

Supplementary Material

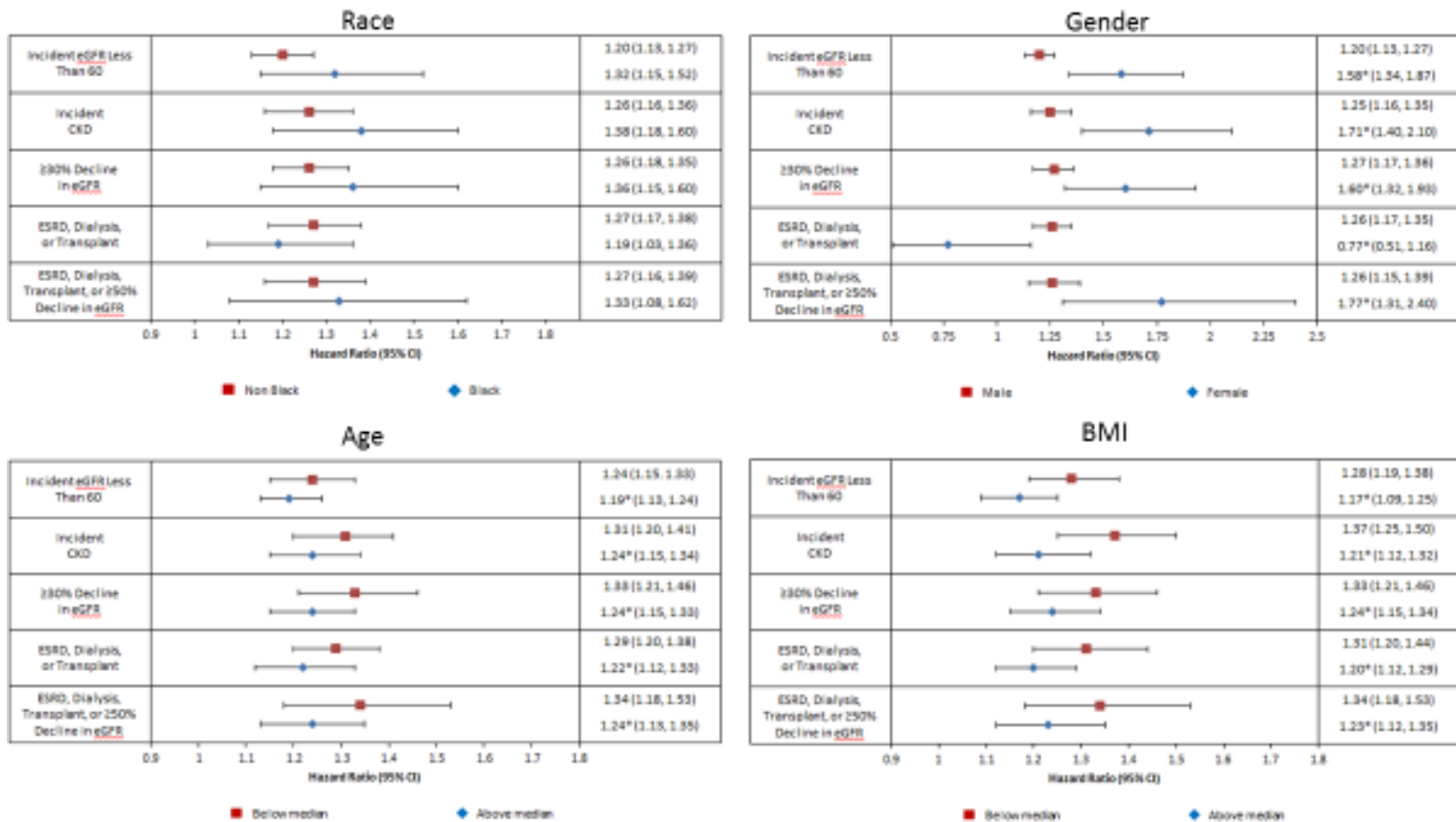
- **Supplemental figure legends**
- **Supplemental figures**
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- **Supplemental methods**
- **References**

Supplemental Figure Legends:

Supplemental Figure 1: Effect modification of the association between PM_{2.5} and risk of kidney outcomes by age, race, gender, and BMI; * denotes a p for interaction <0.001

Supplemental Figure 1

Effect Modification of the Association of PM_{2.5} and Kidney Outcomes



Supplemental Table 1: Risk of renal outcomes by PM_{2.5} concentrations categorized in quartiles

PM_{2.5} Exposure	Measure	Incident eGFR Less Than 60⁺	Incident CKD*	≥ 30% Decline in eGFR	ESRD
Year 2004 Annual Average	N	1,709,761	1,644,351	2,482,737	2,482,737
	Quartile 2 HR (CI)	1.07 (1.01, 1.14)	1.09 (1.01, 1.18)	1.11 (1.05, 1.18)	1.06 (0.98, 1.13)
	Quartile 3 HR (CI)	1.09 (1.04, 1.15)	1.11 (1.04, 1.19)	1.15 (1.09, 1.21)	1.11 (1.04, 1.19)
	Quartile 4 HR (CI)	1.19 (1.13, 1.26)	1.24 (1.15, 1.33)	1.26 (1.20, 1.33)	1.18 (1.10, 1.27)
Time Varying	N	1,702,923	1,637,643	2,473,531	2,473,531
	Quartile 2 HR (CI)	1.02 (0.97, 1.07)	1.04 (0.99, 1.10)	1.02 (0.97, 1.08)	1.12 (1.07, 1.17)
	Quartile 3 HR (CI)	1.07 (1.02, 1.12)	1.10 (1.04, 1.16)	1.06 (1.01, 1.12)	1.09 (1.03, 1.15)
	Quartile 4 HR (CI)	1.14 (1.09, 1.20)	1.19 (1.12, 1.26)	1.18 (1.10, 1.24)	1.18 (1.11, 1.25)
<p>Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty. Quartile 1, consisting of those living in counties with the lowest PM_{2.5}, is the reference category. + Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry. *Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry. Abbreviations: PM_{2.5}, particulate matter <2.5 μm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; CKD, Chronic Kidney Disease; ESRD, end stage renal disease; N, sample size; HR, hazard ratio; CI, 95% confidence interval.</p>					

Supplemental Table 2: Risk of renal outcomes for every 10 µg/m³ increase in PM_{2.5} concentration using data from air monitoring stations within 30, 10, and 5 miles from residential ZIP code centroid of cohort participants.

PM _{2.5} Exposure	Maximum Distance to Nearest Monitoring Station (miles)	Measure	Incident eGFR Less Than 60 ⁺	Incident CKD*	≥ 30% Decline in eGFR	ESRD
Year 2004 Annual Average	30 miles	N	1,303,020	1,251,826	1,891,638	1,891,638
		HR (CI)	1.21 (1.18, 1.24)	1.28 (1.24, 1.32)	1.26 (1.22, 1.29)	1.21 (1.14, 1.27)
	10 miles	N	788,875	756,602	1,141,684	1,141,684
		HR (CI)	1.21 (1.18, 1.25)	1.28 (1.23, 1.34)	1.27 (1.23, 1.31)	1.24 (1.16, 1.32)
	5 miles	N	439,831	421,505	632,650	632,650
		HR (CI)	1.20 (1.15, 1.26)	1.26 (1.19, 1.34)	1.25 (1.19, 1.30)	1.24 (1.13, 1.36)
Time Varying	30 miles	N	792,995	758,292	1,155,167	1,155,167
		HR (CI)	1.29 (1.25, 1.33)	1.43 (1.38, 1.49)	1.38 (1.33, 1.42)	1.30 (1.20, 1.41)
	10 miles	N	363,745	346,454	534,239	534,239
		HR (CI)	1.37 (1.31, 1.44)	1.58 (1.49, 1.67)	1.46 (1.39, 1.53)	1.29 (1.15, 1.46)
	5 miles	N	163,548	155,230	241,553	241,553
		HR (CI)	1.39 (1.28, 1.51)	1.55 (1.43, 1.69)	1.44 (1.33, 1.55)	1.44 (1.19, 1.74)
<p>Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty.</p> <p>+ Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry.</p> <p>*Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry.</p> <p>Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; CKD, Chronic Kidney Disease; eGFR, estimated glomerular filtration rate; ESRD, end stage renal disease; N, sample size; CI, 95% confidence interval; HR, hazard ratio.</p>						

Supplemental table 3: Risk of renal outcomes for every 10 µg/m³ increase in PM_{2.5} concentration in the top 100 counties with highest number of Census population.

PM_{2.5} Exposure	Measure	Incident eGFR Less Than 60⁺	Incident CKD[*]	≥ 30% Decline in eGFR	ESRD
Year 2004 Annual Average	N	499,916	478,244	726,146	726,146
	HR (CI)	1.20 (1.09, 1.33)	1.30 (1.15, 1.47)	1.24 (1.10, 1.40)	1.22 (1.08, 1.38)
Time Varying	N	496,574	474,969	721,629	721,629
	HR (CI)	1.17 (1.04, 1.32)	1.32 (1.13, 1.54)	1.24 (1.07, 1.42)	1.26 (1.07, 1.47)
<p>Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty.</p> <p>+ Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry.</p> <p>*Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry.</p> <p>Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; CKD, Chronic Kidney Disease; ESRD, end stage renal disease; N, sample size; HR, hazard ratio; CI, 95% confidence interval.</p>					

Supplemental table 4: Risk of renal outcomes for every 10 µg/m³ increase in PM_{2.5} concentration using data from air monitoring stations within 5 miles from ZIP code centroid in analyses adjusting for city (termed city adjusted model), and analyses considering differences between and within cities (termed within city model).

PM _{2.5} Exposure	Model	Measure	Incident eGFR Less Than 60 ⁺	Incident CKD*	≥ 30% Decline in eGFR	ESRD‡	ESRD or ≥ 50% Decline in eGFR‡
Year 2004 Annual Average	N		420,818	403,196	604,777	604,777	604,777
	City Adjusted Model	HR (CI)	1.15 (1.07, 1.23)	1.14 (1.06, 1.24)	1.21 (1.14, 1.29)	1.02 (0.86, 1.20)	1.33 (1.20, 1.48)
	Within City Model	Between-City HR (CI)	1.24 (1.18, 1.29)	1.31 (1.24, 1.39)	1.27 (1.22, 1.33)	1.30 (1.17, 1.44)	1.21 (1.14, 1.29)
		Within-City HR (CI)	1.13 (1.03, 1.23)	1.12 (1.01, 1.25)	1.19 (1.08, 1.30)	1.03 (0.86, 1.23)	1.30 (1.12, 1.50)
Time Varying	N		157,059	149,033	231,831	231,831	231,831
	City Adjusted Model	HR (CI)	1.29 (1.18, 1.41)	1.40 (1.26, 1.56)	1.43 (1.31, 1.56)	1.33 (1.01, 1.76)	1.27 (1.12, 1.44)
	Within City Model	Between-City HR (CI)	1.45 (1.31, 1.60)	1.61 (1.47, 1.77)	1.45 (1.33, 1.58)	1.51 (1.21, 1.87)	1.30 (1.13, 1.49)
		Within-City HR (CI)	1.18 (1.02, 1.36)	1.31 (1.09, 1.58)	1.42 (1.24, 1.64)	1.00 (0.65, 1.55)	1.57 (1.24, 1.58)

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty.

+ Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry.

*Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry.

‡ Because the outcome of ESRD is rare, we considered the alternative composite end point of ESRD or ≥ 50% Decline in eGFR in these analyses.

Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; CKD, Chronic Kidney Disease; ESRD, end stage renal disease; N, sample size; HR, hazard ratio; CI, 95% confidence interval.

Supplemental table 5: Risk of renal outcomes for every 10 µg/m³ increase in PM_{2.5} concentration while additionally controlling for 55 US county-level characteristics curated from the 2014 County Health Rankings datasets.

Model	Measure	Incident eGFR Less Than 60 ⁺	Incident CKD [*]	≥ 30% Decline in eGFR	ESRD, Dialysis, or Transplant	ESRD or ≥ 50% Decline in eGFR [‡]
Year 2004 Annual Average	N	1,293,786	1,242,895	1,872,030	1872,030	1,872,030
	HR (CI)	1.24 (1.13, 1.37)	1.36 (1.20, 1.54)	1.29 (1.17, 1.42)	1.06 (0.95, 1.20)	1.31 (1.15, 1.49)
Time Varying	N	1,288,132	1,237,348	1,864,389	1,864,389	1,864,389
	HR (CI)	1.21 (1.11, 1.32)	1.32 (1.19, 1.47)	1.27 (1.17, 1.39)	1.16 (1.05, 1.29)	1.26 (1.09, 1.44)

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, number of outpatient eGFR measurements, number of hospitalizations, and county level variables from the 2014 County Health Rankings dataset.

+ Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry.

*Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry.

‡ Because the outcome of ESRD is rare, we considered the alternative composite end point of ESRD or ≥ 50% Decline in eGFR in these analyses.

Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; CKD, Chronic Kidney Disease; ESRD, end stage renal disease; N, sample size; HR, hazard ratio; CI, 95% confidence interval.

Supplemental table 6: Risk of renal outcomes for every 10 µg/m³ increase in PM_{2.5} concentration while controlling for expanded definition of diabetes and hypertension.

Model	Measure	Incident eGFR Less Than 60 ⁺	Incident CKD*	≥ 30% Decline in eGFR	ESRD, Dialysis, or Transplant
Year 2004 Annual Average	N	1,679,965	1,616,153	2,444,157	2,444,157
	HR (CI)	1.22 (1.15, 1.29)	1.28 (1.19, 1.38)	1.28 (1.19, 1.38)	1.24 (1.15, 1.33)
Time Varying	N	1,673,235	1,609,552	2,435,073	2,435,073
	HR (CI)	1.25 (1.18, 1.33)	1.36 (1.26, 1.47)	1.35 (1.26, 1.45)	1.27 (1.16, 1.39)

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty.

+ Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry.

*Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry.

Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; CKD, Chronic Kidney Disease; ESRD, end stage renal disease; N, sample size; HR, hazard ratio; CI, 95% confidence interval.

Supplemental Table 7: Risk of rapid eGFR decline (eGFR Slope <-5 ml/min/1.73m²/year), and risk of composite renal outcome of ESRD or ≥50% decline in eGFR for every 10 µg/m³ increase in PM_{2.5} concentrations.

Outcome	PM _{2.5} Exposure	N	Measure of Association (CI)
eGFR Slope <-5 ml/min/1.73m ² /year	Year 2004 Annual Average: OR (CI)**	819,984	1.35 (1.22, 1.50)
Composite Outcome of ESRD or ≥50% Decline in eGFR	Year 2004 Annual Average: HR (CI)	2,482,737	1.29 (1.16, 1.44)
	Time Varying: HR (CI)	2,473,531	1.34 (1.18, 1.52)
<p>Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty. *Odds ratio for slope is odds of rapid eGFR decline (eGFR Slope <-5 ml/min/1.73m²/year) vs. stable decline (eGFR Slope <0 to -1 ml/min/1.73m²/year) Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; N, sample size; eGFR, estimated glomerular filtration rate; OR, odds ratio; CI, 95% confidence interval; ESRD, end stage renal disease; HR, hazard ratio.</p>			

Supplemental table 8: Risk of all-cause mortality for every 10 µg/m³ increase in PM_{2.5} concentration and by PM_{2.5} quartiles

Measure	PM _{2.5} Exposure	
	Year 2004 Annual Average	Time Varying
N	2,482,737	2,473,531
A 10 µg/m ³ increase in PM _{2.5} HR (CI)	1.13 (1.07, 1.19)	1.24 (1.18, 1.31)
Quartile 2 HR (CI)	1.07 (1.04, 1.11)	1.07 (1.05, 1.10)
Quartile 3 HR (CI)	1.09 (1.06, 1.12)	1.08 (1.05, 1.11)
Quartile 4 HR (CI)	1.12 (1.09, 1.16)	1.13 (1.11, 1.16)
<p>Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty.</p> <p>Quartile 1, consisting of those living in counties with the lowest PM_{2.5}, is the reference category for quartile measures.</p> <p>Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; N, sample size; HR, hazard ratio; CI, 95% confidence interval.</p>		

Supplemental table 9: Risk of hospital admission due to myocardial infarction for every 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ concentrations:

Measure	$\text{PM}_{2.5}$ Exposure	
	Year 2004 Annual Average	Time Varying
N	2,482,737	2,473,531
A 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ HR (CI)	1.16 (1.01, 1.32)	1.25 (1.17, 1.46)
<p>Models adjusted for age, race, gender, cancer, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T_0 eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, county percent in poverty, and prior history of myocardial infarction.</p> <p>Abbreviations: $\text{PM}_{2.5}$, particulate matter <2.5 μm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; HR, hazard ratio; CI, 95% confidence interval.</p>		

Supplemental table 10: Risk of renal outcomes for every 10 µg/m³ increase in PM_{2.5} concentration using informative censoring sensitivity analysis for competing risk models.

PM_{2.5} Exposure	Measure	Incident eGFR Less Than 60⁺	Incident CKD[*]	≥ 30% Decline in eGFR	ESRD
Year 2004 Annual Average	N	1,709,761	1,644,351	2,482,737	2,482,737
	Censoring as a Risk ^{**} HR (CI)	1.17 (1.11, 1.24)	1.19 (1.12, 1.27)	1.22 (1.14, 1.31)	1.13 (1.07, 1.20)
Time Varying	N	1,702,923	1,637,643	2,473,531	2,473,531
	Censoring as a Risk ^{**} HR (CI)	1.27 (1.19, 1.35)	1.36 (1.27, 1.46)	1.34 (1.25, 1.44)	1.29 (1.23, 1.34)

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty.

+ Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry.

*Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry.

** Censoring as a Risk: Model treats censoring at a competing risk as an event

Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; CKD, Chronic Kidney Disease; ESRD, end stage renal disease; N, sample size; HR, hazard ratio; CI, 95% confidence interval.

Supplemental table 11: Risk of renal outcomes for every one IQR increase in ambient air sodium concentrations (0.046416 µg/m³)

Sodium Exposure	Measure	Incident eGFR Less Than 60 ⁺	Incident CKD*	≥ 30% Decline in eGFR	ESRD	Death
Year 2004 Annual Average	N	948,202	909,229	1,368,122	1,368,122	1,368,122
	HR (CI)**	0.99 (0.99, 1.00)	0.99 (0.98, 0.99)	0.99 (0.98, 1.00)	1.01 (1.00, 1.02)	1.00 (1.00, 1.01)
Time Varying	N	946,991	908,219	1,366,479	1,366,692	1,366,692
	HR (CI)**	0.99 (0.99, 0.99)	0.99 (0.98, 0.99)	0.99 (0.99, 0.99)	1.01 (1.00, 1.02)	1.00 (0.99, 1.00)

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T₀ eGFR, body mass index, smoking status, ACEI/ARB use, county population density, number of outpatient eGFR measurements, number of hospitalizations, and county percent in poverty.
+ Incident eGFR<60 was evaluated in a subcohort of people with no prior history of eGFR≤60 at time of cohort entry.
*Incident CKD was evaluated in a subcohort of people with at least 2 eGFR separated by at least 90 days apart who had no prior history eGFR≤60 at time of cohort entry.
Abbreviations: PM_{2.5}, particulate matter <2.5 µm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; CKD, Chronic Kidney Disease; ESRD, end stage renal disease; N, sample size; HR, hazard ratio; CI, 95% confidence interval.
**Represents for every one IQR increase in sodium (0.046416 µg/m³)

Supplemental Methods:

Data Sources:

We utilized Department of Veterans Affairs datasets including inpatient and outpatient medical SAS datasets (that contain utilization data related to inpatient and outpatient encounters within the VA system) to ascertain patient demographic characteristics, location based on Federal Information Processing Standard (FIPS) county codes, and comorbidity information based on Current Procedural Terminology (CPT) codes, and ICD-9-CM diagnostic and procedure codes corresponding to inpatient and outpatient encounters¹⁻⁴. The VA Decision Support System Laboratory Results file (a detailed database that includes VA-wide results for select laboratory tests obtained in the clinical setting) supplied data on outpatient and inpatient serum creatinine measurements, which were collected during routine medical care^{1, 2, 5}. The VA Vital Status and Beneficiary Identification Records Locator Subsystem (BIRLS) files furnished demographic characteristics and death follow-up through September 30, 2012^{1, 2}. Data from the United States Renal Database System (USRDS) obtained through the VA/Centers for Medicare and Medicaid Services (CMS) was utilized in assessing ESRD status⁶. The Corporate Data Warehouse (CDW) dataset provided data on body mass index (BMI) and systolic blood pressure, smoking status, and angiotensin-converting enzyme inhibitors (ACEIs) / angiotensin receptor blockers (ARBs) and diabetic medication (including oral hypoglycemic agents and insulin) use from the Vital Signs, Health Factors, and RX Outpatient domains, respectively. The Census Bureau's Model-based Small Area Income & Poverty Estimates (SAIPE) supplied annual estimates of county level percent in poverty⁷. Information on county level population density and population size was obtained from the 2000 Census of Population and Housing⁷. Latitude and longitude for ZIP code tabulation area was obtained from the 2000 Census Gazetteer File⁸. Data on the link between ZIP code and metropolitan statistical area (MSA) was obtained from the ZIP Code to Core Based Statistical Area Relationship File based on the Office of Management and Budget 2006 delineation of MSA from the US Census Bureau⁹.

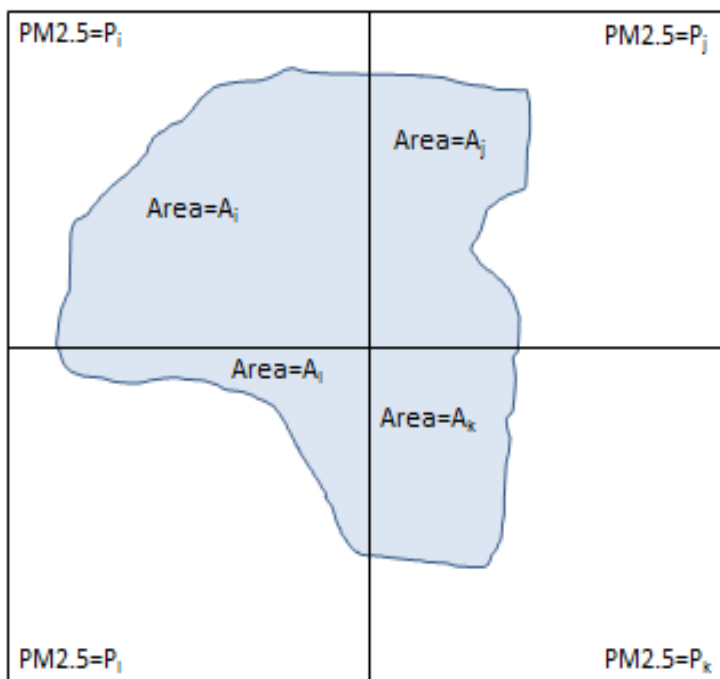
Covariates:

Race/ethnicity was categorized as white, black, or other (Latino, Asian, Native American, or other racial/ethnic minority groups). Comorbidities were assigned on the basis of relevant ICD-9-CM diagnostic and procedures codes and CPT codes in the VA Medical SAS datasets using definitions validated for use in VA datasets¹⁰⁻¹³.

BMI was categorized into underweight (<18.50), normal weight (18.50-24.99), overweight (25.00-29.99), and obese (≥30.00). Smoking status was defined as current, former, or never smoker. ACEI/ARB use was defined as use if there were prescriptions for 90 days or greater during the time before T₀. Number of outpatient eGFR measurements represented the cumulative number of outpatient eGFR values from October 1, 1999 to T₀. Number of hospitalizations was derived from the cumulative number of inpatient stays lasting a full day or longer from October 1, 1999 to T₀. Population density and percent in poverty were assigned based on county of residence at T₀.

PM_{2.5} exposure definition for NASA based data

We considered NASA's spaceborne satellite sensors as an additional source to capture ambient PM_{2.5} exposure. NASA's SEDAC Global Annual PM_{2.5} Grids from MODIS, MISR and SeaWiFS Aerosol Optical Depth (AOD) provided the data on PM_{2.5} estimates at the 10x10 km resolution^{14, 15}. Data is available in three year medians every year from 2003-2011. Patients were censored on Dec 31, 2011 in time varying models. Overlap of 10x10 km resolution PM_{2.5} grids and zip code's geographic area, resulting in surface area weighted PM_{2.5} values for each zip code, was used to define exposure levels (as depicted in the figure below).



Area weighted PM_{2.5} exposure assigned to the above zip code is calculated as:

$$\frac{P_i A_i + P_j A_j + P_k A_k + P_l A_l}{A_i + A_j + A_k + A_l}$$

where P_x is the PM_{2.5} value for grid X, and A_x the area of overlap between the zip code and grid X

Population Attributable Fraction (PAF) and Attributable Burden of Disease (ABD):

PAF was calculated using piecewise constant hazard models for disease incidence^{16, 17}. The PAF for incidence of disease was obtained from the formula:

$$PAF(T^D \leq \min(T^M, a_j)) = 1 - \frac{\sum_{i=1}^n \sum_{j=1}^J \frac{\lambda_{ij}^{*D}}{\lambda_{ij}^{*D} + \lambda_{ij}^{*M}} (S_{i,j-1}^* - S_{ij}^*)}{\sum_{i=1}^n \sum_{j=1}^J \frac{\lambda_{ij}^D}{\lambda_{ij}^D + \lambda_{ij}^M} (S_{i,j-1} - S_{ij})}$$

where D indicates disease, M mortality, n the number of individuals in analysis, J the number of intervals, a_j the survival time, λ_{ij}^O the hazard of incident outcome O for person i and interval j, * indicates the values at the Theoretical Minimum Exposure Level (TMREL), and S the disease free survival from $S_{ij} = S_{ij}^D S_{ij}^M = e^{-\sum_{k=1}^j (\lambda_{ik}^D + \lambda_{ik}^M)(a_k - a_{k-1})}$. The TMREL used for PM_{2.5} was 12 ug/m³ for those with an exposure above 12 ug/m³, and the existing level of exposure for those at or under 12 ug/m³. PAF was estimated using the annual average 2004 PM_{2.5} data. Burden of disease, as the number of incident outcomes per year attributable to PM_{2.5} exposure above the EPA standard of 12 ug/m³, was calculated using literature based estimates of outcome incident rates in the United States^{6, 18} and the 2000 Census contiguous US population, from the equation $ABD = PAF * IR * population$, where ABD is the attributable burden of disease, PAF is the population attributable, IR is the incident rate of the outcome, and population in which the burden is being assessed¹⁹. ABD was additionally calculated using a TMREL defined according to the Global Burden of Disease study methodologies²⁰⁻²². This TMREL was assigned based on a uniform distribution of PM_{2.5} from 2.4–5.9 µg/m³ representing exposure values between the minimum and fifth percentiles of exposure distributions from outdoor air pollution cohort studies²⁰⁻²². As elegantly articulated by Lim et al. the TMREL by its definition should minimize individual (and population level) risk and be *theoretically* possible to achieve, but not necessarily affordable or feasible to achieve²². Maps of the ABD per 100,000 population of incident CKD in each county were generated. Burden of disease uncertainty intervals were based on PAF variance.

Spline analyses:

Cubic spline analyses were performed in adjusted cox proportional hazard regression models with knots placed at PM_{2.5} quartiles²³ using 2004 monitor and modeled data. One percent of counties at each tail end of

the county PM_{2.5} distribution were excluded to reduce influence of potential outliers. For all splines the lowest PM_{2.5} value included in analyses, 5.7 µg/m³, was used as the reference.

Sensitivity analyses:

To test robustness of study findings we undertook a number of sensitivity analyses where we: a) Repeated the primary analyses, assigning PM_{2.5} exposure to each cohort participant based upon the nearest air monitoring station to their residential ZIP code centroid. Distance to nearest monitoring station was calculated using the Haversine formula, the latitude and longitude of the station, and the latitude and longitude of the cohort participant's ZIP code tabulation area²⁴. The analyses were restricted to those who were within 30 miles of the station. Participants were excluded in time varying models if they were considered >30 miles away from a monitoring station at any time. We then repeated this process and further reduced the distance threshold where we assigned exposure to those residing within 10, and 5 miles of air monitoring station;

b) repeated analyses in those who lived in counties which had a population size in the top 100 of all counties in the United States; c) analyzed exposure to assess within city effects in those who lived within 5 miles of an air monitoring station, where city was defined by MSA, using two methods: 1- termed the "city adjusted" model where an indicator variable for MSA was included in the models; 2- termed the "within-city model", used a city wide mean parameter (for between city effects) and a difference from city mean parameter (for within city effects)²⁵. Further details on "city-adjusted" and "within-city analyses" are provided in the section below; d) we additionally controlled for 55 US county-level characteristics using the 2014 County Health Rankings (CHR) Datasets^{26, 27}; county-level variables describe domains including demographics, physical environment, social and economic factors, health behaviors, clinical care, and health outcomes; only variables that were comparable across state were included (and listed in the County Health Rankings section below). Population density and poverty variables used in the primary analyses were excluded as the CHR data includes similar variables; the air pollution measure in the CHR datasets was also excluded as it would overlap with the primary predictor (PM_{2.5}). A principal component analysis was first conducted on the CHR data to address multicollinearity between the county level characteristics, and then factor scores were computed and controlled for in analyses. e) conducted analyses controlling for more sensitive definitions of hypertension and diabetes; the definition of hypertension included relevant diagnostic codes and average systolic blood pressure (treated

as a continuous variable) in the year prior to T_0 ; the definition of diabetes included relevant diagnostic codes as well as use of diabetic medications (including oral hypoglycemic agents and insulin) and HbA1c levels >6.4 . f) examined the association of $PM_{2.5}$ concentrations and the alternative renal outcome of rapid eGFR decline defined as eGFR slope <-5 ml/min/1.73m²/year, where odds of rapid eGFR decline was compared to stable eGFR decline (eGFR slope <0 to -1 ml/min per 1.73 m²/year) using a logistic regression model with the generalized estimating equation method to account for intra-county correlation¹³; g) examined the association of $PM_{2.5}$ concentrations and the alternative composite renal outcome of ESRD, dialysis, kidney transplant, or $\geq 50\%$ decline in eGFR; i) as a measure of calibration, analyzed the association between $PM_{2.5}$ and risk of all-cause mortality (as a positive control) using continuous and quartile exposure definitions; j) considered the risk of myocardial infarction (MI) as an additional positive control, where MI was defined as hospital admission due to myocardial infarction (inpatient admission with a primary diagnosis ICD-9 code of 410.*)²⁸, while additionally controlling for prior history of MI k) conducted sensitivity analyses for the competing risk of death²⁹; l) analyzed exposure to sodium, in baseline and time varying models, and its association with the kidney disease outcomes and death. Sodium exposure was assigned based on the nearest air monitoring station with a sodium measure within 30 miles of a participant's residential zip code's centroid, and was assessed for every 1 IQR (0.046 $\mu\text{g}/\text{m}^3$, based on 2004 distribution) increase.

City adjusted and within-city models:

For city adjusted and within-city models Cox proportional hazard models with a robust sandwich estimator were used.

City Adjusted Model

City adjusted models were built by incorporating a city indicator, using the following equation for the hazard at time t $\lambda(t)$:

$$\lambda(t) = \lambda_0 e^{\beta_1 X_i + \beta_2 C + \gamma Z_i}$$

where λ_0 is the baseline hazard, β_1 the coefficient for $PM_{2.5}$ exposure X for individual i , β_2 the coefficient for city C (the city indicator), and γ the vector of coefficients for covariates Z for individual i .

Within-city Model

For within-city models, PM_{2.5} exposures of all subjects living in zip codes that fell within a city were averaged, providing a “city mean,” \bar{X}_j . For time varying models the city mean was calculated at the beginning of each year. Within-city models were fit using an equation for the hazard at time t for person i in city j $\lambda_{ij}(t)$:

$$\lambda_{ij}(t) = \lambda_0(t)e^{\beta_B \bar{X}_j + \beta_W (X_{ij} - \bar{X}_j) + \gamma Z_i}$$

where λ_0 is the baseline hazard, β_B (the between city effect) the coefficient for city j’s mean PM_{2.5} exposure \bar{X}_j , β_W (the within city effect) the coefficient for the difference between the individual i in city j’s PM_{2.5} exposure X_{ij} and the city j’s mean PM_{2.5} exposure \bar{X}_j , and γ the vector of coefficients for covariates Z for individual i.

County Health Rankings^{26, 27}:

County Health Rankings county level variable definitions and data sources.

Variable	Source	Definition	Dates
Demographics			
Population	Census Population Estimates	Number of people in a county	2012
% below 18 years of age	Census Population Estimates	Percentage of the population below 18 years of age	2012
% 65 and older	Census Population Estimates	Percentage of the population 65 or older	2012
% Non-Hispanic African American	Census Population Estimates	Percentage of the population who are Non-Hispanic African American	2012
% American Indian and Alaska Native	Census Population Estimates	Percentage of the population who are American Indian and Alaska Native	2012
% Asian	Census Population Estimates	Percentage of the population who are Asian	2012
% Native Hawaiian/Other Pacific Islander	Census Population Estimates	Percentage of the population who are Native Hawaiian/Other Pacific Islander	2012
% Hispanic	Census Population Estimates	Percentage of the population who are Hispanic	2012

% Non-Hispanic White	Census Population Estimates	Percentage of the population who are Non-Hispanic White	2012
% not proficient in English	American Community Survey, 5-year estimates	Percentage of the population not proficient in the English language	2008-2012
% Females	Census Population Estimates	Percentage of the population who are female	2012
% Rural	Census Population Estimates	Percentage of the population living in a rural area	2012
Physical Environment			
Drinking water violations	Safe Drinking Water Information System	Population affected by a water violation/Total population with public water	FY 2012-2013
Severe housing problems	HUD, Comprehensive Housing Affordability Strategy	Percentage of households with at least 1 of 4 housing problems: overcrowding, high housing costs, or lack of kitchen or plumbing facilities	2006-2010
Driving alone to work	American Community Survey	Percent of people who drive alone to work	2008-2012
Long commute - driving alone	American Community Survey	Among workers who commute in their car alone, the percentage that commute more than 30 minutes	2008-2012
Social and economic factors			
Some college	American Community Survey	Percent adults age 25-44 with some post-secondary education	2008-2012
Unemployment	Bureau of Labor Statistics	Percent of population age 16+ unemployed and looking for work	2012
Children in poverty	Small Area Income and Poverty Estimates	Percent of children (under age 18) living in poverty	2012
Inadequate Social Support	Behavioral Risk Factor Surveillance System	Percent of adults that report not getting social/emotional support	2005-2010
Children in single-parent households	American Community Survey	Percent of children that live in single-parent households	2008-2012
Injury deaths	CDC WONDER	Injury mortality rate per 100,000	2006-2010
Median household income	Small Area Income and Poverty Estimates	Median household income at which half the households earn	2012

		more and half the households earn less	
Children eligible for free lunch	National Center for Education Statistics	Percentage of children enrolled in public schools eligible for free lunch	2011
Homicide rate	National Center for Health Statistics	Number of deaths from assaults per 100,000 population	2004-2010
Health Behaviors			
Adult smoking	Behavioral Risk Factor Surveillance System	Percent of adults that reported currently smoking	2006-2012
Access to exercise opportunities	OneSource Global Business Browser, Delorme map data, ESRI, & US Census Tigerline Files	Percentage of the population with access to places for physical activity	2010 & 2012
Excessive drinking	Behavioral Risk Factor Surveillance System	Percent of adults that report excessive drinking	2006-2012
Alcohol-impaired driving deaths	Fatality Analysis Reporting System	Percent of driving deaths with alcohol involvement	2008-2012
Teen births	National Center for Health Statistics	Teen births / females ages 15-19 * 1,000	2005-2011
Limited access to healthy foods	USDA Food Environment Atlas	Percentage of the population who are low income and do not live close to a grocery store	2010
Motor vehicle crash deaths	National Center for Health Statistics	Number of deaths due to traffic accidents involving a motor vehicle per 100,000 population	2004-2010
Drug poisoning deaths	CDC WONDER mortality data	Number of deaths due to drug poisoning per 100,000 population	2004-2010
Clinical Care			
Uninsured	Small Area Health Insurance Estimates	Percent of population < 65 without insurance	2011
Primary care physicians	HRSA Area Resource Rile	Number of primary care physicians per 100,000 population	2011
Dentists	HRSA Area Resource Rile	Number of dentists per 100,000 population	2012
Mental health providers	CMS, National Provider Identification	Number of mental health providers per 100,000 population	2013
Preventable hospital stays	Medicare/Dartmouth Institute	Discharges for ambulatory care sensitive	2011

		conditions/Medicare Enrollees * 1,000	
Diabetic monitoring	Medicare/Dartmouth Institute	Percent of Diabetic Medicare enrollees receiving HbA1c test	2011
Mammography screening	Medicare/Dartmouth Institute	Percent of female Medicare enrollees having at least 1 mammogram in 2 yrs (age 67-69)	2011
Uninsured adults	Small Area Health Insurance Estimates	Percentage of the population ages 18 to 65 that has no health insurance coverage	2011
Uninsured children	Small Area Health Insurance Estimates	Percentage of the population under age 19 that has no health insurance coverage	2011
Health Care Costs	Dartmouth Atlas of Health Care	Price-adjusted Medicare reimbursements (part A and B) per enrollee	2011
Could not see doctor due to costs	Behavioral Risk Factor Surveillance System	Percentage of the population who could not see a doctor due to costs	2006-2012
Other primary care providers	CMS, National Provider Identification	Number of other primary care providers per the population of a county	2013
Health Outcomes			
Premature death	National Center for Health Statistics	Age-adjusted years of potential life lost (YPLL) rate per 100,000	2008-2010
Poor or fair health	Behavioral Risk Factor Surveillance System	Percent of adults that report fair or poor health (age-adjusted)	2006-2012
Poor physical health days	Behavioral Risk Factor Surveillance System	Average number of reported physically unhealthy days per month	2006-2012
Poor mental health days	Behavioral Risk Factor Surveillance System	Average number of reported mentally unhealthy days per month	2006-2012
Low birthweight	National Center for Health Statistics	Percent of births with low birth weight (<2500g)	2005-2011
Diabetes	National Center for Chronic Disease Prevention and Health Promotion, Division of Diabetes Translation	Prevalence of diagnosed diabetes in a given county	2010
HIV prevalence rate	National Center for HIV/AIDS, Viral	Number of diagnoses cases of HIV in a	2010

	Hepatitis, STD, and TB prevention	county per 100,000 population	
Premature age-adjusted mortality	CDC WONDER mortality data	Number of deaths among residents under the age of 75 per 100,000 population	2008-2010
Infant mortality	Health Indicators Warehouse	Number of deaths among children less than one year of age per 100,000 population	2002-2008
Child mortality	CDC WONDER mortality data	Number of deaths among children under age 18 per 100,000 population	2007-2010

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