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Association Between Particulate Matter Pollution and CKD Mortality by Social Deprivation

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To the Editor:

Chronic kidney disease (CKD) remains an important driver of mortality in the United States.[1] Traditional risk factors such as diabetes and hypertension can only partially explain the geographical variation in CKD mortality. There is increasing evidence that environmental and socioeconomic factors are key determinants of health outcomes in CKD. Recent findings suggest that air pollution, specifically particulate matter <2.5 microns ($PM_{2.5}$), may be an important risk factor for CKD related morbidity and mortality.[2] Further, social deprivation may increase susceptibility to $PM_{2.5}$-mediated health effects[3], but it is unknown whether this can be extrapolated to CKD. The objective of this study was to quantify the association between PM2.5 and CKD mortality by levels of social deprivation at the county level in the United States.

In this cross-sectional study, CKD mortality is defined as the number of people who died due to CKD. We linked 1999-2019 county-level age-adjusted CKD mortality data from the National Center for Health Statistics (NCHS) Multiple Cause of Death files (underlying cause of death International Classification of Diseases, 10th revision [ICD10]: N18.X) with the Social Deprivation Index (SDI) and chronic (1999-2019) $PM_{2.5}$ exposures. ICD-10 codes have been shown to have a good accuracy in identifying patients with moderate to severe CKD.[4] The SDI, a validated metric of socioeconomic status, grades counties from 1 (least socially deprived) to 100 (most socially deprived).[5] We utilized the 2015 SDI which is generated by incorporating the following American Community Survey estimates (2011-2015) weighted by factor loadings: low income, low education, non-employment, no car ownership, crowded housing, renter-occupied housing, and single parent family home. 1999-2019 county-level $PM_{2.5}$ estimates were generated by QGIS V3.22 utilizing modeled data by the Atmospheric Analysis Group.[6] (Item S1) We grouped counties according to SDI quartile (1-25, 26-50, 51-75, and 76-100). We then used linear regression models to estimate the associations between $PM_{2.5}$ and age-adjusted CKD mortality standardized to the 2000 US Census population (accounting for population change with time). Further, local spatial auto-correlations (Moran's I) were modeled to identify statistically significant clusters of counties with high and low CKD mortality rates and PM2.5 exposures. Institutional Review Board approval and informed consent were not required since data used is publicly available and de-identified.

A total of 469,933 deaths due to CKD were analyzed across 2,304 U.S. counties with mean age-adjusted CKD mortality of 7.70 deaths/100,000 person-years. There was significant regional variation in age-adjusted CKD mortality and in $PM_{2.5}$ (Figure S1). Counties with high social deprivation had higher PM2.5 exposure, albeit with significant overlap in PM2.5 levels between the groups (Figure S2). Univariate linear regression model showed that approximately 18% of intercountry variation in CKD mortality was explained by variation in $PM_{2.5}$ alone, with an increased CKD mortality rate of 0.70 deaths/100,000 person-years for every 1 µg/m^3 increase in $PM_{2.5}$ exposure. The association was attenuated when adding SDI to the model, but both $PM_{2.5}$ (β 0.57 [0.52-0.62], $P<0.001$) and SDI scores (β 0.05 [0.05-0.06], $P<0.001$) remained independently associated with age-adjusted CKD mortality (adjusted $R^2=0.37$). Similar estimates were obtained using random effects stratified by US census region. The association between $PM_{2.5}$ and CKD mortality was strongest among counties with highest SDI (β 0.70 [0.49-0.92]) compared with lowest SDI (β 0.49 [0.41-0.56]), P for interaction <0.001, Figure 1. CKD mortality across the spectrum of PM2.5 and SDI intersections is shown in Figure 2. Positive and negative spatial autocorrelations were noted in PM2.5 and CKD mortality (Figure S3).

In this analysis of roughly half a million CKD deaths, we illustrate that $PM_{2.5}$ is associated with age-adjusted CKD mortality even after adjusting for social deprivation. We further show that the association between $PM_{2.5}$ and CKD is accentuated in counties that are most socially vulnerable, and that 37% of intercountry variation of CKD mortality can be explained by $PM_{2.5}$ and SDI alone.

This analysis highlights the important contributions of social and environmental drivers of CKD. Air pollutants can increase risk of CKD via multiple mechanisms, including inflammation, oxidative stress, thrombosis, and elevations in blood pressure and glycemia[7–9]. We additionally demonstrate that socially deprived areas may be disproportionately impacted by air pollution, which is similar to what has been observed for cardiovascular disease[3], extrapolating both social deprivation-related susceptibility and vulnerability effects to air pollution to CKD. The mechanisms driving this disproportionate increase in PM2.5 related CKD mortality among socially-deprived individuals may include healthcare access, behavioral risk factors, work-related exposures, as well as the prevalence of other comorbidities which might signal increased susceptibility to the effects of air pollution.[10]

A main limitation of this study is that the accuracy of CKD mortality defined by ICD-10 codes has not been validated. Further, our analysis is limited by using population-level data which may not account for all confounders, using modeled environmental exposures, temporal heterogeneity of data, and possible misclassification of cause of death. We tried to minimize these limitations by using large scale age-adjusted mortality and adjusting for SDI, a conglomerate of socio-economic variables.

Our findings call for increased recognition of geographical disparities in CKD mortality and their socio-environmental drivers. Interventions curbing $PM_{2.5}$ pollutions may be most impactful to reduce CKD mortality in socio-economically deprived areas.

Article Information

Authors' Contributions: research idea and study design: IM, SA-K; data acquisition: IM, JS, MEEM; data analysis/interpretation: IM, JS, MEEM, SA-K; statistical analysis: IM, JS, SA-K; supervision or mentorship: MD, MR, SR, SA-K. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

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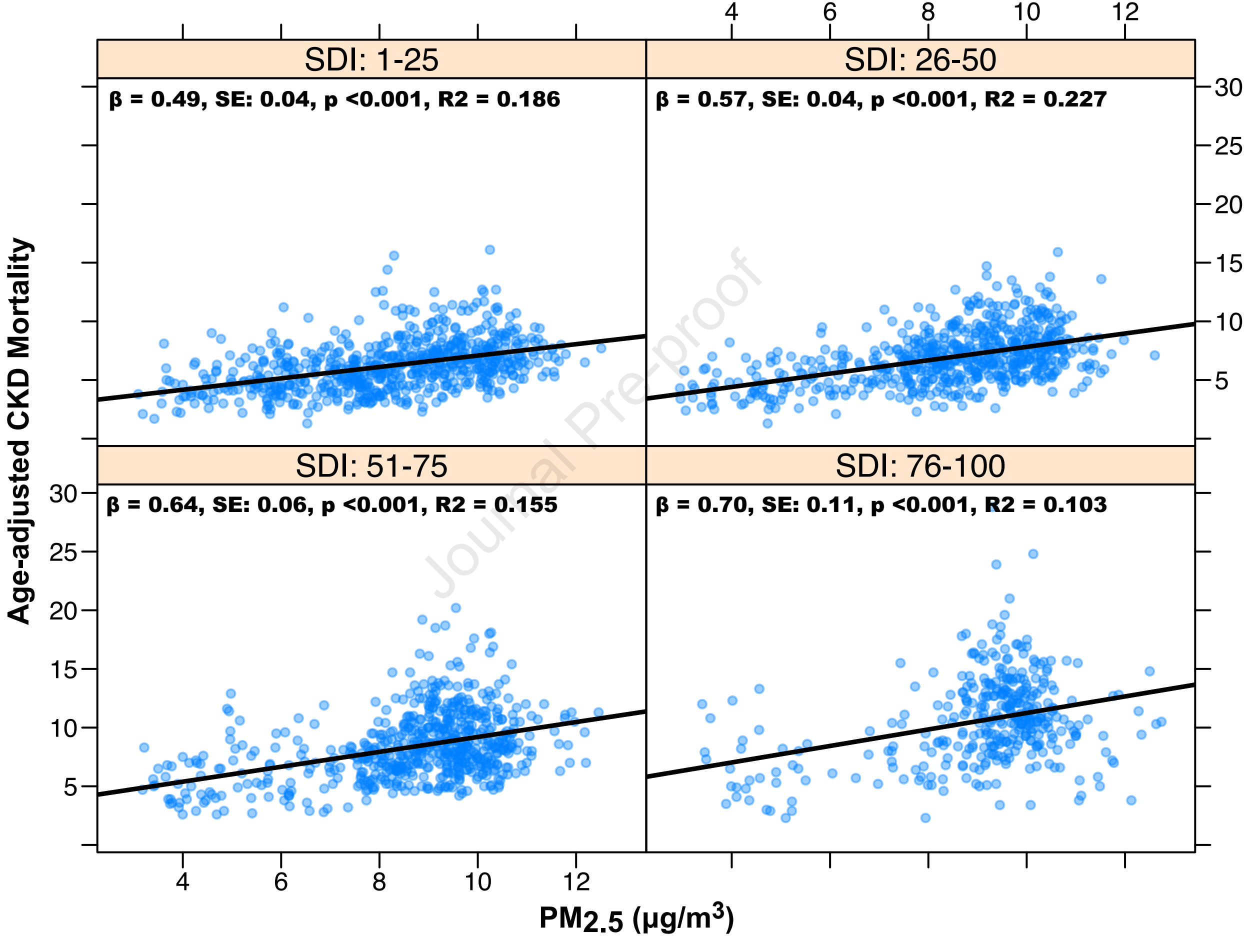
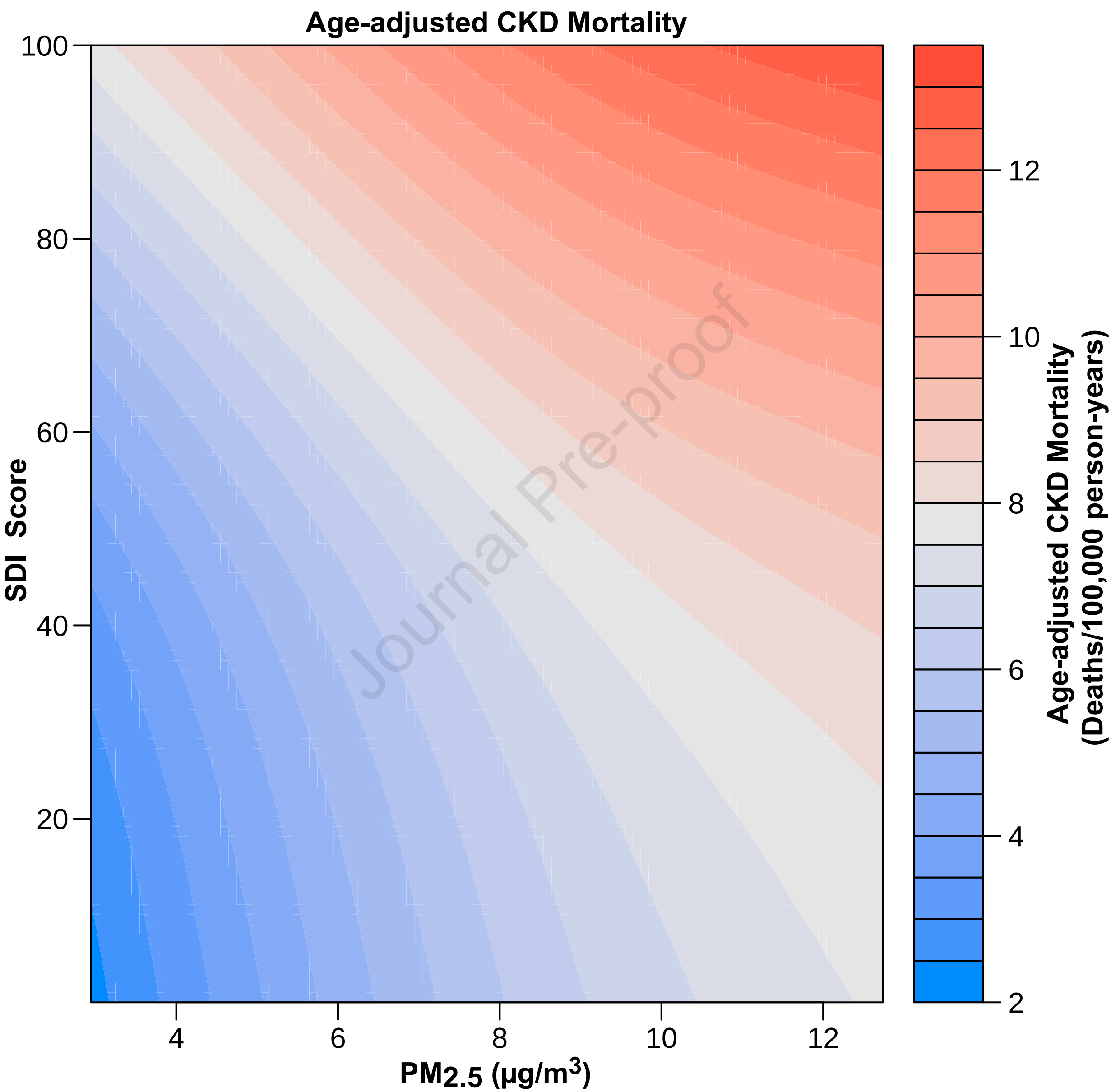
Figure 1: Association between PM2.5 and age-adjusted chronic kidney disease (CKD) mortality (rate per 100,000) by social deprivation index (SDI).

Figure 2: Association between particulate matter < 2.5 microns (PM2.5) and chronic kidney disease (CKD) mortality with social deprivation index (SDI) interaction; highest (red) and lowest (blue) CKD mortality rates are achieved when PM2.5 and SDI are simultaneously high or low, respectively.


SDI: 1-25
β = 0.49, SE: 0.04, p <0.001, R2 = 0.186
SDI: 26-50
β = 0.57, SE: 0.04, p <0.001, R2 = 0.227
SDI: 51-75
β = 0.64, SE: 0.06, p <0.001, R2 = 0.155
SDI: 76-100
β = 0.70, SE: 0.11, p <0.001, R2 = 0.103
Age-adjusted CKD Mortality
PM2.5 (μg/m3)
4
6
8
10
12
5
10
15
20
25
30



Age-adjusted CKD Mortality
100
80
60
40
20
SDI Score
4
6
8
10
12
PM2.5 (μg/m3)
12
10
8
6
4
2
Age-adjusted CKD Mortality
(Deaths/100,000 person-years)