodemographic characteristics (model 1), indoor air pollution (model 2), and additional health variables such as BUN, UA, and kidney disease status (model 3).

Restricted cubic splines (RCSs) with three knots (10th, 50th, and 90th percentiles) were employed to explore the concentration–response (C–R) relationships between air pollutants and eGFR decline rates. Subgroup analyses stratified by sex, age, education level, residence, lifestyle, CKD status, and eGFR classification were conducted to investigate potential interactive effects.

The 'mediation' R package was utilized to determine whether the relationship between air pollution exposure and eGFR decline was mediated by lifestyle categories, with 10,000 bootstraps applied. The interaction between air pollution and lifestyle was further examined using weighted quantile sum (WQS) regression [47], implemented with the '*gWQS*' package (version 3.0.5), and quantile g-computation [48], performed with the '*qgcomp*' package (version 2.15.2). These models evaluated the combined effects of multi-pollutant exposures on eGFR decline rates. The WQS index (ranging from 0 to 1) quantified the relative contribution of each pollutant to the combined effect, while quantile g-computation addressed limitations of the uniform directionality assumption inherent in WQS models. To ensure robustness, two sets of sensitivity analyses were conducted. First, we recalculated eGFR using the CKD-EPIcr and CKD-EPIcys equations [49]. Second, we applied linear mixed-effects models using the '*lme4*' package (version 1.1-37), treating eGFR as the dependent variable and incorporating both time (years since baseline) and pollutant-by-time interaction terms. Random intercepts were included for individual participants to account for within-subject correlation. All statistical analyses were performed using R software (version 4.4.2) (R Project for Statistical Computing, Vienna, Austria), with a two-sided $p < .05$ considered statistically significant.

3. Results

3.1. Baseline characteristics

Table 2 summarizes the baseline characteristics of CHARLS participants. Among the 5306 participants, the mean age (±SD) was 59.99 ± 9.27 years, with 53.81% female and 46.19% male. Lifestyle categorization revealed that 813 participants had an unfavorable lifestyle, 2877 had an intermediate lifestyle, and 1616 had a favorable lifestyle. Participants with a favorable lifestyle were generally younger, more likely to be female, better educated, and more often resided in rural areas. Smoking and alcohol consumption were disproportionately common among participants with an unfavorable lifestyle. Key health and behavioral factors, including physical activity, sleep duration, social participation, non-HDL cholesterol, BMI, diabetes prevalence, and blood pressure, were lowest in the favorable lifestyle group. Although the prevalence of kidney disease did not vary across lifestyle categories, BUN and UA levels were lowest among participants with a favorable lifestyle. The average exposure levels of the air pollutants PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3 were 32.03 ± 10.18, 57.61 ± 18.89, 97.64 ± 33.40, 30.50 ± 9.90, and 84.76 ± 6.59 μg/m^3, respectively. As shown in Table 2, there were no statistically significant differences in outdoor (PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3) or indoor (solid fuel use for cooking or heating) air pollution exposure across the different lifestyle subgroups (all $p > .05$).

3.2. Association between air pollution exposure, lifestyle, and eGFR slope

Generalized linear regression analyses were conducted to evaluate the associations between air pollution exposure and the annual eGFR slope. Results from both continuous exposure models and median-dichotomized models (high vs. low exposure) are detailed in Table 3.

In models using air pollutant concentrations as continuous variables, significant inverse associations were observed for PM_1 ($\beta = -0.04$, 95% CI: −0.05, −0.03), $PM_{2.5}$ ($\beta = -0.02$, 95% CI: −0.03, −0.02), PM_{10} ($\beta = -0.01$, 95% CI: −0.02, −0.01),

Table 2. Baseline characteristic of the enrolled participants according to different lifestyle categories.

	Total (n = 5306)	Unfavorable (n = 817)	Intermediate (n = 2778)	Favorable (n = 1711)	p Value
Age, years	59.99 ± 9.27	61.30 ± 8.81	60.50 ± 9.29	58.55 ± 9.26	<.0001
Sex					<.01
Female	2855 (53.81)	412 (50.43)	1474 (53.06)	969 (56.63)	
Male	2451 (46.19)	405 (49.57)	1304 (46.94)	742 (43.37)	
Education					<.0001
Above high school	390 (7.36)	45 (5.52)	182 (6.56)	163 (9.53)	
Below high school	4911 (92.64)	770 (94.48)	2594 (93.44)	1547 (90.47)	
Residence					<.0001
Rural	3499 (65.94)	489 (59.85)	1837 (66.13)	1173 (68.56)	
Urban	1807 (34.06)	328 (40.15)	941 (33.87)	538 (31.44)	
South/north					.25
North	2484 (46.81)	385 (47.12)	1272 (45.79)	827 (48.33)	
South	2822 (53.19)	432 (52.88)	1506 (54.21)	884 (51.67)	
Nationality					.95
Han	4937 (93.06)	762 (93.38)	2580 (92.87)	1595 (93.22)	
Others	298 (5.62)	43 (5.27)	159 (5.72)	96 (5.61)	
NA	70 (1.32)	11 (1.35)	39 (1.40)	20 (1.17)	
Solid fuel use for cooking	3090 (58.50)	466 (57.11)	1606 (58.04)	1018 (59.92)	.32
Solid fuel use for heating	3053 (62.27)	442 (59.41)	1638 (63.44)	973 (61.70)	.12
Kidney disease	294 (5.60)	48 (5.96)	149 (5.42)	97 (5.72)	.82
BUN, mg/dL	15.81 ± 4.48	16.22 ± 4.58	15.87 ± 4.45	15.50 ± 4.45	<.001
UA, mg/dL	4.43 ± 1.25	4.78 ± 1.39	4.47 ± 1.22	4.18 ± 1.17	<.0001
Smoking	2058 (38.88)	406 (49.82)	1122 (40.51)	530 (31.03)	<.0001
BMI, kg/m^2	23.56 ± 3.86	25.50 ± 4.14	23.71 ± 3.94	22.39 ± 3.12	<.0001
Non-HDL, mg/dL	142.39 ± 38.60	189.83 ± 38.40	146.13 ± 30.76	113.68 ± 21.43	<.0001
DM	801 (15.10)	309 (37.82)	366 (13.17)	126 (7.36)	<.0001
Pre-DM	1174 (22.15)	262 (32.15)	665 (23.96)	247 (14.44)	<.0001
HbA1c, %	5.27 ± 0.81	5.91 ± 1.46	5.21 ± 0.61	5.05 ± 0.41	<.0001
SBP, mmHg	131.03 ± 21.84	146.01 ± 20.10	133.63 ± 21.73	119.69 ± 16.56	<.0001
DBP, mmHg	75.63 ± 12.18	83.18 ± 11.84	76.81 ± 11.99	70.11 ± 10.02	<.0001
Nighttime sleep duration, hour	6.34 ± 1.90	6.08 ± 2.08	6.21 ± 1.96	6.69 ± 1.65	<.0001
Alcohol consumption					<.01
Drink more than once a month	1312 (24.79)	221 (27.12)	719 (25.97)	372 (21.77)	
Drink less than once a month	388 (7.33)	70 (8.59)	186 (6.72)	132 (7.72)	
Never drink	3593 (67.88)	524 (64.29)	1864 (67.32)	1205 (70.51)	
Social participation (score ≥80)	1253 (23.61)	139 (17.01)	591 (21.27)	523 (30.57)	<.0001
Physical activity (score ≥80)	1414 (26.65)	178 (21.79)	739 (26.60)	497 (29.05)	<.001
Ambient air pollutants					
PM_1, μg/m^3	32.03 ± 10.18	32.08 ± 10.83	31.81 ± 10.13	32.35 ± 9.94	.22
$PM_{2.5}$, μg/m^3	57.61 ± 18.89	58.01 ± 20.02	57.18 ± 18.81	58.13 ± 18.45	.21
PM_{10}, μg/m^3	97.64 ± 33.40	97.61 ± 35.09	96.73 ± 33.16	99.14 ± 32.92	.06
NO_2, μg/m^3	30.50 ± 9.90	30.39 ± 10.27	30.32 ± 9.88	30.83 ± 9.75	.24
O_3, μg/m^3	84.76 ± 6.59	84.43 ± 6.70	84.73 ± 6.62	84.98 ± 6.47	.13

and NO_2 (β = −0.03, 95% CI: −0.04, −0.02) in the fully adjusted model (model 3, all p < .0001). O_3 was not significantly associated with eGFR slope as a continuous variable (β = −0.01, 95% CI: −0.02, 0.01, p = .32), which was consistent with the results in other models.

Similar trends were observed in the dichotomized models comparing high ($Q2$) vs. low ($Q1$) exposure groups. High exposure to all pollutants, including O_3, was significantly associated with accelerated decline in eGFR. For example, high NO_2 exposure was associated with a significantly eGFR decline (β = −0.93, 95% CI: −1.16, −0.71, p < .0001), and for $PM_{2.5}$, β = −0.51 (95% CI: −0.72, −0.31, p < .0001). The consistency of results across both continuous and categorical models strengthens the validity of the observed associations. Covariate adjustments in models 1 to 3 had little impact on the direction or statistical significance of the associations.

Comparable trends were observed for NO_2, PM_1, PM_{10}, and O_3, with high exposure to each pollutant significantly associated with an accelerated eGFR decline (p < .0001). However, the analysis did not find evidence for a mediating effect of lifestyle on the relationship between air pollution and eGFR decline (Supplementary Material, Fig. S2).

3.3. Lifestyle-stratified analysis

Figure 2 depicts the joint effects of lifestyle categories (favorable, intermediate, unfavorable) and air pollution exposure levels ($Q1$: low exposure vs. $Q2$: high exposure) on the annual eGFR slope (Supplementary Material, Table S1). The fully adjusted model (model 3) revealed significantly accelerated eGFR decline rates among participants in the high pollution exposure group ($Q2$) compared to those in the low exposure

Table 3. Association between air pollutant and eGFR slope.

	PM_1		$PM_{2.5}$		PM_{10}		NO_2		O_3	
	Continuous	*p* Value	Continuous	*p* Value	Continuous	*p* Value	Continuous	*p* Value	Continuous	*p* Value
Crude model	−0.03 (−0.04, −0.02)	<.0001	−0.01 (−0.02, −0.01)	<.0001	−0.01 (−0.01, 0.00)	<.001	−0.02 (−0.03, −0.01)	<.0001	0.00 (−0.02, 0.01)	.85
Model 1	−0.04 (−0.05, −0.03)	<.0001	−0.02 (−0.03, −0.02)	<.0001	−0.01 (−0.02, −0.01)	<.0001	−0.04 (−0.05, −0.03)	<.0001	−0.01 (−0.03, 0.00)	.11
Model 2	−0.04 (−0.05, −0.03)	<.0001	−0.02 (−0.03, −0.02)	<.0001	−0.01 (−0.02, −0.01)	<.0001	−0.03 (−0.04, −0.02)	<.0001	−0.01 (−0.03, 0.01)	.24
Model 3	−0.04 (−0.05, −0.03)	<.0001	−0.02 (−0.03, −0.02)	<.0001	−0.01 (−0.02, −0.01)	<.0001	−0.03 (−0.04, −0.02)	<.0001	−0.01 (−0.02, 0.01)	.32
	*Q*2 vs. *Q*1	*p* Value	*Q*2 vs. *Q*1	*p* Value	*Q*2 vs. *Q*1	*p*	*Q*2 vs. *Q*1	*p*	*Q*2 vs. *Q*1	*p*
Crude model	−0.68 (−0.87, −0.49)	<.0001	−0.49 (−0.69, −0.30)	<.0001	−0.53 (−0.73, −0.34)	<.0001	−0.66 (−0.85, −0.46)	<.0001	−0.24 (−0.44, −0.05)	.02
Model 1	−0.81 (−1.01, −0.60)	<.0001	−0.55 (−0.75, −0.35)	<.0001	−0.78 (−0.99, −0.57)	<.0001	−0.92 (−1.13, −0.70)	<.0001	−0.49 (−0.70, −0.27)	<.0001
Model 2	−0.81 (−1.02, −0.60)	<.0001	−0.54 (−0.75, −0.34)	<.0001	−0.82 (−1.04, −0.60)	<.0001	−0.96 (−1.18, −0.74)	<.0001	−0.52 (−0.75, −0.30)	<.0001
Model 3	−0.79 (−1.00, −0.57)	<.0001	−0.51 (−0.72, −0.31)	<.0001	−0.78 (−1.01, −0.56)	<.0001	−0.93 (−1.16, −0.71)	<.0001	−0.51 (−0.74, −0.28)	<.0001

Low exposure (*Q*1) was used as the reference group. Model 1: sex, age, education, residence, and south/north. Model 2: sex, age, education, residence, south/north, solid fuel use for cooking, solid fuel use for heating. Model 3: sex, age, education, residence, south/north, solid fuel use for cooking, solid fuel use for heating, BUN, UA, and kidney disease status.

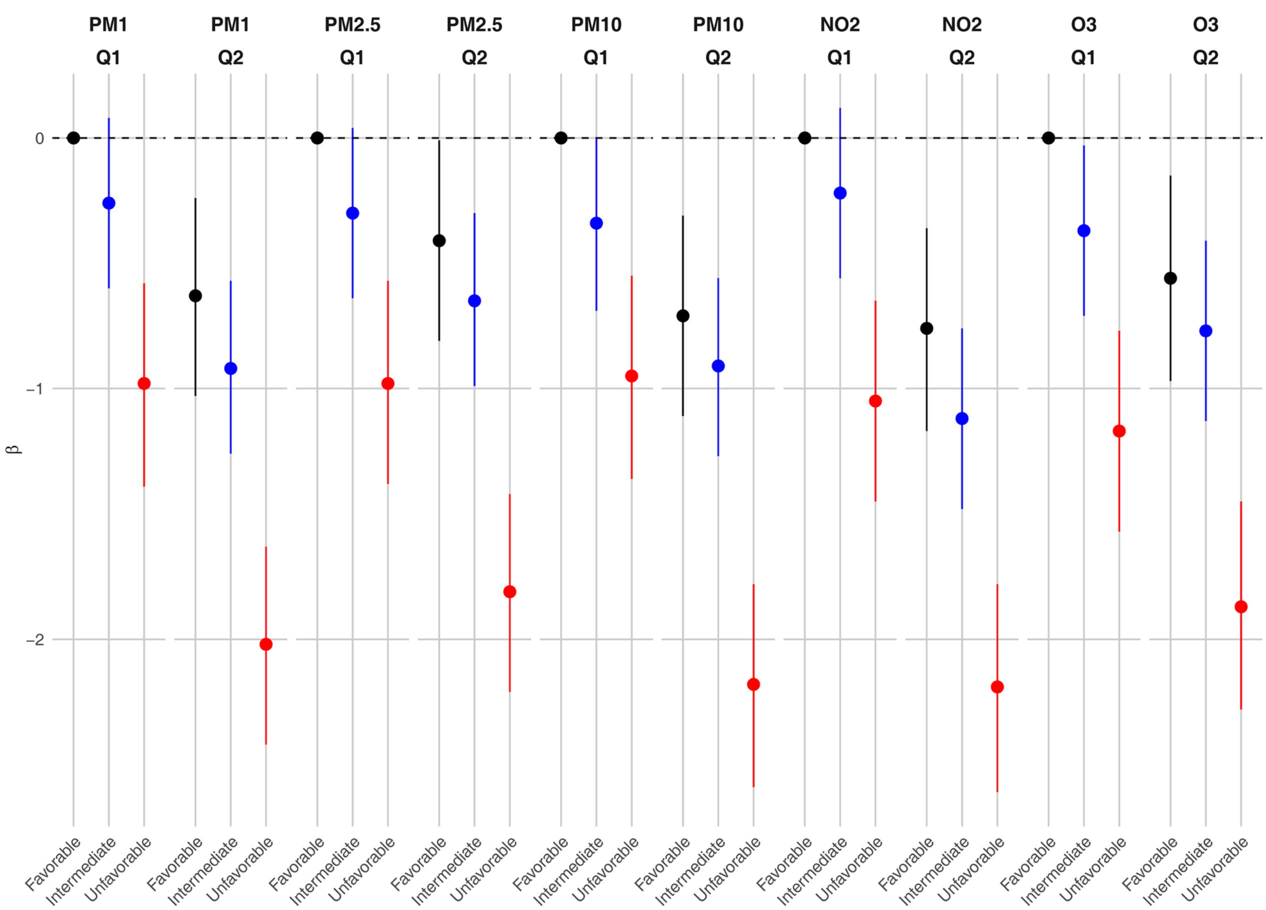

Figure 2. Combined effects of lifestyle and air pollutant exposure on eGFR slope. Joint effects of lifestyle categories (favorable, intermediate, unfavorable) and air pollution exposure levels (*Q*1: low exposure; *Q*2: high exposure) on eGFR slope, with a favorable lifestyle as the reference group. All tests for trend were statistically significant ($p < .001$). Model adjusted for sex, age, education, residence, south/north, solid fuel use for cooking, solid fuel use for heating, BUN, UA, and kidney disease status. CI: confidence interval; NO_2: nitrogen dioxide; O_3: ozone; PM_1: particulate matter with an aerodynamic diameter less than 1 µm; $PM_{2.5}$: particulate matter with an aerodynamic diameter less than 2.5 µm; PM_{10}: particulate matter with an aerodynamic diameter < 10 µm.

group (*Q*1) across all pollutants and lifestyle categories. Lifestyle demonstrated a critical moderating influence on these associations. The annual eGFR decline rate was highest in the unfavorable lifestyle group under all exposure conditions, followed by the intermediate lifestyle group, whereas a favorable lifestyle substantially mitigated the adverse effects of air pollution on kidney function. For example, under high PM_1 exposure (*Q*2), the eGFR decline rate in the favorable lifestyle group was −0.69 (95% CI: −1.06, −0.33, $p < .001$), which was significantly lower than the rates observed in the intermediate lifestyle group (−1.03, 95% CI: −1.35, −0.71, $p < .0001$) and the unfavorable lifestyle group ($\beta = -2.20$, 95% CI: −2.65, −1.75, $p < .0001$). This pattern was consistent across other pollutants ($PM_{2.5}$, PM_{10}, NO_2, and O_3). For instance, under high NO_2 exposure, the eGFR decline rates for the favorable, intermediate, and unfavorable lifestyle groups were −1.01 (95% CI: −1.38, −0.64, $p < .0001$), −1.27 (95% CI: −1.60, −0.93, $p < .0001$), and −2.44 (95% CI: −2.91, −1.98, $p < .0001$), respectively.

3.4. C–R relationships

The C–R relationships between air pollution exposure and the annual eGFR slope are depicted in Figure 3. Significant linear relationships were observed for PM_{10}, O_3, and $PM_{2.5}$ with the annual eGFR slope, as indicated by the analysis (*p*-nonlinear >.05). In contrast, the C–R curves for NO_2 and PM_1 exhibited statistically significant nonlinear relationships (*p*-nonlinear <.05), suggesting potential threshold effects at specific exposure levels. These nonlinear relationships indicate that the effects of air pollutants on kidney function may vary depending on exposure intensity, suggesting potential threshold effects at specific exposure levels.

3.5. Subgroup analysis

The results of subgroup analyses are summarized in Figure 4. No significant interactions were observed across age groups, sexes, education levels, or geographic regions (*p*-interaction >.05). However, urban residence amplified the impact of PM_1, $PM_{2.5}$, and PM_{10} exposure on eGFR decline. Except for NO_2 and O_3, improvements in lifestyle significantly mitigated the adverse effects of air pollution on kidney function. Analysis of CKD subgroups revealed that as kidney function declined, higher air pollution exposure was associated with steeper eGFR decline rates, although only some results reached statistical significance.

3.6. Combined air pollution exposure and eGFR decline

Spearman's rank correlation analysis revealed strong correlations among PM_1, $PM_{2.5}$, and PM_{10} concentrations ($\rho > 0.8$; Figure 5(A)), while NO_2 and O_3 were relatively independent from the other pollutants. Based on the WQS regression model, PM_1 and $PM_{2.5}$ contributed the most to the combined effect of air pollution on the annual eGFR slope, with $PM_{2.5}$ accounting for the highest proportion (87.3%; Figure 5(B)). The WQS index curve demonstrated a negative linear relationship between air pollution mixtures and eGFR decline rates (Figure 5(C)). Each quartile increase in air pollution mixture exposure was significantly associated with an accelerated annual eGFR decline ($\beta = -0.33$, 95% CI: −0.45, −0.22, $p = 1.7e-8$).

Consistent findings were observed in the quantile g-computation analysis (Figure 5(D)), which further emphasized the roles of PM_1 and $PM_{2.5}$ as the primary drivers of the negative effects, whereas NO_2 contributed the most to positive overall effects. Combined exposure to air pollution mixtures was significantly associated with an accelerated eGFR decline ($\beta = -0.25$, 95% CI: −0.42, −0.09, $p = .003$).

3.7. Sensitivity analysis

Sensitivity analyses using eGFR values calculated with the CKD-EPI_{cr} and CKD-EPI_{cys} formulas to compute the annual eGFR slope yielded findings consistent with the primary analysis (Supplementary Material, Tables S2–S3). Subgroup analyses exploring potential interactions between air pollution and lifestyle showed trends consistent with the main findings, although some results did not reach statistical significance (Supplementary Material, Figures S3–S4).

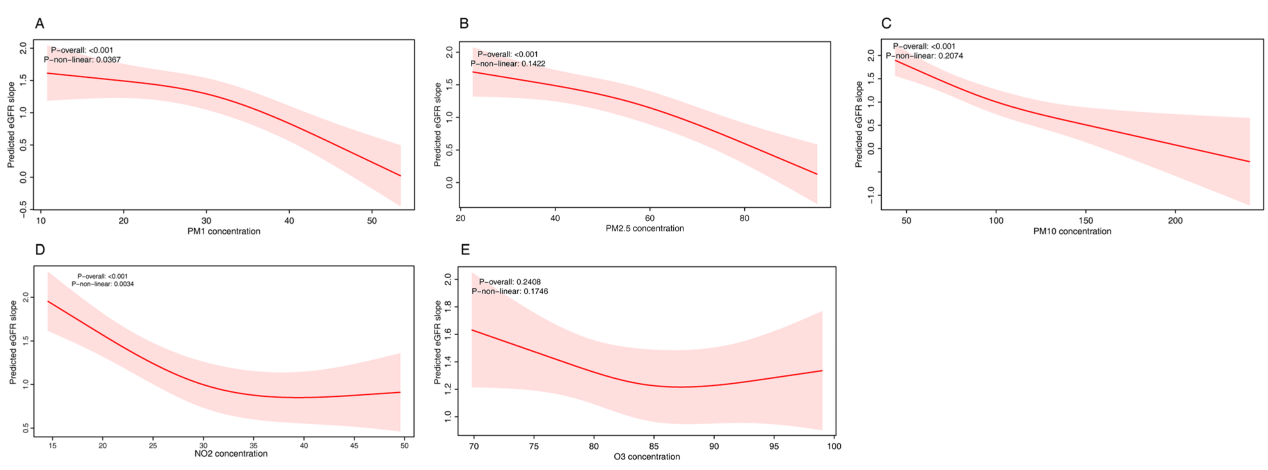

Figure 3. Concentration–response associations of five air pollutants with eGFR slope. Dashed area represents the 95% confidence interval (CI). Model adjusted for sex, age, education, residence, south/north, solid fuel use for cooking, solid fuel use for heating, BUN, UA, and kidney disease status. NO_2: nitrogen dioxide; O_3: ozone; PM_1: particulate matter with an aerodynamic diameter less than 1 µm; $PM_{2.5}$: particulate matter with an aerodynamic diameter less than 2.5 µm; PM_{10}: particulate matter with an aerodynamic diameter < 10 µm.

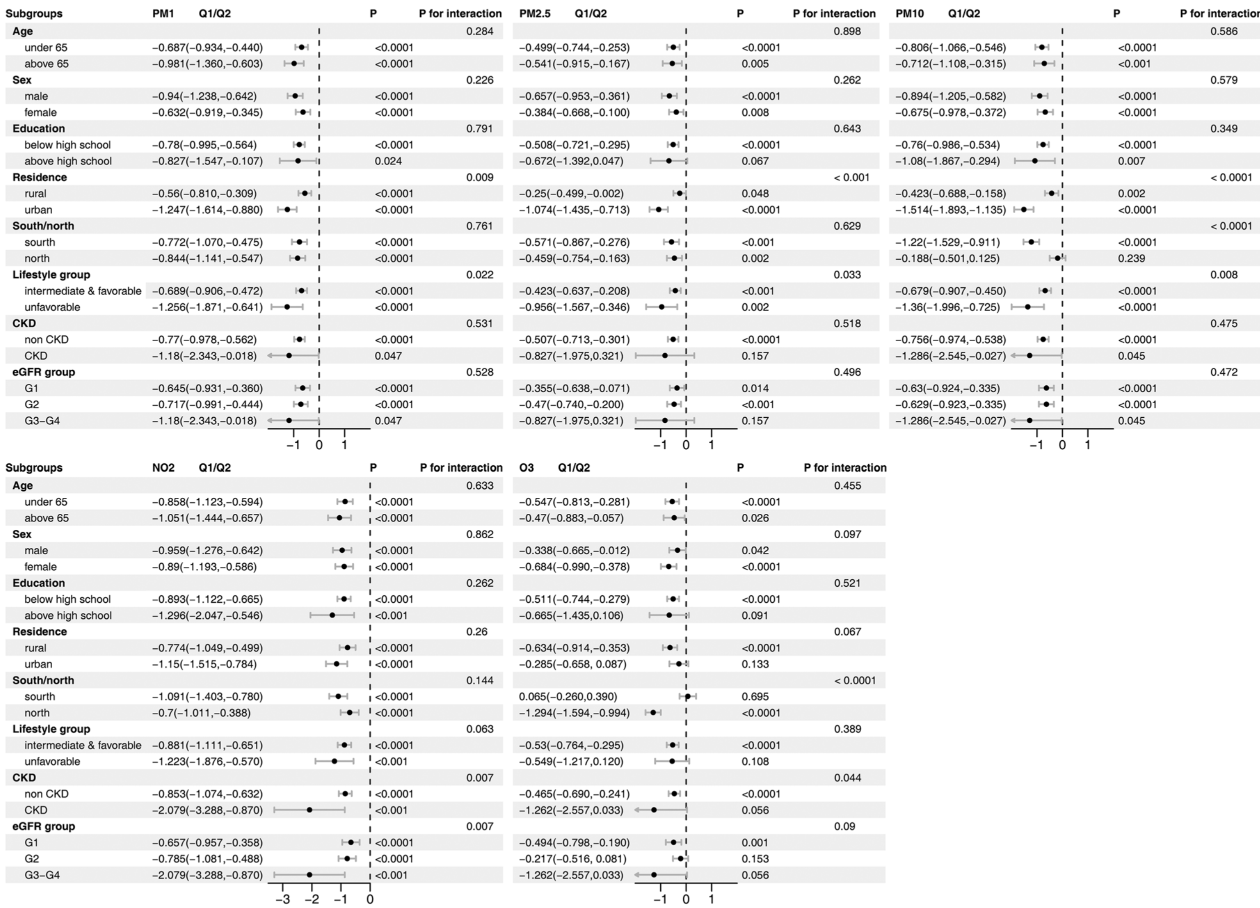

Figure 4. Subgroup analyses of air pollutants with eGFR slope. Forest plot illustrating subgroup analyses of the association between air pollutant exposure and eGFR slope, using low exposure (*Q*1) as the reference group. Chronic kidney disease (CKD) is defined as an eGFR <60 mL/min/1.73 m^2. Model adjusted for sex, age, education, residence, south/north, solid fuel use for cooking, solid fuel use for heating, BUN, UA, and kidney disease status. CI: confidence interval; NO_2: nitrogen dioxide; O_3: ozone; PM_1: particulate matter with an aerodynamic diameter less than 1 µm; $PM_{2.5}$: particulate matter with an aerodynamic diameter less than 2.5 µm; PM_{10}: particulate matter with an aerodynamic diameter < 10 µm.

Additionally, linear mixed-effects model analyses accounting for repeated eGFR measurements produced results highly consistent with those of the primary analysis (Table 4). For most pollutants (PM_1, $PM_{2.5}$, PM_{10}, and NO_2), both the continuous exposure models and the median-dichotomized comparisons (higher vs. lower exposure groups) showed statistically significant associations with eGFR decline in the expected directions. Notably, for O_3, the continuous exposure model yielded a non-significant association, whereas the categorical comparison revealed a significant association – a pattern consistent with the primary eGFR slope-based analysis. These findings further validate the robustness of our conclusions across different modeling approaches.

4. Discussion

This nationwide cohort study examined the relationship between air pollution exposure and changes in kidney function, measured as the eGFR slope, while exploring the protective role of healthy lifestyles. We found that high concentrations of air pollutants, such as PM_1, $PM_{2.5}$, NO_2, and PM_{10}, significantly accelerated eGFR decline. Importantly, adopting healthy lifestyle behaviors consistently mitigated these adverse effects, demonstrating their robust and independent benefits across various pollution levels.

Our findings align with prior evidence that high air pollution exposure is strongly associated with accelerated eGFR decline, reaffirming air pollution as a significant risk factor for kidney health [27,50,51]. Unlike previous studies focusing on static outcomes [52,53], such as CKD incidence or baseline eGFR, this study utilized the annual eGFR slope as a dynamic measure, offering a deeper understanding of the progressive impact of air pollution.

The effects of O_3 on kidney function remain less clear. While some studies suggest a negative association between O_3 levels and eGFR [54], others propose potential protective effects at low concentrations for CKD management [55]. Our RCS analysis identified a nonlinear relationship between O_3 exposure and eGFR decline, suggesting threshold effects. This complexity may be influenced by geographical and meteorological factors affecting O_3 distribution, such as long-range transport of O_3 precursors [56]. Broader geographical studies are needed to resolve these inconsistencies.

This study also evaluated the combined effects of multiple pollutants, addressing a critical gap in the literature. Using quantile g-computation and WQS regression models, we identified

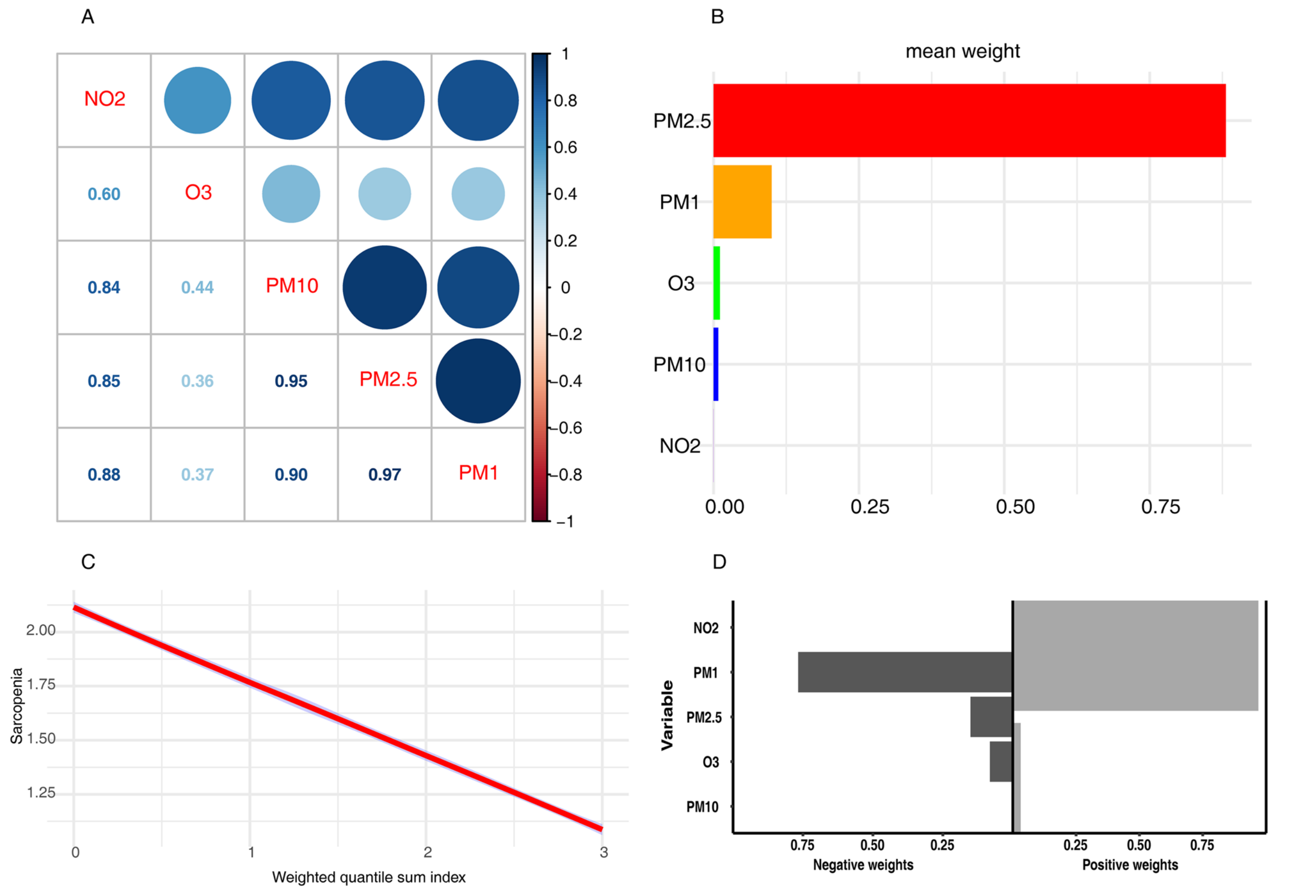

Figure 5. Combined effects of air pollution mixtures on eGFR slope. (A) Correlation analysis of air pollutants; (B) contribution of individual pollutants to the combined effects of air pollution on eGFR slope based on the WQS regression model; (C) relationship between air pollution mixtures and eGFR slope as modeled by the WQS index; (D) results of the quantile g-computation analysis.

Table 4. Associations between air pollutants and eGFR decline based on linear mixed-effects models.

Pollutant	Exposure type	β (95% CI)	p Value
PM_1	Continuous	−0.03 (−0.04, −0.02)	2.87e−07
PM_1	Q2 vs. Q1	−0.66 (−0.86, −0.46)	1.66e−10
$PM_{2.5}$	Continuous	−0.01 (−0.02, −0.01)	1.23e−06
$PM_{2.5}$	Q2 vs. Q1	−0.48 (−0.68, −0.27)	3.8e−06
PM_{10}	Continuous	0.00 (−0.01, 0.00)	2.17e−03
PM_{10}	Q2 vs. Q1	−0.52 (−0.72, −0.32)	3.94e−07
NO_2	Continuous	−0.02 (−0.03, −0.01)	2.45e−03
NO_2	Q2 vs. Q1	−0.67 (−0.87, −0.47)	8.21e−11
O_3	Continuous	0 (−0.01, 0.02)	.85
O_3	Q2 vs. Q1	−0.25 (−0.45, −0.05)	.01

Low exposure (Q1) was used as the reference group. Sex, age, education, residence, south/north, solid fuel use for cooking, solid fuel use for heating, BUN, UA, and kidney disease status.

fine particulate matter (PM_1 and $PM_{2.5}$) as the primary contributors to the adverse effects of combined air pollution exposure on eGFR decline, with $PM_{2.5}$ accounting for the largest proportion. While the biological mechanisms remain incompletely understood, $PM_{2.5}$ is known to induce oxidative stress [57], mitochondrial dysfunction, and inflammation, which can lead to kidney damage [58,59]. The specific mechanisms through which PM_1 affects kidney function warrant further investigation.

A key finding of this study is the protective role of healthy lifestyles in mitigating the adverse impact of air pollution on kidney function. Using a comprehensive lifestyle scoring system based on the 'Life's Essential 8' framework, we assessed modifiable factors, including smoking, alcohol consumption, physical activity, weight management, and social participation [60]. This multidimensional approach offers a more nuanced evaluation of lifestyle compared to single-factor assessments. Consistent with prior research [61–63], our findings demonstrate that healthy lifestyles significantly reduce the risks of CKD onset, progression, and related adverse outcomes. Moreover, this study extends existing evidence by showing that healthy lifestyles can attenuate eGFR decline across all levels of air pollution exposure. These protective effects, independent of pollutant concentrations, highlight the importance of promoting healthy behaviors, especially in highly polluted environments. Likely mechanisms include reductions in oxidative stress and chronic inflammation [64,65], as well as improved regulation of blood pressure, glucose, and lipid levels [66–70].

Stratified analyses revealed no significant interactions between air pollution and demographic factors, such as sex, age, or education. However, urban populations were more susceptible to the harmful effects of fine particulate matter [71], likely due to dietary differences. Urban residents consume more protein-rich and processed foods [72,73], which are independently associated with CKD risk [74,75] through mechanisms involving oxidative stress and mitochondrial dysfunction

[76]. Furthermore, antioxidant-rich diets in rural populations may offer additional protection against the metabolic impact of $PM_{2.5}$ exposure [77,78]. Populations in northern regions were particularly affected by O_3 exposure, potentially due to winter heating practices that exacerbate air pollution [79].

CKD patients were found to be particularly vulnerable to air pollution, with steeper eGFR declines observed in association with NO_2 and O_3 exposure [52,53]. Interestingly, the eGFR decline plateaued in CKD stages G3–G4, consistent with prior studies suggesting that advanced CKD stages are less affected by air pollution [80]. This plateau may be attributed to the protective effects of medical treatments, such as angiotensin receptor blockers, angiotensin converting enzyme inhibitors, and statins, which reduce oxidative stress and mitigate pollutant-related damage [81–83]. However, the lack of medication data in the CHARLS dataset limited further exploration of this hypothesis.

While this study provides valuable insights, several limitations should be acknowledged. First, the absence of detailed residential address data restricted individual-level air pollution exposure assessments, potentially introducing estimation bias. Second, the reliance on self-reported questionnaires for constructing lifestyle scores may have introduced reporting bias. Third, the lack of data on dietary patterns and medication use limited the comprehensiveness of the findings. Fourth, mortality information during the 2015–2016 follow-up wave was unavailable, preventing us from distinguishing between participants lost to follow-up due to death and those who disengaged for other reasons. This limitation may have introduced survivor bias, as individuals with higher exposure levels and poorer health may have been underrepresented in the final analytic sample. Future studies should incorporate precise exposure assessments, such as personal air pollution monitoring devices, and include data on dietary and medication variables. Such efforts will enhance our understanding of the mechanisms underlying air pollution's impact on kidney health and inform targeted prevention strategies.

5. Conclusions

This study provides robust evidence of the detrimental effects of air pollution on kidney function and highlights the independent protective role of healthy lifestyles. Promoting healthy behaviors represents an effective strategy to slow kidney function decline, particularly in high-pollution environments. These findings underscore the need for targeted interventions and public health policies to address the growing burden of air pollution on kidney health.

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Author contributions

CRediT: **Leying Zhao**: Conceptualization, Data curation, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing; **Cong Zhao**: Conceptualization, Data curation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing; **Zhen Wang**: Formal analysis, Visualization, Writing – original draft; **Zhenjie Chen**: Data curation, Methodology, Writing – original draft; **Huijuan Zheng**: Investigation, Validation, Writing – original draft; **Sinan Ai**: Investigation, Methodology, Writing – original draft; **Jiayin Tao**: Data curation, Software, Writing – original draft; **Danting Li**: Data curation, Validation, Writing – original draft; **Weiwei Sun**: Conceptualization, Data curation, Project administration, Validation, Writing – original draft, Writing – review & editing; **Yaoxian Wang**: Conceptualization, Funding acquisition, Project administration, Writing – original draft, Writing – review & editing.

Ethical approval

This study was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11014 and IRB00001052-11015).

Consent form

Informed consent was obtained from all individual participants included in the study.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data can be accessed from the China Health and Retirement Longitudinal Study (CHARLS) (http://charls.pku.edu.cn/) with application.

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