

Association of PM2.5 Changes with Advanced Kidney Disease Progression and Mortality in Patients with Early CKD: A Nationwide Retrospective Cohort Study in Taiwan

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Abstract

Background

Fine particulate matter (PM_{2.5}) is an increasingly recognized risk factor for kidney disease. However, evidence on the kidney-protective effects of improvements in PM_{2.5} exposure is limited. Early intervention in chronic kidney disease (CKD) is essential. We aimed to explore the association of changes in long-term PM_{2.5} exposure with advanced CKD progression and mortality among early-stage CKD patients.

Methods

This retrospective cohort study enrolled 423,855 early CKD patients (stages 1–3a) between 2012 and 2021, with follow-up through 2022. PM_{2.5} change (Δ PM_{2.5}) was defined as the difference between the 365-day mean concentration before enrollment and the 365-day mean before follow-up end. Multivariate Cox proportional hazards models assessed associations of Δ PM_{2.5} with advanced CKD progression, dialysis initiation, and mortality, both per 1 $\mu\text{g}/\text{m}^3$ change and across tertiles of Δ PM_{2.5}. Restricted cubic spline analyses characterized concentration-response relationships.

Results

Each 1 $\mu\text{g}/\text{m}^3$ reduction in PM_{2.5} was associated with 8%, 5%, and 7% lower risks of advanced CKD progression, dialysis initiation, and mortality, respectively. Compared with the reference tertile, participants in the most improved tertile exhibited 19%, 9%, and 28% lower risks, whereas those in the most deteriorated tertile had 2.25-, 1.59-, and 1.94-fold higher risks. Spline analyses indicated near-linear relationships, with protective effects in CKD progression and mortality plateauing beyond a 15 $\mu\text{g}/\text{m}^3$ reduction.

Conclusions

Improvements in PM_{2.5} exposure are associated with reduced risks of advanced CKD progression, dialysis initiation, and mortality among early CKD patients. Public health strategies promoting air quality may represent effective early interventions to protect kidney health.

Background

Fine particulate matter (PM_{2.5}) is a well-established risk factor for adverse health outcomes. Over the past two decades, evidence has linked PM_{2.5} exposure to stroke, coronary artery disease, chronic obstructive pulmonary disease, hypertension, rheumatoid arthritis, and diabetes mellitus [1–6]. Recent studies in last decade also showed its association with both the development and progression of kidney disease [7–11]. Despite these risks, over 99% of the global population lives in regions where long-term PM_{2.5} concentrations exceed World Health Organization standards [12]. Many countries have therefore prioritized air quality improvement as a public health policy.

Chronic kidney disease (CKD) affects more than 10% of the global population and imposes a major healthcare and socioeconomic burden [13]. Progression to advanced CKD and subsequent end-stage kidney disease (ESKD) magnifies this impact [14–16]: although only 0.038% of the global population has ESKD, they account for over 2–4% of healthcare expenditure in some countries [17]. In Taiwan, treated ESKD patients comprise 0.36% of the population but consume over 9% of National Health Insurance reimbursements [18]. To address this, the Taiwan government launched a national Pre-ESKD Care Program for advanced CKD patients (stages 3b–5, eGFR < 45 ml/min/1.73m²) in 2007, later extending coverage to earlier stages (stages 1–3a, eGFR $\geq$ 45 ml/min/1.73m²) through the Early CKD Care Program in 2011 [19]. However, most preventive efforts have targeted traditional risk factors such as diabetes and hypertension, with limited focus on environmental hazards including air pollution [20, 21]. Emerging

evidence has revealed the plausible pathophysiology of how PM_{2.5} induces kidney injury, including oxidative stress, immune response, inflammation, endothelial injury, apoptosis and genotoxic effect [22, 23].

Taiwan has the world's highest incidence and prevalence of treated ESKD and ranks fourth among OECD countries in PM_{2.5} exposure [24, 25]. Although ambient PM_{2.5} has declined since 2005 due to regulatory efforts, evidence on whether such reductions mitigate CKD progression remains scarce. Recent findings by Chen et al. (2025) suggest that lowering long-term PM_{2.5} exposure reduces the risks of dialysis progression and mortality in advanced CKD [26], however, it remains uncertain whether these results can be extrapolated to patients with early-stage CKD. Early intervention for CKD is widely recognized as a key component of the global public health agenda [27]. This study examines the association of changes in long-term ambient PM_{2.5} (Δ PM_{2.5}) level and the risks of progression to advanced CKD and mortality among patients with early CKD (stages 1–3a, eGFR $\geq$ 45 ml/min/1.73m²).

Methods

This retrospective, nationwide, population-based cohort study integrated data from the Taiwan Air Quality Monitoring Database (TAQMD) and the National Health Insurance Research Database (NHIRD) to investigate the association between changes in ambient fine particulate matter (Δ PM_{2.5}) and the risk of progression to advanced CKD (including initiation of maintenance dialysis), initiation of maintenance dialysis, and all-cause mortality among patients with early CKD. The TAQMD, established by the Ministry of Environment (MOENV), provides daily measurements of six air pollutants (PM_{2.5}, PM₁₀, O₃, CO, SO₂, and NO₂) from 84 monitoring stations across Taiwan. Data accuracy is ensured through annual calibration against reference standards, adjustments for environmental factors, inter-station comparisons, internal and external audits, and independent verification using mobile monitoring systems, all conducted in accordance with international standards, including ISO 9001 [28]. The NHIRD encompasses de-identified administrative and healthcare data covering over 99.8% of Taiwan's population enrolled in the compulsory National Health Insurance (NHI) program. The database, maintained by the Health and Welfare Data Science Center (HWDC), contains comprehensive information on patient demographics, diagnoses, procedures, and medical expenditures, enabling full-population epidemiological research [29, 30]. Since 2011, the NHI has implemented the Early CKD Care Program, which provides multidisciplinary care to patients with CKD stages 1–3a [19]. Diseases were coded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) before December 2015 and both ICD-9-CM and Tenth Revision (ICD-10-CM) thereafter. This study was approved by the Research Ethics Review Committee of New Taipei City Hospital (protocol No. NTPC 114002-N).

Eligible participants included adults aged $\geq$ 18 years with early CKD (stages 1–3a, eGFR $\geq$ 45 ml/min/1.73m²) who resided in areas with continuous PM_{2.5} monitoring for at least 12 consecutive months between January 1, 2012, and December 31, 2021. Residential location was determined based on the medical institution visited for outpatient care of acute upper respiratory tract infection (ICD-9-CM: 460; ICD-10-CM: J00) or allergic rhinitis/sinusitis (ICD-9-CM: 472, 473, 477; ICD-10-CM: J30–J32) before enrollment. For individuals without such records, residential information was derived from employment data in the Registry for Beneficiaries database [26]. The enrollment date in the Early CKD Care Program was designated as the index date. Among 1,001,131 patients enrolled during the study period, those with missing demographic information (n = 4,108), age < 18 or $\geq$ 100 years (n = 2,115), prior enrollment in the Pre-ESKD Care Program (n = 4,924), follow-up duration < 365 days (n = 25,524), or progression to end-stage kidney disease (ESKD) requiring maintenance dialysis within 365 days (n = 217) were excluded. Patients residing in postal areas lacking air-quality monitoring stations (n = 532,868) and those in regions without available PM_{2.5} data (n = 7,520) were also excluded. The final analytic cohort comprised 423,855 adults with early CKD (Fig. 1).

The change in PM_{2.5} concentration (Δ PM_{2.5}) for each participant was calculated in three steps. First, the mean daily PM_{2.5} concentration during the 365 days preceding the index date (concentration A) was determined. Second, the mean daily concentration during the 365 days before the end of follow-up (concentration B) was calculated. Third, Δ PM_{2.5} was defined as B – A (μ g/m³), where negative values indicated improved air quality and positive values represented deterioration [26]. For categorical analyses, Δ PM_{2.5} was stratified into tertiles in ascending order, with tertile 1 representing the largest reduction in PM_{2.5}, tertile 2 denoting minimal change, and tertile 3 indicating the greatest increase in PM_{2.5} exposure.

The primary outcome of this study was progression to advanced CKD, including the initiation of maintenance dialysis. This was defined as the date on which patients with early CKD participated in the pre-ESKD Care Program (for CKD stages 3b-5, eGFR < 45 ml/min/1.73m²) or applied for the catastrophic illness card for maintenance dialysis. Participation in both the Early CKD Care Program and the Pre-ESKD Care Program was identified using Taiwan NHI reimbursement codes. The other outcome was all-cause mortality occurring beyond 365 days after the index date. Mortality data—including date and causes of death—were obtained by linking patient records to the Taiwan Death Registry within the HWDC. For patients who experienced an outcome, follow-up ended at the time of the event; for those who did not, follow-up continued until December 31, 2022.

Baseline covariates included demographic characteristics (age, sex, and monthly insurance salary), comorbid conditions (diabetes mellitus, hypertension, chronic obstructive pulmonary disease, coronary artery disease, liver cirrhosis, heart failure, stroke, and malignancy), and the Charlson Comorbidity Index (CCI) score. Comorbidities were identified from inpatient and outpatient claims recorded during the 12 months preceding the index date. Zip code area-level covariates included the degree of urbanization, categorized into four levels (lowest, low, high, and highest) according to the classification proposed by Liu et al. (2006) [31], corresponding to city, town, suburban, and rural areas [32], as well as annual changes in concentrations of NO₂, CO, and SO₂.

Statistical Analysis

Baseline characteristics of patients across the $\Delta PM_{2.5}$ tertiles were assessed using linear contrasts from the general linear model for continuous variables and the Cochran–Armitage trend test for categorical variables. Cox proportional hazards models were applied to evaluate the association between $\Delta PM_{2.5}$ and the risks of outcomes, with all baseline characteristics listed in Table 1 included as covariates. Three models were specified: (a) Model 1, unadjusted, incorporating only $\Delta PM_{2.5}$; (b) Model 2, adjusted for individual-level covariates, including age, sex, monthly income, all comorbidities as well as the CCI score, and the index year of enrollment; and (c) Model 3, further adjusted for urbanization level of the residence and the annual change of NO₂ and SO₂. CO was not included in the multivariable Cox model owing to its strong collinearity with NO₂.

Table 1
Baseline characteristics of patients with early CKD according to the tertile groups of annual PM_{2.5} change

Variable	Total (n = 423 855)	Tertile 1 (n = 139 850)	Tertile 2 (n = 139 908)	Tertile 3 (n = 144 097)	P trend
Range of PM _{2.5} change, µg/m ³	-28.0 to 21.2	-28.0 to -10.2	-10.2 to -4.9	-4.9 to 21.2	-
Mean change of air-pollutants					
PM _{2.5} , µg/m ³	-8.4 ± 5.7	-15.2 ± 3.7	-7.4 ± 1.5	-2.8 ± 1.4	< 0.001
NO ₂ , ppb	-3.7 ± 2.2	-5.3 ± 1.9	-3.7 ± 1.7	-2.0 ± 1.7	< 0.001
CO, ppm	-1.2 ± 0.8	-1.7 ± 0.8	-1.1 ± 0.7	-0.8 ± 0.7	< 0.001
SO ₂ , ppb	-1.6 ± 1.0	-2.2 ± 1.1	-1.6 ± 0.8	-1.1 ± 0.6	< 0.001
Age, year	64.2 ± 13.3	63.4 ± 12.8	64.3 ± 13.4	64.8 ± 13.7	< 0.001
Age ≥ 65 years	210 940 (49.8)	65 093 (46.5)	70 233 (50.2)	75 614 (52.5)	< 0.001
Male sex	221 583 (52.3)	71 604 (51.2)	73 381 (52.5)	76 598 (53.2)	< 0.001
Urbanization level of the residence					< 0.001
The lowest level	12 552 (3.0)	6 010 (4.3)	3 496 (2.5)	3 046 (2.1)	
Low level	107 292 (25.3)	37 498 (26.8)	38 738 (27.7)	31 056 (21.6)	
High level	212 495 (50.1)	69 829 (49.9)	73 443 (52.5)	69 223 (48.0)	
The highest level	91 516 (21.6)	26 513 (19.0)	24 231 (17.3)	40 772 (28.3)	
Monthly income, NTD					0.735
≤ 19,047	113 843 (26.9)	36 704 (26.3)	37 503 (26.8)	39 636 (27.5)	
19,047 – 26,400	164 891 (38.9)	56 196 (40.2)	54 570 (39.0)	54 125 (37.6)	
≥ 26,400	145 121 (34.2)	46 950 (33.6)	47 835 (34.2)	50 336 (34.9)	
Comorbidity					
Diabetes mellitus	256 745 (60.6)	79 589 (56.9)	85 193 (60.9)	91 963 (63.8)	< 0.001
Hypertension	286 329 (67.6)	93 955 (67.2)	94 776 (67.7)	97 598 (67.7)	0.002
Coronary artery disease	73 450 (17.3)	23 505 (16.8)	24 718 (17.7)	25 227 (17.5)	< 0.001
COPD	23 625 (5.6)	6 685 (4.8)	8 131 (5.8)	8 809 (6.1)	< 0.001
Liver cirrhosis	6 225 (1.5)	1 697 (1.2)	2 026 (1.5)	2 502 (1.7)	< 0.001
Heart failure	5 941 (1.4)	1 153 (0.8)	2 097 (1.5)	2 691 (1.9)	< 0.001
Stroke	6 165 (1.5)	1 789 (1.3)	2 140 (1.5)	2 236 (1.6)	< 0.001
Malignancy	33 299 (7.9)	9 053 (6.5)	10 985 (7.9)	13 261 (9.2)	< 0.001
Charlson Comorbidity Index	3.0 ± 2.1	2.7 ± 1.9	3.1 ± 2.1	3.3 ± 2.3	< 0.001
Abbreviation: CKD, chronic kidney disease; ESRD, end stage renal disease; PM, particulate matter; NTD, New Taiwan Dollar; COPD, chronic obstructive pulmonary disease;					
Data are presented as frequency (%) or mean ± standard deviation.					

To further delineate the exposure–response relationship, the continuous $\Delta PM_{2.5}$ was modeled as a flexible restricted cubic spline (RCS) variables, with adjustments for the same covariates specified in Model 3. The knots were positioned at the 10th, 50th, and 90th percentiles of the distribution. Effect modification by baseline characteristics was assessed through stratified analyses according to age (< 65 or $\geq$ 65 years), sex, absence or presence of diabetes, and monthly salary ($\leq$ 19,047 NTD [level 1] vs. >19,047 NTD [levels 2–3]). RCS analyses were conducted in R version 4.3.2 (R Foundation for Statistical Computing) using the rms package, while all other statistical analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). A two-sided P value < 0.05 was considered statistically significant. All analyses were carried out on-site at the HWDC facility.

Results

This study included 423,855 adults with early CKD residing in regions with available $PM_{2.5}$ measurements between 2012 and 2021. The mean age of the cohort was 64.2 years, and 49.8% were older than 65 years. Males represented 52.3% of the participants. With respect to monthly insured salary, 38.9% of patients were classified in the NT\$19,047–26,400 category, 34.2% in the $\geq$ NT\$26,400 category, and 26.9% in the $\leq$ NT\$19,047 category.

The distribution of $\Delta PM_{2.5}$ ranged from -28.0 to $21.2 \mu g/m^3$. Based on tertile classification, 139,850 patients were assigned to tertile 1 (-28.0 to $-10.2 \mu g/m^3$), 139,908 to tertile 2 (-10.2 to $-4.9 \mu g/m^3$), and 144,097 to tertile 3 (-4.9 to $21.1 \mu g/m^3$). Significant differences across tertiles were noted for nearly all baseline characteristics, including age, selected comorbidities, CCI score, changes in mean concentrations of gaseous pollutants (NO_2 , CO, SO_2), and residential urbanization level, whereas monthly income did not differ significantly (Table 1).

According to the multivariable Cox proportional hazards model, each $1\text{-}\mu g/m^3$ reduction in $\Delta PM_{2.5}$ (indicating improved ambient $PM_{2.5}$) was associated with an approximate 8% lower risk of progression to advanced CKD (hazard ratio [HR], 0.923; 95% confidence interval [CI], 0.920–0.926), an equivalently 5% lower risk of dialysis initiation (HR, 0.953; 95% CI, 0.947–0.960), and a nearly 7% lower risk of mortality (HR, 0.925; 95% CI, 0.923–0.927) (Model 3 in Table 2). When tertile 2 ($\Delta PM_{2.5}$ -10.2 to $-4.9 \mu g/m^3$, reflecting the smallest change in $PM_{2.5}$) was used as the reference, patients in tertile 1 ($\Delta PM_{2.5}$ -28.0 to $-10.2 \mu g/m^3$) experienced a 19% lower risk of progression to advanced CKD, a 9% lower risk of dialysis initiation, and a 28% lower risk of mortality. Conversely, participants in tertile 3 ($\Delta PM_{2.5}$ -4.9 to $21.2 \mu g/m^3$) had a 2.25-fold higher risk of progression to advanced CKD, a 1.59-fold higher risk of dialysis initiation, and a 1.94-fold higher risk of mortality (Model 3 in Table 3).

Table 2

The association between the annual PM_{2.5} change (as continuous variable, per µg/m³ decrease) and the risk of outcomes in various adjustment models

Outcome / Model	Hazard ratio (95% CI)	P value
Advance CKD		
Model 1	0.787 (0.784–0.789)	< 0.001
Model 2	0.791 (0.788–0.794)	< 0.001
Model 3	0.923 (0.920–0.926)	< 0.001
Chronic dialysis		
Model 1	0.835 (0.830–0.841)	< 0.001
Model 2	0.835 (0.830–0.841)	< 0.001
Model 3	0.953 (0.947–0.960)	< 0.001
All-cause death		
Model 1	0.809 (0.807–0.811)	< 0.001
Model 2	0.821 (0.819–0.823)	< 0.001
Model 3	0.925 (0.923–0.927)	< 0.001
Abbreviation: PM, particulate matter; CI, confidence interval;		
Model 1: Crude model without adjustment;		
Model 2: Adjusted for age, sex, monthly income, all comorbidities as well as the Charlson Comorbidity Index score, the index year of enrollment;		
Model 3: Further adjusted for urbanization level of the residence and the annual change of NO ₂ and SO ₂ .		

Table 3
The association between the tertile of annual PM_{2.5} change (as categorical variable) and the risk of outcomes in various adjustment models

Outcome / Model / PM _{2.5} change	No. of patients	Incidence rate (95% CI)†	Hazard ratio (95% CI)	P value
Advance CKD				
Model 1				
Tertile 1	139 893	6.8 (6.6–6.9)	0.37 (0.35–0.38)	< 0.001
Tertile 2	139 828	11.3 (11.1–11.5)	Reference	
Tertile 3	144 134	30.8 (30.2–31.4)	4.16 (4.03–4.29)	< 0.001
Model 2				
Tertile 1	139 893	6.8 (6.6–6.9)	0.38 (0.36–0.39)	< 0.001
Tertile 2	139 828	11.3 (11.1–11.5)	Reference	-
Tertile 3	144 134	30.8 (30.2–31.4)	4.04 (3.92–4.16)	< 0.001
Model 3				
Tertile 1	139 893	6.8 (6.6–6.9)	0.81 (0.78–0.84)	< 0.001
Tertile 2	139 828	11.3 (11.1–11.5)	Reference	
Tertile 3	144 134	30.8 (30.2–31.4)	2.25 (2.17–2.32)	< 0.001
Chronic dialysis				
Model 1				
Tertile 1	139 893	2.0 (1.9–2.1)	0.36 (0.34–0.39)	< 0.001
Tertile 2	139 871	2.5 (2.4–2.6)	Reference	-
Tertile 3	144 091	3.1 (2.9–3.2)	2.78 (2.57–3.00)	< 0.001
Model 2				
Tertile 1	139 893	2.0 (1.9–2.1)	0.37 (0.34–0.39)	< 0.001
Tertile 2	139 871	2.5 (2.4–2.6)	Reference	-
Tertile 3	144 091	3.1 (2.9–3.2)	2.75 (2.55–2.97)	< 0.001
Model 3				
Tertile 1	139 893	2.0 (1.9–2.1)	0.91 (0.85–0.98)	0.009
Tertile 2	139 871	2.5 (2.4–2.6)	Reference	-
Tertile 3	144 091	3.1 (2.9–3.2)	1.59 (1.47–1.73)	< 0.001
All-cause death				
Abbreviation: PM, particulate matter; CI, confidence interval;				
† Number of events per 1,000 person-years;				
Model 1: Crude model without adjustment;				
Model 2: Adjusted for age, sex, monthly income, all comorbidities as well as the Charlson Comorbidity Index score, the index year of enrollment;				
Model 3: Further adjusted for urbanization level of the residence and the annual change of NO ₂ and SO ₂ .				

Outcome / Model / PM _{2.5} change	No. of patients	Incidence rate (95% CI)†	Hazard ratio (95% CI)	P value
Model 1				
Tertile 1	139 850	16.6 (16.4–16.8)	0.33 (0.32–0.34)	< 0.001
Tertile 2	139 908	28.6 (28.3–29.0)	Reference	-
Tertile 3	144 097	53.2 (52.5–54.0)	3.25 (3.19–3.32)	< 0.001
Model 2				
Tertile 1	139 850	16.6 (16.4–16.8)	0.36 (0.35–0.37)	< 0.001
Tertile 2	139 908	28.6 (28.3–29.0)	Reference	-
Tertile 3	144 097	53.2 (52.5–54.0)	3.05 (2.99–3.11)	< 0.001
Model 3				
Tertile 1	139 850	16.6 (16.4–16.8)	0.72 (0.70–0.73)	< 0.001
Tertile 2	139 908	28.6 (28.3–29.0)	Reference	-
Tertile 3	144 097	53.2 (52.5–54.0)	1.94 (1.90–1.99)	< 0.001
Abbreviation: PM, particulate matter; CI, confidence interval;				
† Number of events per 1,000 person-years;				
Model 1: Crude model without adjustment;				
Model 2: Adjusted for age, sex, monthly income, all comorbidities as well as the Charlson Comorbidity Index score, the index year of enrollment;				
Model 3: Further adjusted for urbanization level of the residence and the annual change of NO ₂ and SO ₂ .				

The RCS analyses which used $\Delta\text{PM}_{2.5} = 0 \mu\text{g}/\text{m}^3$ as the reference point, revealed that increases in PM_{2.5} levels ($\Delta\text{PM}_{2.5} > 0 \mu\text{g}/\text{m}^3$) were associated with a progressively higher risk of advanced CKD, whereas reductions in PM_{2.5} ($\Delta\text{PM}_{2.5} < 0 \mu\text{g}/\text{m}^3$) corresponded to a lower risk. However, the risk reduction reached a plateau in participants experiencing substantial improvements in air quality ($\Delta\text{PM}_{2.5} < -15 \mu\text{g}/\text{m}^3$) (Fig. 2A). For maintenance dialysis, the RCS model demonstrated an approximately linear positive association with $\Delta\text{PM}_{2.5}$ (although the *P* for linearity and non-linearity < 0.001), although the slope was slightly attenuated in regions with $\Delta\text{PM}_{2.5} < -7 \mu\text{g}/\text{m}^3$ (Fig. 2B). With respect to mortality, the RCS analysis likewise indicated that worsening air quality ($\Delta\text{PM}_{2.5} > 0 \mu\text{g}/\text{m}^3$) was linked to an increased risk (*P* for linearity and non-linearity < 0.001), whereas improvements in PM_{2.5} ($\Delta\text{PM}_{2.5} < 0 \mu\text{g}/\text{m}^3$) were protective. Nevertheless, the survival benefit plateaued once reductions in PM_{2.5} exceeded approximately 15 $\mu\text{g}/\text{m}^3$ (Fig. 2C).

Stratified analyses, in alignment with the Cox regression results, demonstrated that improvements in ambient PM_{2.5} were associated with lower risks of outcomes. A 1- $\mu\text{g}/\text{m}^3$ reduction in $\Delta\text{PM}_{2.5}$ yielded a greater decrease in the risk of progression to advanced CKD (including transition to maintenance dialysis) among patients aged ≥ 65 years (HR, 0.918 vs. 0.928; *P* for interaction < 0.001), females (HR, 0.914 vs. 0.927; *P* for interaction < 0.001), and individuals with a monthly income $\leq 19,047$ NT\$ (HR, 0.908 vs. 0.927; *P* for interaction < 0.001), compared with their respective counterparts (Fig. 3A). Regarding mortality, stratified analyses revealed a greater risk reduction with a 1- $\mu\text{g}/\text{m}^3$ decrease in $\Delta\text{PM}_{2.5}$ among patients aged < 65 years (HR, 0.919 vs. 0.928; *P* for interaction < 0.001), females (HR, 0.921 vs. 0.927; *P* for interaction < 0.001), and those with diabetes (HR, 0.923 vs. 0.927; *P* for interaction = 0.004), compared with their respective counterparts (Fig. 3B).

Discussion

This study demonstrated that improvements in long-term PM_{2.5} air quality were associated with a reduced risk of progression to advanced CKD and maintenance dialysis among patients with early CKD, whereas worsening ambient PM_{2.5} was linked to increased disease progression. These findings are consistent with prior studies reporting the health benefits of reduced PM_{2.5} exposure, such as lower hypertension incidence, improved cardiovascular outcomes, and decreased COPD prevalence [33–35]. Importantly, our results align with limited research directly demonstrating the beneficial effects of PM_{2.5} reduction on CKD development and progression to maintenance dialysis [26, 36]. Bo et al. (2021b) reported a 25% lower risk of CKD development per 5 µg/m³ reduction in ambient PM_{2.5} among Taiwanese adults, with an approximately linear exposure–response relationship [36], while Chen et al. (2025) found that a 1 µg/m³ reduction in PM_{2.5} was associated with an 11% lower risk of dialysis progression, also showing a near-linear relationship between ΔPM_{2.5} and dialysis incidence in patients with advanced CKD [26]. In the current study, although the ΔPM_{2.5}–dialysis relationship was nearly linear, the protective effect on progression to advanced CKD plateaued among early CKD patients once PM_{2.5} improvements exceeding 15 µg/m³.

We further observed that long-term reductions in PM_{2.5} exposure were associated with decreased mortality in early CKD patients, although the protective effect plateaued beyond a 15 µg/m³ improvement. This finding aligns with limited prior studies reporting mortality reductions following air pollution improvement in the general population [37, 38] and complements earlier work linking higher PM_{2.5} exposure to greater mortality risk in CKD and ESKD populations [39–41]. Notably, our results are consistent with Chen et al. (2025), who reported that PM_{2.5} improvement reduced mortality in advanced CKD, with a plateaued protective effect beyond a 5 µg/m³ improvement [26]. This plateau phenomenon, together with the plateaued effect on progression to advanced CKD described above, may reflect the intrinsic vulnerability of CKD patients with complex comorbidities to disease progression and premature mortality [42, 43], wherein residual confounding and comorbidity burden exert stronger influences than environmental PM_{2.5} reduction. Consequently, even substantial improvements in air quality may not fully mitigate mortality risk in the most vulnerable early CKD population.

Several biological mechanisms may underlie these observed associations. Miller (2017) demonstrated that inhaled particulate matter can translocate systemically and damage extrapulmonary organs, including the kidneys [44]. Additionally, PM_{2.5}-induced pulmonary inflammation may trigger systemic inflammation, endothelial injury, oxidative stress, metabolic disturbances, autophagy & pyroptosis, and genotoxicity, ultimately contributing to renal damage [22, 23, 45, 46]. These mechanistic insights provide biological plausibility for the observed reductions in disease progression and mortality associated with long-term improvements in PM_{2.5} exposure among CKD patients, as shown in our study. To our knowledge, this is the first population-based study to evaluate ΔPM_{2.5} in relation to advanced CKD progression, dialysis initiation, and mortality in early-stage CKD, offering valuable evidence to inform public health strategies for kidney health promotion and air quality improvement.

After adjustment for baseline characteristics such as age, sex, diabetes, and monthly insured salary, the significant association between lowering PM_{2.5} exposure and reduced risks of progression to advanced CKD (including transition to maintenance dialysis) and mortality remained. Subgroup analyses showed that early CKD patients aged ≥ 65 experienced a greater reduction in the risk of progression to advanced CKD per 1-µg/m³ decrease in PM_{2.5}, whereas those aged < 65 exhibited larger reductions in mortality risk compared with their older counterparts. Hallan et al. (2024) observed that among patients with early CKD, the mean ESKD rate per 1,000 person-years was lower in those aged ≥ 65 than in those aged < 65, whereas the mean mortality rate per 1,000 person-years was higher in the older group [47]. Ito and Mori (2025) reported that early CKD in younger individuals—especially those with early-onset hypertension—tends to progress more rapidly to ESKD, while in older adults, advancement to severe stages occurs at a slower pace [48]. These findings support the age-specific subgroup analyses in our study.

Regarding the effect of sex, our study revealed that each 1-µg/m³ reduction in PM_{2.5} conferred a greater decrease in the risks of progression to advanced CKD and mortality in females compared with males. These results echo previous studies demonstrating that males have a higher risk of CKD development and that male CKD patients exhibit a greater mortality risk under comparable increases in long-term PM_{2.5} exposure compared with females [8, 49]. The higher risk of PM_{2.5}-associated CKD development and mortality in men compared with women may result from interactions between PM_{2.5} and male-specific factors, including hormonal profiles, occupational exposures, and lifestyle behaviors [50].

Our study found that among early CKD patients, those with diabetes—the most common underlying cause of CKD—experienced a greater reduction in the risk of mortality per 1- $\mu\text{g}/\text{m}^3$ decrease in long-term $\text{PM}_{2.5}$ exposure compared with non-diabetic patients. This observation is consistent with prior evidence demonstrating that, given comparable increases in long-term $\text{PM}_{2.5}$ exposure, CKD patients with diabetes exhibit a lower relative increase in the hazards of eGFR decline or mortality compared with non-diabetic CKD patients [39, 51, 52]. Persistent hyperglycemia accelerates the formation of advanced glycation end products, promoting reactive oxygen species generation, chronic inflammation, and endothelial dysfunction, ultimately contributing to diabetic complications [53]. Given the intrinsically heightened inflammatory state in diabetic CKD and the baseline elevated risks of mortality, reductions in long-term $\text{PM}_{2.5}$ exposure are likely to confer greater benefits in mitigating CKD-related mortality.

Our study demonstrated that among early CKD patients, individuals with lower monthly income experienced a greater decrease in the risk of progression to advanced CKD per 1- $\mu\text{g}/\text{m}^3$ reduction in long-term $\text{PM}_{2.5}$ exposure compared with those with higher income. These results diverge from prior research examining the impact of socioeconomic status (SES) on CKD-related outcomes, which demonstrates that lower SES is associated with increased disease severity, accelerated progression, and a higher risk of ESKD [54, 55]. This difference suggests that, although income is a key indicator of socioeconomic status, relying on it alone in research may introduce potential bias.

This study has several strengths. First, it employs a large, nationwide cohort to investigate the association between $\Delta\text{PM}_{2.5}$ and progression to advanced CKD or mortality in early CKD, allowing for comprehensive adjustment for baseline confounders and providing sufficient statistical power for subgroup analyses, thereby enhancing the reliability and generalizability of the findings. Second, $\Delta\text{PM}_{2.5}$ was evaluated not only in single-pollutant models but also with adjustment for co-pollutants, further strengthening the robustness of the results. Third, to our knowledge, this is the first study to specifically assess the impact of $\Delta\text{PM}_{2.5}$ on progression to advanced CKD, dialysis initiation, and mortality among patients with early CKD, thereby laying the groundwork for future research on air pollution mitigation and early kidney health interventions.

However, several limitations warrant consideration. First, ambient $\text{PM}_{2.5}$ was estimated from fixed-site monitoring stations, which may not fully capture individual indoor exposures, potentially resulting in exposure misclassification. Nonetheless, evidence indicates that indoor $\text{PM}_{2.5}$ derived from outdoor sources can substantially contribute to adverse health outcomes [56]. Second, seasonal variations in $\text{PM}_{2.5}$ concentrations in Taiwan may affect $\Delta\text{PM}_{2.5}$ estimation [57], though this impact was mitigated by employing a 12-month measurement window. Third, the use of 3-digit zip code–level data may not precisely reflect proximity to air-quality monitoring stations [58]; however, previous studies indicate consistent associations with mortality risk even within a 10 km radius. Furthermore, non-differential exposure misclassification typically biases results toward the null [59], yet significant associations were still observed, underscoring the robustness of our findings. Fourth, the NHIRD does not include information on lifestyle behaviors, anthropometric measures, or biochemical parameters related to kidney function, which may also introduce bias. Fifth, as this was an observational study, it is not capable to infer a causal relationship between $\Delta\text{PM}_{2.5}$ and the health outcomes.

In conclusion, reductions in ambient $\text{PM}_{2.5}$ were associated with lower risks of progression to advanced CKD, initiation of dialysis, and mortality, whereas deteriorating air quality was linked to increased risks among patients with early CKD. These findings underscore the importance of air pollution mitigation as an early intervention to preserve kidney health and reduce disease progression and mortality in this population.

Abbreviations

CKD
chronic kidney disease
ESKD
end-stage kidney disease
TAQMD
the Taiwan Air Quality Monitoring Database
NHIRD
the National Health Insurance Research Database

MOENV
the Ministry of Environment
NHI
National Health Insurance
HWDC
the Health and Welfare Data Science Center
ICD-9-CM
the International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CM
the International Classification of Diseases, Tenth Revision, Clinical Modification
CCI
the Charlson Comorbidity Index
RCS
restricted cubic spline
HR
hazard ratio
CI
confidence interval
SES
socioeconomic status

Declarations

Ethics approval

This study was approved by the Research Ethics Review Committee of New Taipei City Hospital (protocol No. NTPC 114002-N) on June 5, 2025. The organization and operation of this Institutional Review Board (IRB) complied with the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines.

Competing interests

The authors disclose the following potential competing interests: Shih-Feng Chen has received financial support from New Taipei City Hospital, Sanchung Branch, and is employed by the same institution. The remaining authors report no known financial interests or personal relationships that could have influenced the work presented in this study.

Conflict of interest

None

Clinical trial number

Not applicable

Consent to participate

Not applicable (This retrospective cohort study utilized de-identified data from the NHIRD, which is protected under regulations governing beneficiary privacy established by the Taiwanese government.)

Supplementary material

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Author Contribution

S.F.C. conceived and designed the study, developed the methodology, performed data analysis, drafted the original manuscript, and manuscript revision. Y.C.L. contributed to project administration, data analysis, and investigation. Y.H.C. was responsible for data curation, formal analysis, and investigation. K.C.H. assisted with methodological development, investigation, data interpretation, and manuscript revision. I.W.W. supervised the study, validated the findings, and contributed to study conceptualization, methodological design, and critical manuscript review. All authors read and approved the final version of the manuscript.

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Data Availability

The first dataset utilized in this study was obtained from the National Health Insurance Research Database (NHIRD), which is maintained by the Health and Welfare Data Science Center (HWDC). As the NHIRD is not publicly accessible, researchers must submit a formal application to the HWDC, Department of Statistics, Ministry of Health and Welfare, Taiwan (<https://dep.mohw.gov.tw/DOS/cp-5119-59201-113.html>) to obtain access. The second dataset was derived from the Taiwan Air Quality Monitoring Database (TAQMD), managed by the Ministry of Environment, Taiwan. Unlike the NHIRD, the TAQMD is publicly available, and historical ambient temperature and air quality data can be downloaded from the Air Quality Index (AQI) platform: Air Quality Index (AQI) | 環境資訊網. <https://data.moenv.gov.tw/>

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Figures

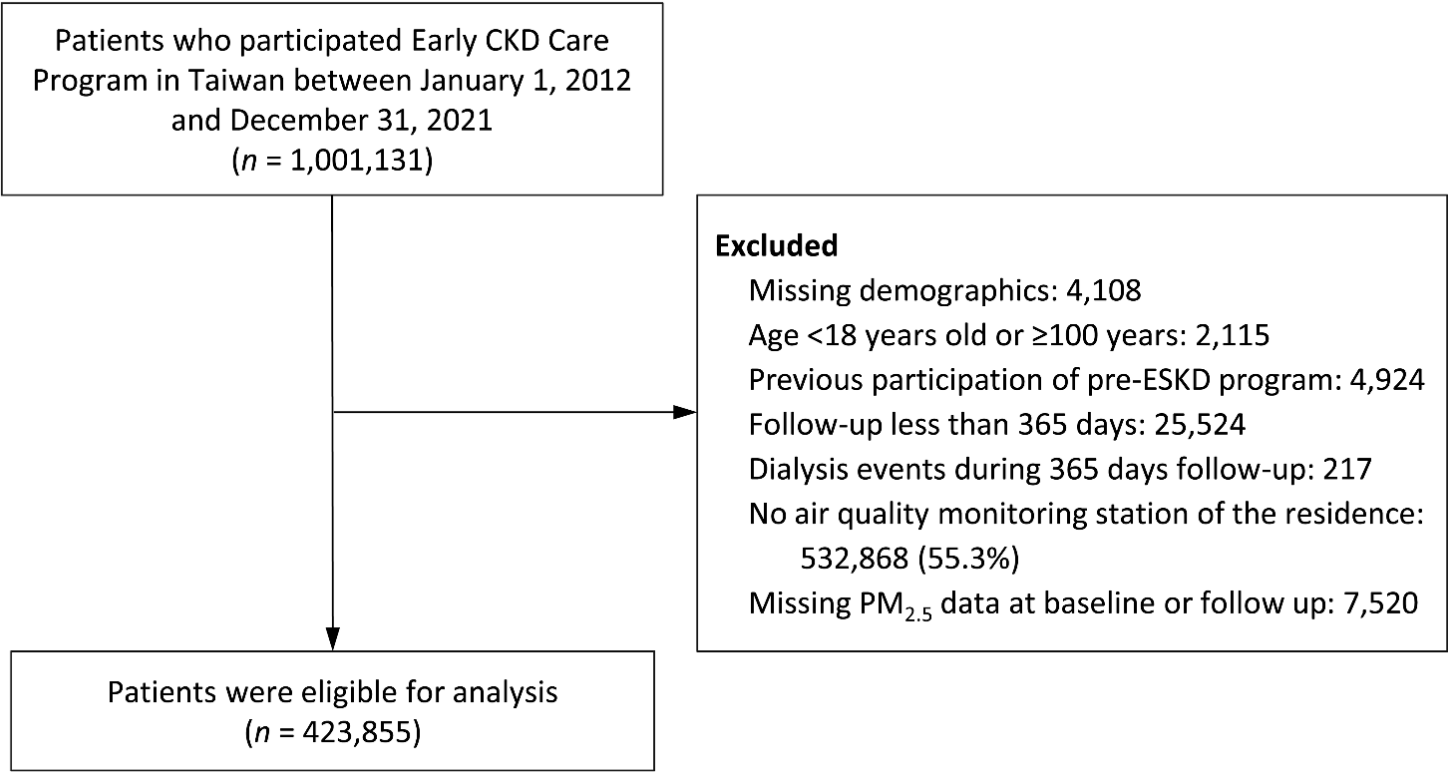
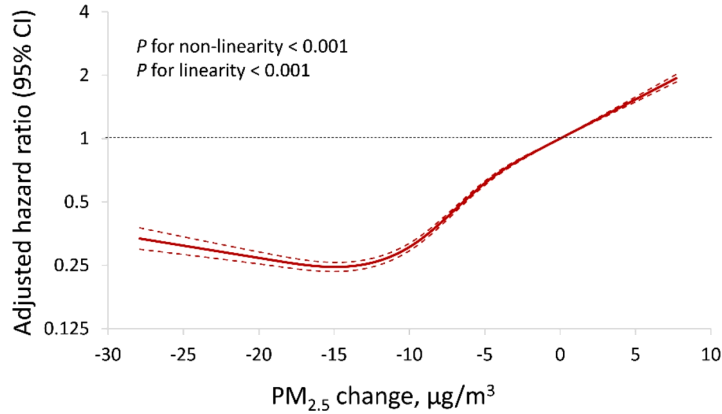


Figure 1

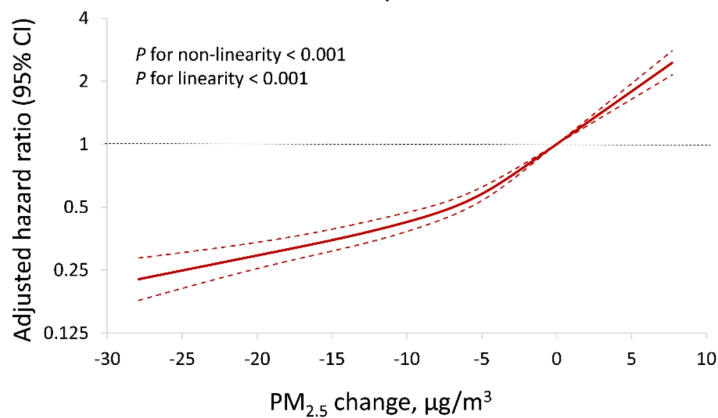
Flowchart illustrating the inclusion and exclusion process of study participants.

CKD, chronic kidney disease; ESKD, end-stage kidney disease; PM, particulate matter.

A. Progression to advanced CKD



B. ESKD with maintenance dialysis



C. All-cause death

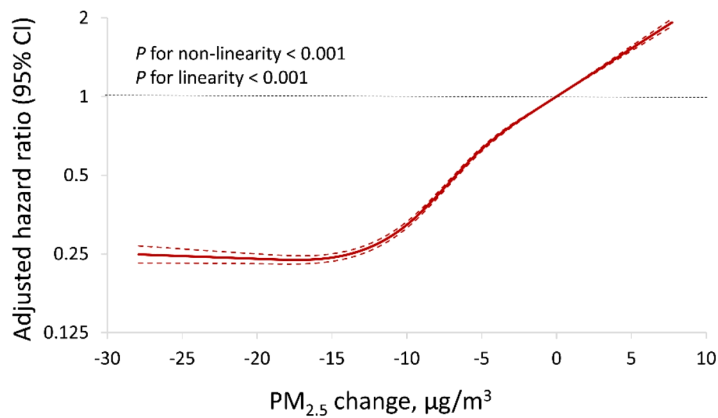
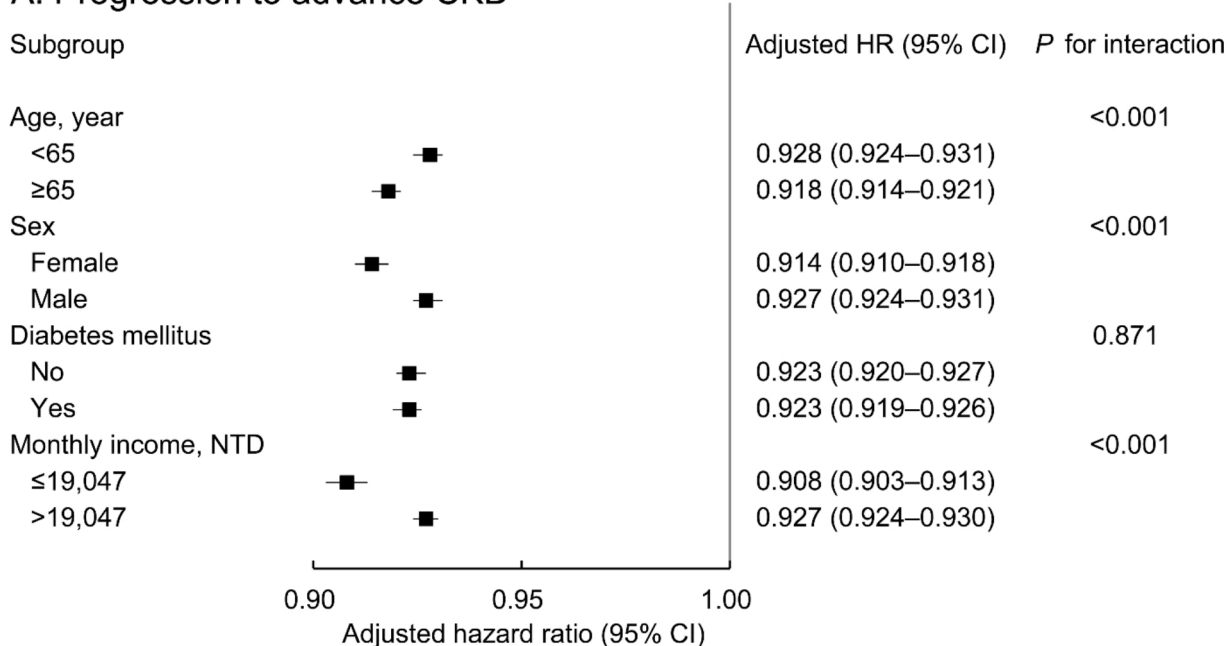


Figure 2

Association between changes in PM_{2.5} levels and the risk of progression to advanced CKD (A), ESKD requiring maintenance dialysis (B), and all-cause mortality (C) among patients with early CKD. Changes in PM_{2.5} were modeled using restricted cubic splines. All covariates listed in Table 1 were adjusted in the multivariable Cox proportional hazards model.

CKD, chronic kidney disease; ESKD, end-stage kidney disease; PM, particulate matter; CI, confidence interval; CKD, chronic kidney disease; PM, particulate matter.

A. Progression to advance CKD



B. All-cause death

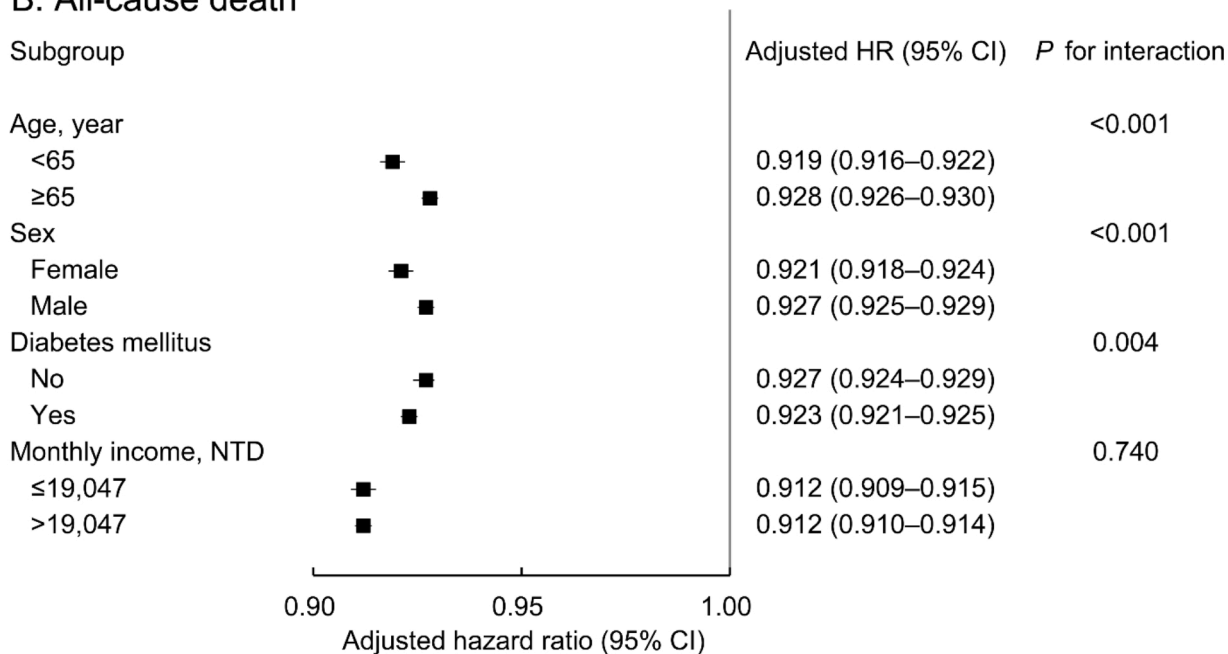


Figure 3

Subgroup analyses of the association between changes in PM_{2.5} levels and the risk of progression to advanced CKD (including initiation of maintenance dialysis) (A) and all-cause mortality (B) among patients with early CKD.

CCI, Charlson's Comorbidity Index; CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; NTD, New Taiwan Dollar; PM, particulate matter.