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Ambient Air Pollution and Mortality Among Older Patients Initiating Maintenance Dialysis

Yijing Feng, MHS[1], **Miranda R. Jones, PhD**[2], **Nadia M. Chu, PhD MPH**[1,2], **Dorry L. Segev, MD PhD**[1,2], **Mara McAdams-DeMarco, PhD**[1,2]

[(1)]Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD

[(2)]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Abstract

Background: Fine particulate matter ($PM_{2.5}$) is associated with chronic kidney disease progression and may impact the health of patients living with kidney failure. While older (aged≥65) adults are most vulnerable to the impact of $PM_{2.5}$, it is unclear whether older patients on dialysis are at elevated risk of mortality when exposed to fine particulate matter.

Methods: Older adults initiating dialysis (2010–2016) were identified from US Renal Data System. $PM_{2.5}$ concentrations were obtained from NASA's SEDAC Global Annual $PM_{2.5}$ Grids. We investigated the association between $PM_{2.5}$ and all-cause mortality using Cox proportional hazard models with linear splines [knot at the current Environmental Protection Agency (EPA) National Ambient Air Quality Standard for $PM_{2.5}$ of 12 μg/m^3] and robust variance.

Results: For older dialysis patients who resided in areas with high $PM_{2.5}$, a 10 μg/m^3 increase in $PM_{2.5}$ was associated with 1.16-fold (95%CI:1.08–1.25) increased risk of mortality; furthermore, those who were female (aHR=1.26, 95%CI:1.13–1.42), Black (aHR=1.31, 95%CI:1.09–1.59) or had diabetes as primary cause of kidney failure (aHR=1.25, 95%CI:1.13–1.38) were most vulnerable to high $PM_{2.5}$. While the mortality risk associated with $PM_{2.5}$ was stronger at higher levels (aHR=1.19, 95%CI:1.08–1.32), even at lower levels (≤12 μg/m^3), $PM_{2.5}$ was significantly associated with mortality risk (aHR=1.04, 95%CI:1.00–1.07) among patients aged≥75 ($P_{slope\ difference}$=0.006).

Conclusions: Older adults initiating dialysis who resided in ZIP codes with $PM_{2.5}$ levels>12 μg/m^3 are at increased risk of mortality. Those aged >75 were at elevated risk even at levels below the EPA Standard for $PM_{2.5}$.

Contact Information: Mara McAdams-DeMarco, PhD, Associate Professor, Departments of Epidemiology and Surgery, Johns Hopkins, 615 N Wolfe Street, Room W6033, Baltimore, MD 21205, 410-614-3822 (tel) 410-614-2079 (fax) mara@jhu.edu.
AUTHOR CONTRIBUTIONS
MMD, YF, MJ, and DLS designed the study; all authors drafted and revised the manuscript; all authors approved the final version of the manuscript.

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DATA AVAILABILITY STATEMENT
The data underlying this article were provided by *USRDS* under license / by permission. Data will be shared on request to the corresponding author with permission of *USRDS*.

Keywords

Air Pollution; kidney failure; Mortality

INTRODUCTION

Elevated levels of fine particulate matter (particulate matter with diameter<2.5μM [$PM_{2.5}$]) are a well-recognized risk factor for cardiovascular mortality,[1] and are associated more broadly with an increased risk of death as well as a reduced life expectancy.[2–5] Older adults are one of the most vulnerable groups to the harmful effect of air pollution.[1, 6, 7] It was estimated that more than 2 million deaths among older adults were attributed to ambient particulate matter globally in 2015.[8]

Furthermore, there is a high global burden of kidney disease that is attributable to ambient air pollution.[9, 10] Experimental studies showed that pollutants in the air such as diesel exhaust and heavy metal could promote oxidative stress, inflammation, and DNA damages in renal tissues.[11, 12] In the United States (US), elevated levels of fine particulate matter, are associated with incident chronic kidney disease, decline in estimated glomerular filtration rate (eGFR), and progression to kidney failure.[13, 14] In fact, proximity to major roads and increased levels of $PM_{2.5}$ leads to reduced eGFR.[15]

Previous studies also suggested that those with diabetes or preexisting coronary disease were susceptible to the harmful effect of $PM_{2.5}$.[1, 16, 17] Therefore, older patients undergoing dialysis were extremely vulnerable to air pollution given their advanced age and high burden of comorbidity.[18] However, it remains unclear whether older dialysis patients who live in areas with elevated levels of fine particulate matter are at increased risk of mortality and whether the current US Environmental Protection Agency (EPA) National Ambient Air Quality Standard for annual $PM_{2.5}$ (≤12μg/m^3)[19] is sufficient to protect this vulnerable population.

Our a priori hypothesis was that older dialysis patients were at elevated risk of mortality when living in a ZIP code with high ambient air pollution exposure. Understanding the role of air pollution on mortality among older patients undergoing dialysis will help inform policy discussions and clinical practice in the US. Therefore, we estimated the risk of mortality by level of fine particulate matter among adults aged≥65 years who initiated dialysis in the US.

MATERIALS AND METHODS

Study population and data source

Older kidney failure patients aged≥65 years at dialysis initiation, who started maintenance dialysis (either hemodialysis or peritoneal dialysis) between 1/1/2010–12/31/2016 without a previous solid organ transplant were identified from US Renal Data System (USRDS). USRDS is a national data system that collects, analyzes and distributes information about chronic kidney disease and kidney failure in the US. The database includes kidney failure patient demographic and diagnosis data, biochemical values, dialysis claims and information on treatment history, hospitalization events and physician/supplier services. The data in USRDS originated from The Centers for Medicare & Medicaid Service, the Organ Procurement and Transplantation Network, the Centers for Disease Control, the ESRD Networks, the US Census and select data from past and current USRDS Special Studies.[20] This study was reviewed by the Johns Hopkins School of Medicine Institutional Review Board and was determined to be exempt.

Only older patients who were diagnosed with renal failure and received their first chronic dialysis treatment were included in our analysis. Among 396,259 older patients who initiated dialysis between 2010–2016, we excluded those who had missing or unidentified ZIP codes or lived in ZIP codes without available air pollution data (N=9,183). We also excluded older patients who lived in ZIP code areas without available socioeconomic status (SES) data (N=1,333) and older patients with missing age, sex, race/ethnicity, body mass index (BMI), cause of kidney failure, smoking status, nephrology care, and comorbidities (N=1,467). Our analytic sample included 384,276 (97% of original population) older patients.

Ambient air pollution exposure

The primary exposure of our analysis was annual $PM_{2.5}$ concentration at the ZIP code level. Ambient air pollution data gridded at 0.01 degrees between 2010–2016 was obtained from NASA's Socioeconomic Data and Application Center (SEDAC) Global Annual $PM_{2.5}$ Grids from NASA Moderate Resolution Imaging Spectroradiometer, Multi-angle Imaging Spectroradiometer, and the Sea-Viewing Wide Field-of-View Sensor Aerosol Optical Depth with Geographically Weighted Regression.[21, 22] $PM_{2.5}$ data was then aggregated to ZIP code level by year. We linked older kidney failure patients and the $PM_{2.5}$ data through their ZIP code of residence and the year of first dialysis. In this analysis, we defined a concentration $\leq 12 \mu g/m^3$ as lower level and $>12 \mu g/m^3$ as higher level of $PM_{2.5}$, as is suggested by the US EPA National Ambient Air Quality Standard for annual $PM_{2.5}$.

Mortality

The outcome of interest in the study was all-cause mortality. USRDS obtained death dates of the patients from multiple sources including CMS Medicare Enrollment Database, CMS forms 2746 and 2728 (1995–2005), Organ Procurement and Transplantation Network transplant follow-up form, CROWNWeb database and Inpatient Claims.[20] Older patients were followed from the date of their first dialysis through date of death, date of transplant, or administrative censoring (12/31/2017), whichever came first. We also explored the association between $PM_{2.5}$ and cause-specific mortality. Given the large number of missingness in the data for cause of deaths, we only classified cause-specific mortality by three categories: CVD, other, and unknown.

Patient and geographic factors

Individual-level factors were obtained from USRDS database (patient profile and CMS-2728 Form), including demographics (age, sex, race/ethnicity) and health-related factors (cause of kidney failure, smoking status, BMI and nephrology care status). Considering comorbidities are potential mediators in the association between $PM_{2.5}$ and mortality, we did not include them in the models of our main analysis.

ZIP code-level SES factors included percent below 200% of the federal poverty line, mean years of education, median household income, median housing cost per month, percent non-Hispanic Black, percent Hispanics, population density and urbanicity. Population density was obtained from SEDAC Gridded Population of the World 2010.[23] Urbanicity of the area in the year of 2013 was retrieve from the Census Bureau TIGER/Line shapefiles, and was categorized into urban, urban clusters (incorporating places that contained at least 2,500 but less than 50,000 people within its boundaries) and rural.[24] Other ZIP code-level characteristics were abstracted from 2014 American Community Survey.[25]

Statistical analysis

Baseline characteristics were summarized by levels of ZIP code-level $PM_{2.5}$ exposure ($\leq 12\mu g/m^3$, $>12\mu g/m^3$). Continuous variables were presented as median (IQR) while categorical variables were presented as frequency (%).

Cox proportional hazard models with robust variance accounting for cluster effect of ZIP codes were used to investigate the unadjusted and adjusted continuous association between $PM_{2.5}$ and all-cause and cause-specific mortality among the study population. Considering the variation of air pollution by different time periods and that more than 50% of the older patients with $PM_{2.5}$ exposure level higher than $12\mu g/m^3$ came from California, we allowed different baseline hazard functions by the year of dialysis initiation and whether the older patients lived in California. We accounted for demographics, health-related factors and ZIP code-level factors in our adjusted models. We fit linear spline models with a knot at $12\mu g/m^3$ to allow for different dose-response associations below and above the current EPA National Ambient Air Quality Standard. To explore other potential non-linear exposure-outcome associations, we additionally fit restricted cubic spline models.

To investigate whether the association between ZIP code-level $PM_{2.5}$ concentration and all-cause mortality among older dialysis population varied by age (<75 and ≥75 years), sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic Black, and Hispanic/Latino, other), history of smoking (current and non-current), and cause of kidney failure (diabetes, hypertension, glomerular nephritis and other), we fit linear spline models within different subgroups.

Considering the levels and composition of $PM_{2.5}$ can vary greatly across the US, we further investigated the association within different regions of the country. We grouped our study population by their states of residence into eight regions [Figure 1]. Adjusted Cox proportional hazard models were used to obtain the linear association between continuous $PM_{2.5}$ and all-cause mortality in different regions, separately.

In our sensitivity analysis, we further adjusted for comorbidities (cardiovascular disease, chronic obstructive pulmonary disease and cancer) in our linear spline models as additional potential confounders. The first six months after dialysis initiation was a complicated period with high mortality, we did additional analysis among those who survived the first three and six months of maintenance dialysis. Considering a large proportion of the older patients resided in areas with higher level of $PM_{2.5}$ concentration were from California, we also conducted analyses separately for older patients who came from California and those who were from other states to see if the association was consistent between the two groups.

Statistical analyses were conducted using Stata SE, version 15 (Stata Corp, College Station, TX) and R 3.6.1,[26],[27] and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Older adults initiating dialysis

There were 384,276 older patients (across 25,100 ZIP codes) who initiated dialysis between 2010 and 2016 and were followed for a median of 1.84 (IQR:0.77–3.25) years. Overall, 14% were female, 63% were non-Hispanic white, 20% were non-Hispanic Black, and 11% were Hispanic/Latino. The median age at dialysis initiation was 74 years (IQR:69–80).

Ambient air pollution ($PM_{2.5}$)

The median ZIP code-level $PM_{2.5}$ concentration for older patients was 9.17μg/m^3 (IQR:7.63–10.78, range 0.70–23.62 μg/m^3). Among our study population, 48,885 (13%) had ZIP-code level $PM_{2.5}$ concentration >12μg/m^3. Furthermore, the distribution of ZIP code-level $PM_{2.5}$ varied across the US with the highest ZIP code-level air pollution occurring in Far west region.

When compared to those residing in areas with lower $PM_{2.5}$ concentrations (≤12μg/m^3), older patients in areas with higher level of concentration ($PM_{2.5}$ >12μg/m^3) were less likely to be non-Hispanic white (49% vs 65%) and more likely to be Hispanic/Latino (20% vs 10%). Only 23% of the older patients living in areas with higher level of $PM_{2.5}$ had been on nephrology care for more than 12 months at the time of dialysis initiation, compared to 32% in the older patients with lower exposure [Table 1].

The older patients in ZIP codes with higher levels of $PM_{2.5}$ concentrations were more likely to live in ZIP codes with a higher proportion of Hispanic residents (median 19.0% vs 6.9%), population density (median 1,974/KM^2 vs 393/KM^2), and housing cost (median $1,145 vs $928 USD/month). Furthermore, they were more likely to be in urban areas; 93.0% of the older patients in high $PM_{2.5}$ concentration ZIP codes lived in urban areas compared to 73.3% in the lower group [Table 1].

Ambient air pollution and mortality among older dialysis patients

Overall, 117,091 patients residing in areas with low $PM_{2.5}$ level and 29,995 patients in areas with high $PM_{2.5}$ died during the follow-up period, among which 84,109 (34%) died from CVD, 94,923 (38%) died from other causes, and 69,093 (28%) had unknown cause of death.

Restricted cubic spline model suggested that there was non-linear association between $PM_{2.5}$ and mortality risk and shown that the dose-response association changed when $PM_{2.5}$ level reached ~12μg/m^3 [Figure 2].

In the unadjusted linear spline model, a 10μg/m^3 increase in $PM_{2.5}$ was associated with a 1.03-fold (95%CI:1.01–1.06) increased risk of mortality when $PM_{2.5}$ was at lower level; a 10μg/m^3 increase in $PM_{2.5}$ was associated with a 1.21-fold (95%CI:1.11–1.33) increased risk of mortality when $PM_{2.5}$ was at higher level. After accounting for demographics, health-related factors and ZIP code-level characteristics, no association was found between $PM_{2.5}$ and mortality risk when the $PM_{2.5}$ level was below 12μg/m^3 (HR=1.01 per 10μg/m^3 increase, 95%CI:0.99–1.03). However, when $PM_{2.5}$ was above 12 μg/m^3, 10μg/m^3 increase was associated with 1.16-fold (95%CI:1.08–1.25) increase in mortality risk among older dialysis patients [Table 2].

At higher levels, increased $PM_{2.5}$ was associated with an increased risk of CVD mortality (HR=1.38; 95%CI 1.21–1.58) and unknown causes of mortality (HR=1.33; 95%CI 0.1.14–1.55), but not death from other cause [Table S1].

Ambient air pollution and mortality among subgroups of older patients initiating dialysis

The association between $PM_{2.5}$ concentration and mortality varied across different subgroups of older patients initiating dialysis [Figure 3]. At higher levels, we found that older patients who were female (HR=1.26 per 10μg/m^3 increase, 95%CI:1.13–1.42), Black (HR=1.31 per 10μg/m^3 increase, 95%CI:1.09–1.59) or had diabetes (HR=1.25 per 10μg/m^3 increase, 95%CI:1.13–1.38) as the primary cause of kidney failure had higher $PM_{2.5}$ associated mortality risk than the overall study population.

Although the risk of mortality was stronger when $PM_{2.5}$ was above 12 μg/m^3 (HR=1.19 per 10 μg/m^3 increase, 95%CI:1.08–1.32), even at lower levels, $PM_{2.5}$ was significantly associated with increased mortality risk among older patients who were aged>75 years (HR=1.04 per 10 μg/m^3 increase, 95%CI:1.00–1.07).

Ambient air pollution and mortality by geographic region

Across eight geographic regions, the Great Lakes region had the highest median ZIP code-level $PM_{2.5}$ concentration (median=11.17μg/m^3), while the Rocky Mountains had the lowest (median=5.77μg/m^3) [Figure 1].

Significant associations between $PM_{2.5}$ and mortality risk were only found in the Far West region (Median $PM_{2.5}$=10.22μg/m^3), where per 10 μg/m^3 increase in $PM_{2.5}$ was associated with 1.06-fold (95%CI:1.01–1.11) increase in mortality risk. We also found marginally significant exposure-outcome association in the Great Lakes region (HR=1.08 per 10 μg/m^3 increase, 95%CI:1.00–1.16). No association was observed in other regions with lower $PM_{2.5}$ level [Figure 1].

Sensitivity analysis

Further adjustment for comorbidities did not significantly change the inferences from the main analyses; for every 10μg/m^3 increase, $PM_{2.5}$ was associated with 1.14-fold (95%CI:1.07–1.22) increase in mortality risk for higher levels, and no association was observed at lower air pollution levels. After excluding patients who died within first three and six months of maintenance dialysis, the result remained consistent. The exposure-outcome association was similar between older patients from California and other states [Table S1]. Mortality rates among our study population between 2010–2016 are shown in table S2.

DISCUSSION

In this study of 384,276 older patients initiating dialysis between 2010–2016 in the US, the median ZIP code-level $PM_{2.5}$ concentration was 9.17μg/m^3, and 13% lived in ZIP code with $PM_{2.5}$ level >12μg/m^3. A 10 μg/m^3 increase in $PM_{2.5}$ was associated with 1.23-fold (95%CI:1.14–1.32) increase in mortality among older patients initiating dialysis when at higher level of $PM_{2.5}$ and 1.05-fold (95%CI:1.02–1.07) increase when at lower level after adjusting for demographics and ZIP code-level socioeconomic status. When further adjusted for health-related factors, the association was attenuated such that $PM_{2.5}$ was associated with mortality only at levels above 12 μg/m^3 (HR=1.15, 95%CI:1.07–1.23). We also found that $PM_{2.5}$ was associated with elevated mortality risk among older patients who were aged>75 years at dialysis initiation even at lower levels of $PM_{2.5}$. However, older patients who were female, Black or had diabetes as primary cause of kidney failure were most vulnerable when exposed to higher levels of $PM_{2.5}$ (>12 μg/m^3).

To our knowledge, while many cohort studies have evaluated the association between long-term exposure of air pollution and mortality risk in the general population[3, 28–30], this is the first study to examine this relationship with a focus on older patients with kidney failure in the US. We observed a positive association between long-term exposure to $PM_{2.5}$ and all-cause and CVD mortality among older patients initiating dialysis, which is consistent with a recent study in Hong Kong (median $PM_{2.5}$ concentration=38.9μg/m^3). Ran et.al[31] found an interquartile change (4 μg/m^3) in $PM_{2.5}$ was associated with 14% (95%CI:1.01–1.30) increase in mortality, which could be translated into more than 35% increase in mortality every 10 μg/m^3 increase in $PM_{2.5}$, among kidney failure patients. This larger effect size observed in Hong Kong could potentially be explained by the higher levels of air pollution persisting in the region in comparison to the Unites States. Furthermore, patients with kidney failure in Hong Kong was quite different from those in the Unites States in terms of primary renal diagnosis.[32] Another recent study investigating short-term effect of wildfire smoke conducted among hemodialysis patients in the United Sates (US) found that a 10 μg/m^3 increase in wildfire $PM_{2.5}$ was associated with 1.04-fold (95%CI:1.01–1.17) increase in the same-day mortality.[33] All these findings supports that air pollution is a potential threat to the health of patients with kidney failure.

Many of the studies found linear or supralinear (characterized by decrease slope with increased exposure level) concentration-response associations between $PM_{2.5}$ and mortality, where increased air pollution associated mortality risk occurred even at very low levels of $PM_{2.5}$.[3, 29, 34–36] Specifically, a study conducted among the Medicare population found that per 10 μg/m^3 increase in $PM_{2.5}$ was linearly associated with 7.3% (95%CI:7.1–7.5%) increase in all-cause mortality without any thresholds[3] while another study conducted among a Canadian census cohort observed that $PM_{2.5}$ was associated with a steep increase in relative mortality risk at levels below 5 μg/m^3, with associations attenuating at higher levels.[29] However, in this study, the reverse was observed; we found that there was increased mortality risk only when $PM_{2.5}$ was >12 μg/m^3, and no association when $PM_{2.5}$ was at lower levels among the overall study population. Previous studies suggested that air pollution could affect health by inducing systematic inflammation.[1] When compared to general population, older patients with kidney failure are more likely to have a high inflammatory state.[37, 38] It is possible that, at low levels of $PM_{2.5}$, the proinflammatory effect from air pollution is small relative to the already high state of inflammation experienced by this vulnerable population, such that there is no observed increase in mortality risk. However, when the $PM_{2.5}$ increased to a specific level, the effect was large enough to lead to adverse outcomes among older patients with kidney failure. This could also explain the comparable or even stronger association we observed at higher levels of air pollution than in other US studies.[3, 28, 30] Additionally, this potential mechanism was also supported by our findings of significant exposure-outcome associations in regions with highest levels of $PM_{2.5}$ (Great Lakes and Far West).

In this study, patients >75 years of age with kidney failure were more vulnerable to air pollution compared to their younger counterparts (65–75 years), such that elevated mortality risk was observed even at low levels of $PM_{2.5}$. This finding is in line with other studies demonstrating the susceptibility of the oldest older adults in general to harmful effects of air pollution,[1, 16, 17] supporting current EPA recommendations for them to take extra precautions during high pollution days.[39] A previous study had found that older adults (aged≥65) who were frail were more vulnerable to the adverse effects of air pollution than their non-frail counterparts.[40] The higher vulnerability to air pollution among older dialysis patients observed in our study may be attributable to frailty, a condition characterized by higher vulnerability to stressors,[41] considering that the prevalence of frailty increases with age and more than 25% of the kidney transplant candidates aged≥65 years-old were frail.[42–44] Meanwhile, the higher prevalence of comorbidities including cardiovascular disease and respiratory disease among older patients initiating dialysis could also contribute to the vulnerability of this population.[1]

In this population of older dialysis patients, we found that the effect of air pollution on mortality differed by racial/ethnic groups, with older non-Hispanic Black patients being more vulnerable to the effects of $PM_{2.5}$ at levels above the current EPA standard, and non-Hispanic White patients at increased risk of mortality even at levels below the current EPA standard. One potential cause for this difference could be the geographical distribution of racial/ethnic groups as the composition of particulate matter varies greatly by region[45] and the particle compositions were found to be associated with mortality.[46, 47] Furthermore, Black patients are also more likely to be disproportionately affected by other risk factors such as low SES, which may increase their vulnerability to environmental stressors and thus contribute to this observed difference, yet the role of race/ethnicity on the association between air pollution and mortality remains inconclusive.

Older patients initiating dialysis are a vulnerable group with high baseline mortality,[18] such that even a small increase in relative risk would result in a relatively large increase in absolute mortality. Consequently, it is especially critical for this population to avoid unnecessary excess mortality risk from $PM_{2.5}$ exposure. Although air pollution has long been considered to be a threat to health, recent studies on air quality awareness among US adults found that only 29.2% of participants believed that air pollution was bad and 14.7% would change their behavior when there was low air quality; similar results were found among participants with heart disease.[48, 49] Under these circumstances, there is a need for healthcare providers, like geriatricians, to discuss the potential harms of air pollution with their vulnerable older patients and provide recommendations for behavioral changes. This study identified different subgroups of older patients initiating dialysis with varying vulnerability to air pollution, which could help geriatricians and nephrologists target air pollution exposure mitigation strategies for older patients most in need of them.

Our study has the strength of using the geographically diverse, registry-based data capturing the majority of older patients with kidney failure in the US. Data from a national registry database allowed us to adjusted for key health-related factors which were most relevant to older patients initiating dialysis. Additionally, the large sample size enabled us to do individual analysis in different subgroups and regions.

This study has its limitations in the measurements of exposure and confounders and ascertainment of outcomes. Air pollution concentration was assessed at the ZIP code level and we were not able to account for the indoor air pollution; this could result in potential exposure misclassification as variations in $PM_{2.5}$ can exist within a ZIP code and this level may not reflect all locations where older patients may spend time. Even within the same area, individual exposure of $PM_{2.5}$ could be affected by many factors such as proximation to major road ways and outdoor activity level. Due to the limited availability of other data, we only investigated the effect of $PM_{2.5}$ in this study and was not able to control for other pollutants such as ozone and NO_2. Therefore, part of the observed effect of might be contributed to other types of pollutants. However, previous studies suggested that further controlling for other pollutants did not significantly change the estimated effects of PM2.5.[3, 50] We only have the ZIP code and health-related information for the patient at the time of listing, such that we were not able to account for time varying exposure of $PM_{2.5}$ and other time-varying confounding. The ZIP code information was obtained solely from USRDS patient profile and we were not able to confirm whether the patients actually resided within the ZIP code area at the time of dialysis initiation and during the follow-up. However, the ZIP code data had been used to link ZIP code-level exposure in other studies [51, 52] and this is the only data we have regarding the patients' area of residence. For SES confounders, we were only able to measure at ZIP code level, which could lead to residual confounding. In terms of outcome ascertainment, the large number of missingness in cause-of-death data limited our ability to investigate and interpret the association between $PM_{2.5}$ and cause-specific mortality.

In conclusion, ambient air pollution, measured by $PM_{2.5}$, was associated with all-cause mortality among older patients initiating dialysis. More notably, increased mortality risk was observed among patients aged>75 years, even at levels below current EPA National Ambient Air Quality Standard for $PM_{2.5}$. Our results suggested that the current EPA standard for $PM_{2.5}$ might not be enough to protect the most vulnerable populations. Geriatricians and nephrologists should consider ambient air pollution as an important environmental exposure and implement ambient air pollution exposure mitigation strategies for their vulnerable older patients and actively engage in advocacy for population-level solutions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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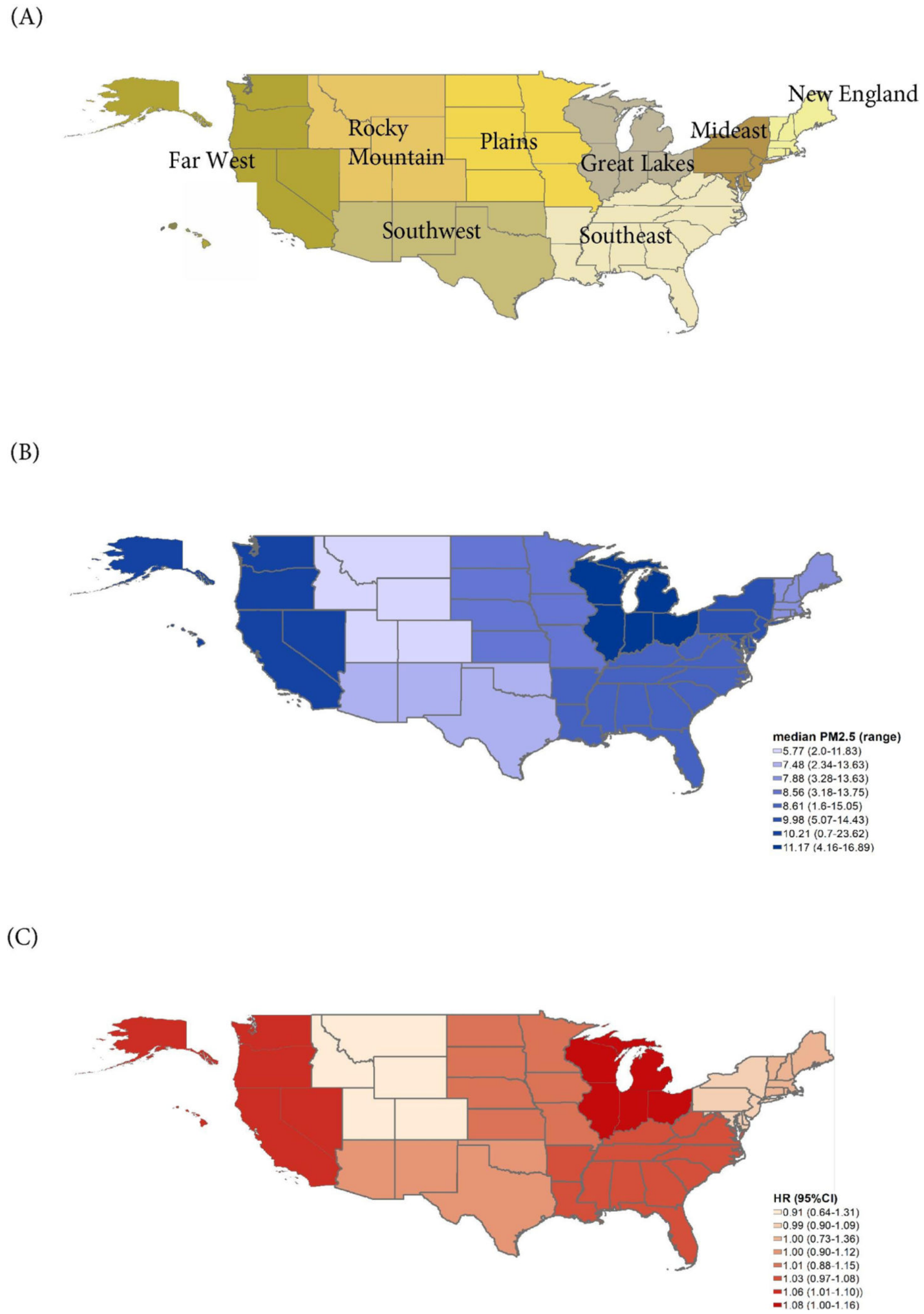

Figure 1.

$PM_{2.5}$ level and $PM_{2.5}$-mortality association in eight regions of the US

(A) Eight regions in the Unites States; (B) $PM_{2.5}$ level by regions; (C) $PM_{2.5}$-mortality association in eight regions; HR: Hazard Ratio for mortality per 10 μg/m^3 increase in $PM_{2.5}$

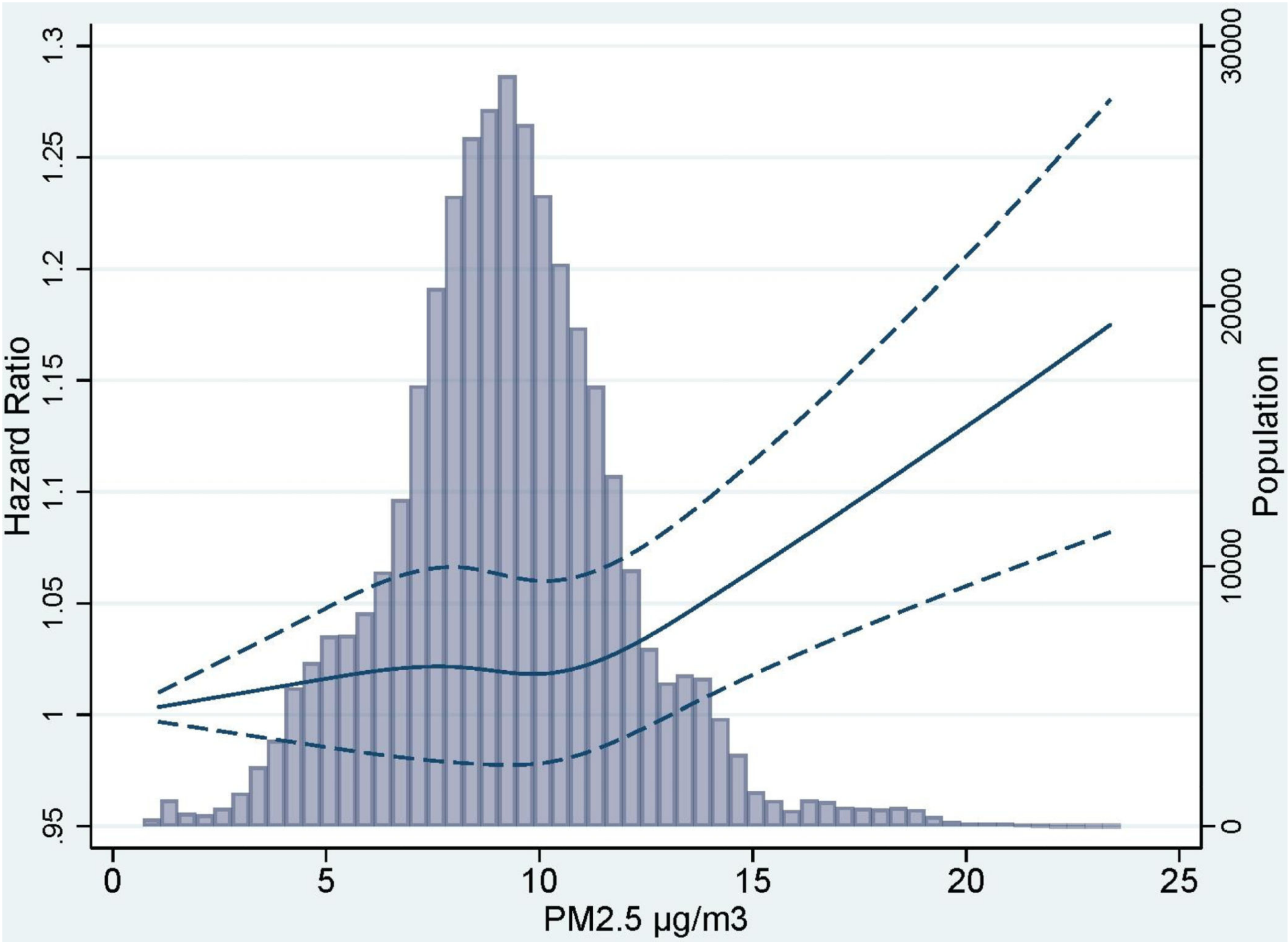

Figure 2.

Concentration-response function of $PM_{2.5}$ and mortality among older (aged≥65) patients initiating dialysis:

Dose-response function was estimated using restrict-cubic spline model. Association adjusted for demographics (age, sex, race), ZIP-code level characteristics (percent below 200% of the federal poverty line, mean years of education, median household income, median housing cost per month, percent Black, percent Hispanics, population density and urbanicity), health related factors (cause of kidney failure, smoking status, BMI and nephrology care status)

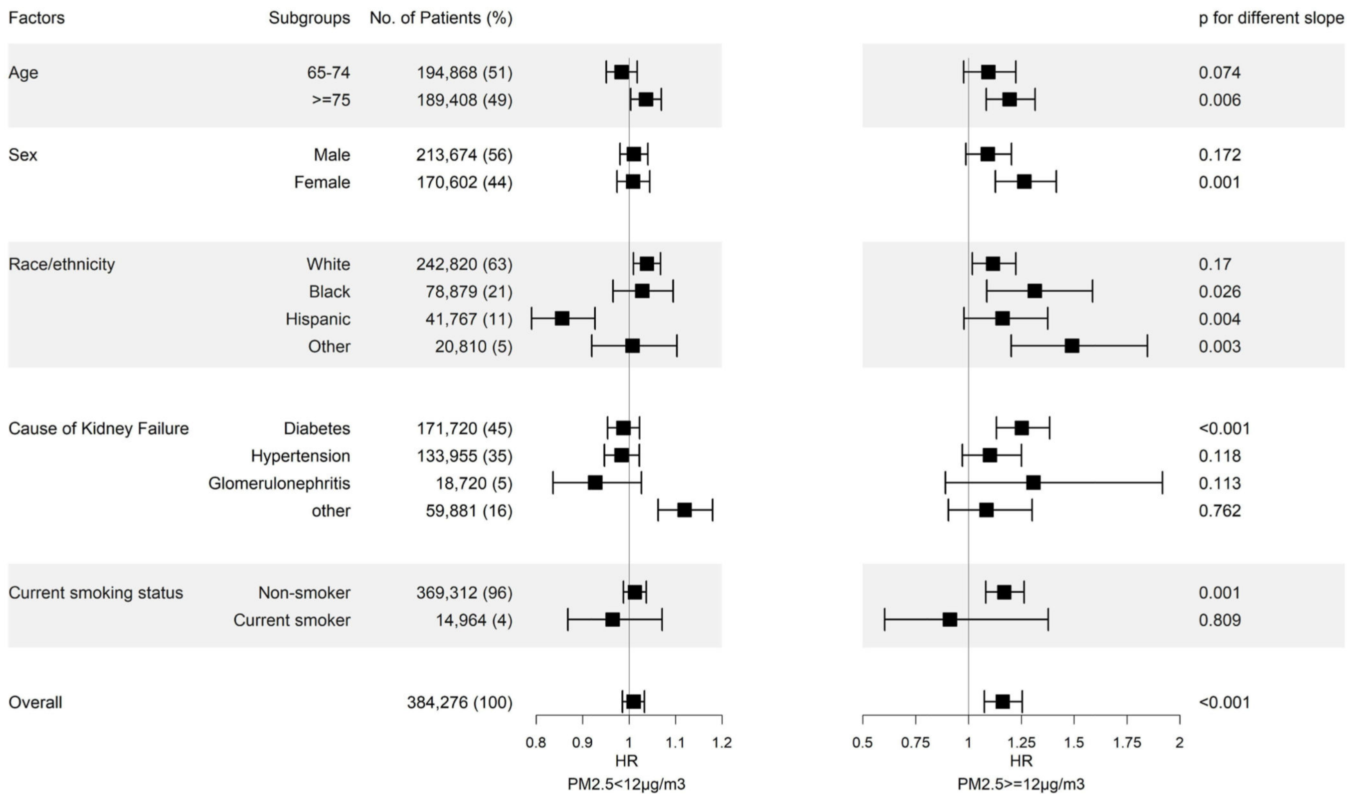

Figure 3.

$PM_{2.5}$ and all-cause morality among subgroups of older patients on dialysis in the US (N=384,276)

HR: Hazard ratio for mortality per 10 μg/m^3 increase in $PM_{2.5}$; *p* for slope difference indicated the *p* effect difference of per 10 μg/m^3 increase in $PM_{2.5}$ between areas with $PM_{2.5}$≤12 and areas with PM2.5>12; Association adjusted for adjusted for demographics (age, sex, race), ZIP-code level characteristics (percent below 200% of the federal poverty line, mean years of education, median household income, median housing cost per month, percent Black, percent Hispanics, population density and urbanicity), health related factors (cause of kidney failure, smoking status, BMI and nephrology care status)

Table 1.

Baseline characteristics of older (aged≥65) patients initiating dialysis by $PM_{2.5}$ levels (N=384,276).

Factor		$PM_{2.5}$≤12μg/m^3	$PM_{2.5}$>12μg/m^3
N		335,391	48,885
Individual level characteristics			
Age at dialysis initiation (years)		74 (69, 80)	75 (69, 81)
Female		148,233 (44.2%)	22,369 (45.8%)
Race/ethnicity	White	218,650 (65.2%)	24,170 (49.4%)
	Black	68,831 (20.5%)	10,048 (20.6%)
	Hispanic	32,161 (9.6%)	9,606 (19.7%)
	Other	15,749 (4.7%)	5,061 (10.4%)
BMI[a] (kg/m^2)		27.4 (23.5, 32.3)	26.6 (23.1, 31.5)
Primary cause of kidney failure	Diabetes	148,217 (44.2%)	23,503 (48.1%)
	Hypertension	117,073 (34.9%)	16,882 (34.5%)
	Glomerulonephritis	16,817 (5.0%)	1,903 (3.9%)
	Other	53,284 (15.9%)	6,597 (13.5%)
Current smoker		13,565 (4.0%)	1,399 (2.9%)
Nephrology care at dialysis initiation	No care	74,798 (22.3%)	10,921 (22.3%)
	Unknown care	43,655 (13.0%)	10,589 (21.7%)
	<6 months of care	44,806 (13.4%)	7,949 (16.3%)
	6–12 months	63,555 (19.0%)	8,204 (16.8%)
	>12 months	108,566 (32.4%)	11,221 (23.0%)
ZIP code-level characteristics			
Percent Black		6.2 (1.7, 21.1)	5.2 (2.0, 17.6)
Percent Hispanic		6.9 (2.7, 18.4)	19.0 (4.6, 50.0)
Population density		393 (71, 1,275)	1,974 (873, 3,761)
Mean education year		13.2 (12.6, 14.0)	13.0 (12.2, 13.8)
Median income		48,520 (38,583, 63,677)	50,083 (39,222, 64,211)
Monthly housing cost		928 (721,1245)	1,145 (871, 1437)
Percent below 200% FPL		36.0 (24.5, 47.3)	39.9 (27.2, 52.1)
Urbanicity	Urban	243,681 (72.7%)	45,017 (92.1%)
	Urban cluster	62,219 (18.6%)	2,989 (6.1%)
	Rural	29,491 (8.8%)	879 (1.8%)

Continuous variables were presented as [median (IQR)], categorical variables were presented as [frequency (%)]

[a]BMI: Body Mass Index; FPL: Federal poverty line

Table 2.

Associations between $PM_{2.5}$ and all-cause mortality among older (aged≥65) patients initiating dialysis (N=384,276).

	HR (95%CI)		p for slope difference
	$PM_{2.5}$≤12μg/m^3	$PM_{2.5}$>12μg/m^3	
Unadjusted	1.03 (1.01–1.06)	1.21 (1.11–1.33)	0.002
Model1[a]: Demographic adjusted	1.03 (1.01–1.05)	1.26 (1.17–1.36)	<0.001
Model2[b]: Model1+ ZIP code factors	1.05 (1.02–1.07)	1.23 (1.14–1.32)	<0.001
Model3[c]: Model2+ health-related factors	1.01 (0.99–1.03)	1.16 (1.08–1.25)	0.001

HR: Hazard Ratio for mortality per 10 μg/m^3 increase in $PM_{2.5}$; p for slope difference indicated the p effect difference of per 10 μg/m^3 increase in $PM_{2.5}$ between areas with $PM_{2.5}$≤12 and areas with PM2.5>12

[a]Model1 adjusted for demographics (age, sex, race)

[b]Model2 adjusted for demographics + ZIP-code level characteristics (percent below 200% of the federal poverty line, mean years of education, median household income, median housing cost per month, percent Black, percent Hispanics, population density and urbanicity)

[c]Model3 adjusted for demographics + ZIP-code level characteristics + health-related factors (cause of kidney failure, smoking status, BMI and nephrology care status)