# **Supplementary Material**

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#### **Supplemental Figure Legends:**

Supplemental Figure 1: Effect modification of the association between PM2.5 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<sub>2.5</sub> and Kidney Outcomes



Supplemental Table 1: Risk of renal outcomes by PM2.5 concentrations categorized in quartiles

| PM <sub>2.5</sub><br>Exposure | Measure    | Incident<br>eGFR<br>Less Than<br>60 <sup>+</sup> | Incident<br>CKD* | ≥ 30%<br>Decline in<br>eGFR | ESRD         |
|-------------------------------|------------|--|------------------|-----------------------------|--------------|
| Year 2004<br>Annual           | Ν          | 1,709,761  | 1,644,351        | 2,482,737                   | 2,482,737    |
| Average                       | Quartile 2 | 1.07   | 1.09             | 1.11                        | 1.06         |
|                               | HR (CI)    | (1.01, 1.14)                                     | (1.01, 1.18)     | (1.05, 1.18)                | (0.98,1.13)  |
|                               | Quartile 3 | 1.09   | 1.11             | 1.15                        | 1.11         |
|                               | HR (CI)    | (1.04, 1.15)                                     | (1.04, 1.19)     | (1.09, 1.21)                | (1.04, 1.19) |
|                               | Quartile 4 | 1.19   | 1.24             | 1.26                        | 1.18         |
|                               | HR (CI)    | (1.13, 1.26)                                     | (1.15, 1.33)     | (1.20, 1.33)                | (1.10, 1.27) |
| Time Varying                  | Ν          | 1,702,923  | 1,637,643        | 2,473,531                   | 2,473,531    |
|                               | Quartile 2 | 1.02   | 1.04             | 1.02                        | 1.12         |
|                               | HR (CI)    | (0.97, 1.07)                                     | (0.99, 1.10)     | (0.97, 1.08)                | (1.07, 1.17) |
|                               | Quartile 3 | 1.07   | 1.10             | 1.06                        | 1.09         |
|                               | HR (CI)    | (1.02, 1.12)                                     | (1.04, 1.16)     | (1.01, 1.12)                | (1.03, 1.15) |
|                               | Quartile 4 | 1.14   | 1.19             | 1.18                        | 1.18         |
|                               | HR (CI)    | (1.09, 1.20)                                     | (1.12, 1.26)     | (1.10, 1.24)                | (1.11, 1.25) |

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T<sub>0</sub> 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<sub>2.5</sub>, 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.

**Supplemental Table 2:** Risk of renal outcomes for every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration using data from air monitoring stations within 30, 10, and 5 miles from residential ZIP code centroid of cohort participants.

| PM <sub>2.5</sub><br>Exposure | Maximum<br>Distance to<br>Nearest<br>Monitoring<br>Station<br>(miles) | Measure | Incident<br>eGFR<br>Less Than<br>60⁺ | Incident<br>CKD*     | ≥ 30%<br>Decline in<br>eGFR | ESRD                 |
|-------------------------------|---|---------|--------------------------------------|----------------------|-----------------------------|----------------------|
| Year 2004                     | 20 miles  | Ν       | 1,303,020                            | 1,251,826            | 1,891,638                   | 1,891,638            |
| Annual<br>Average             | 30 miles  | HR (CI) | 1.21<br>(1.18, 1.24)                 | 1.28<br>(1.24, 1.32) | 1.26<br>(1.22, 1.29)        | 1.21<br>(1.14, 1.27) |
|                               |   | N       | 788,875                              | 756,602              | 1,141,684                   | 1,141,684            |
|                               | 10 miles  | HR (CI) | 1.21<br>(1.18, 1.25)                 | 1.28<br>(1.23, 1.34) | 1.27<br>(1.23, 1.31)        | 1.24<br>(1.16, 1.32) |
|                               |   | N       | 439,831                              | 421,505              | 632,650                     | 632,650              |
|                               | 5 miles   | HR (CI) | 1.20<br>(1.15, 1.26)                 | 1.26<br>(1.19, 1.34) | 1.25<br>(1.19, 1.30)        | 1.24<br>(1.13, 1.36) |
| Time Varying                  |   | N       | 792,995                              | 758,292              | 1,155,167                   | 1,155,167            |
|                               | 30 miles  | HR (CI) | 1.29<br>(1.25, 1.33)                 | 1.43<br>(1.38, 1.49) | 1.38<br>(1.33, 1.42)        | 1.30<br>(1.20, 1.41) |
|                               |   | N       | 363,745                              | 346,454              | 534,239                     | 534,239              |
|                               | 10 miles  | HR (CI) | 1.37<br>(1.31, 1.44)                 | 1.58<br>(1.49, 1.67) | 1.46<br>(1.39, 1.53)        | 1.29<br>(1.15, 1.46) |
|                               |   | N       | 163,548                              | 155,230              | 241,553                     | 241,553              |
|                               | 5 miles   | HR (CI) | 1.39<br>(1.28, 1.51)                 | 1.55<br>(1.43, 1.69) | 1.44<br>(1.33, 1.55)        | 1.44<br>(1.19, 1.74) |

Models adjusted for age, race, gender, cancer, cardiovascular disease, 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, 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<sub>2.5</sub>, 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.

Supplemental table 3: Risk of renal outcomes for every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration in the top 100 counties with highest number of Census population.

| PM <sub>2.5</sub><br>Exposure | Measure | Incident eGFR<br>Less Than 60 <sup>+</sup> | Incident<br>CKD*     | ≥ 30%<br>Decline in<br>eGFR | ESRD                 |
|-------------------------------|---------|--|----------------------|-----------------------------|----------------------|
| Year 2004                     | Ν       | 499,916                                    | 478,244              | 726,146                     | 726,146              |
| Annual<br>Average             | HR (CI) | 1.20<br>(1.09, 1.33)                       | 1.30<br>(1.15, 1.47) | 1.24<br>(1.10, 1.40)        | 1.22<br>(1.08, 1.38) |
| Time Varying                  | Ν       | 496,574                                    | 474,969              | 721,629                     | 721,629              |
|                               | HR (CI) | 1.17<br>(1.04, 1.32)                       | 1.32<br>(1.13, 1.54) | 1.24<br>(1.07, 1.42)        | 1.26<br>(1.07, 1.47) |

Models adjusted for age, race, gender, cancer, cardiovascular disease, 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, 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.

**Supplemental table 4:** Risk of renal outcomes for every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> 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 <sub>2.5</sub><br>Exposure | Model                  | Measure                     | Incident<br>eGFR Less<br>Than 60⁺ | Incident<br>CKD*     | ≥ 30%<br>Decline in<br>eGFR | ESRD‡                | ESRD or ≥<br>50% Decline<br>in eGFR‡ |
|-------------------------------|------------------------|-----------------------------|-----------------------------------|----------------------|-----------------------------|----------------------|--------------------------------------|
| Year 2004<br>Annual           | N                      |                             | 420,818                           | 403,196              | 604,777                     | 604,777              | 604,777                              |
| Average                       | City Adjusted<br>Model | HR (CI)                     | 1.15<br>(1.07, 1.23)              | 1.14<br>(1.06, 1.24) | 1.21<br>(1.14, 1.29)        | 1.02<br>(0.86, 1.20) | 1.33<br>(1.20, 1.48)                 |
|                               | Within City            | Between-<br>City<br>HR (CI) | 1.24<br>(1.18, 1.29)              | 1.31<br>(1.24, 1.39) | 1.27<br>(1.22, 1.33)        | 1.30<br>(1.17, 1.44) | 1.21<br>(1.14, 1.29)                 |
|                               | Model                  | Within-<br>City<br>HR (CI)  | 1.13<br>(1.03, 1.23)              | 1.12<br>(1.01, 1.25) | 1.19<br>(1.08, 1.30)        | 1.03<br>(0.86, 1.23) | 1.30<br>(1.12, 1.50)                 |
| Time Varying                  | N                      |                             | 157,059                           | 149,033              | 231,831                     | 231,831              | 231,831                              |
|                               | City Adjusted<br>Model | HR (CI)                     | 1.29<br>(1.18, 1.41)              | 1.40<br>(1.26, 1.56) | 1.43<br>(1.31, 1.56)        | 1.33<br>(1.01, 1.76) | 1.27<br>(1.12, 1.44)                 |
|                               | Within City<br>Model   | Between-<br>City<br>HR (CI) | 1.45<br>(1.31, 1.60)              | 1.61<br>(1.47, 1.77) | 1.45<br>(1.33, 1.58)        | 1.51<br>(1.21, 1.87) | 1.30<br>(1.13, 1.49)                 |
|                               |                        | Within-<br>City<br>HR (CI)  | 1.18<br>(1.02, 1.36)              | 1.31<br>(1.09, 1.58) | 1.42<br>(1.24, 1.64)        | 1.00<br>(0.65, 1.55) | 1.57<br>(1.24, 1.58)                 |

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T<sub>0</sub> 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.

**Supplemental table 5:** Risk of renal outcomes for every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration while additionally controlling for 55 US county-level characteristics curated from the 2014 County Health Rankings datasets.

| Model        | Measure | Incident<br>eGFR Less<br>Than 60 <sup>+</sup> | Incident<br>CKD* | ≥ 30%<br>Decline in<br>eGFR | ESRD,<br>Dialysis, or<br>Transplant | ESRD or ≥<br>50% Decline<br>in eGFR‡ |
|--------------|---------|---|------------------|-----------------------------|-------------------------------------|--------------------------------------|
| Year 2004    | N       | 1,293,786                                     | 1,242,895        | 1,872,030                   | 1872,030                            | 1,872,030                            |
| Annual       | HR (CI) | 1.24  | 1.36             | 1.29                        | 1.06                                | 1.31                                 |
| Average      |         | (1.13, 1.37)                                  | (1.20, 1.54)     | (1.17, 1.42)                | (0.95, 1.20)                        | (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  | 1.32             | 1.27                        | 1.16                                | 1.26                                 |
|              |         | (1.11, 1.32)                                  | (1.19, 1.47)     | (1.17, 1.39)                | (1.05, 1.29)                        | (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.

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

**Supplemental table 6**: Risk of renal outcomes for every 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration while controlling for expanded definition of diabetes and hypertension.

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

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T<sub>0</sub> 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.

**Supplemental Table 7:** Risk of rapid eGFR decline (eGFR Slope <-5 ml/min/1.73m<sup>2</sup>/year), and risk of composite renal outcome of ESRD or  $\geq$ 50% decline in eGFR for every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentrations.

| Outcome                 | PM <sub>2.5</sub> Exposure | Ν         | Measure of Association<br>(CI) |
|-------------------------|----------------------------|-----------|--------------------------------|
| eGFR Slope <-5          | Year 2004                  | 819,984   | 1.35                           |
| ml/min/1.73m²/year      | Annual Average: OR (CI)**  |           | (1.22, 1.50)                   |
| Composite Outcome of    | Year 2004                  | 2,482,737 | 1.29                           |
| ESRD or ≥50% Decline in | Annual Average: HR (CI)    |           | (1.16, 1.44)                   |
| eGFR                    | Time Varying: HR (CI)      | 2,473,531 | 1.34<br>(1.18, 1.52)           |

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T<sub>0</sub> 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/1.73m<sup>2</sup>/year) vs. stable decline (eGFR Slope <0 to -1 ml/min/1.73m<sup>2</sup>/year)

Abbreviations: PM<sub>2.5</sub>, 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.

**Supplemental table 8:** Risk of all-cause mortality for every 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration and by PM<sub>2.5</sub> quartiles

|  | PM <sub>2.5</sub> Exposure  |                      |  |  |
|--|-----------------------------|----------------------|--|--|
| Measure  | Year 2004<br>Annual Average | Time Varying         |  |  |
| Ν  | 2,482,737                   | 2,473,531            |  |  |
| A 10 μg/m <sup>3</sup> increase in PM <sub>2.5</sub><br>HR<br>(CI) | 1.13<br>(1.07, 1.19)        | 1.24<br>(1.18, 1.31) |  |  |
| Quartile 2<br>HR (CI)  | 1.07<br>(1.04, 1.11)        | 1.07<br>(1.05, 1.10) |  |  |
| Quartile 3<br>HR (CI)  | 1.09<br>(1.06, 1.12)        | 1.08<br>(1.05, 1.11) |  |  |
| Quartile 4<br>HR (CI)  | 1.12<br>(1.09, 1.16)        | 1.13<br>(1.11, 1.16) |  |  |

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T<sub>0</sub> eGFR, body mass index, 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<sub>2.5</sub>, is the reference category for quartile measures.

Abbreviations:  $PM_{2.5}$ , particulate matter <2.5  $\mu$ m in aerodynamic diameter; N, sample size; HR, hazard ratio; CI, 95% confidence interval.

**Supplemental table 9:** Risk of hospital admission due to myocardial infarction for every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentrations:

|  | PM <sub>2.5</sub> Exposure  |                      |  |  |
|--|-----------------------------|----------------------|--|--|
| Measure  | Year 2004<br>Annual Average | Time Varying         |  |  |
| Ν  | 2,482,737                   | 2,473,531            |  |  |
| A 10 μg/m <sup>3</sup> increase in PM <sub>2.5</sub><br>HR<br>(CI) | 1.16<br>(1.01, 1.32)        | 1.25<br>(1.17, 1.46) |  |  |

Models adjusted for age, race, gender, cancer, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T<sub>0</sub> 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.

Abbreviations: PM<sub>2.5</sub>, particulate matter <2.5 µm in aerodynamic diameter; eGFR, estimated glomerular filtration rate; HR, hazard ratio; CI, 95% confidence interval.

**Supplemental table 10:** Risk of renal outcomes for every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration using informative censoring sensitivity analysis for competing risk models.

| PM <sub>2.5</sub><br>Exposure | Measure                             | Incident<br>eGFR Less<br>Than 60 <sup>+</sup> | Incident CKD*        | ≥ 30% Decline<br>in eGFR | ESRD                 |
|-------------------------------|-------------------------------------|---|----------------------|--------------------------|----------------------|
| Year 2004<br>Annual           | Ν                                   | 1,709,761                                     | 1,644,351            | 2,482,737                | 2,482,737            |
| Average                       | Censoring as a<br>Risk**<br>HR (CI) | 1.17<br>(1.11,1.24)                           | 1.19<br>(1.12, 1.27) | 1.22<br>(1.14, 1.31)     | 1.13<br>(1.07, 1.20) |
| Time Varying                  | Ν                                   | 1,702,923                                     | 1,637,643            | 2,473,531                | 2,473,531            |
|                               | Censoring as a<br>Risk**<br>HR (CI) | 1.27<br>(1.19, 1.35)                          | 1.36<br>(1.27, 1.46) | 1.34<br>(1.25, 1.44)     | 1.29<br>(1.23, 1.34) |

Models adjusted for age, race, gender, cancer, cardiovascular disease, 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, 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

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

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

Models adjusted for age, race, gender, cancer, cardiovascular disease, chronic lung disease, diabetes mellitus, hyperlipidemia, hypertension, T<sub>0</sub> 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<sub>2.5</sub>, 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 encounters<sup>1-4</sup>. 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<sup>1, 2, 5</sup>. The VA Vital Status and Beneficiary Identification Records Locator Subsystem (BIRLS) files furnished demographic characteristics and death follow-up through September 30, 2012<sup>1,2</sup>. 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 status<sup>6</sup>. 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 poverty<sup>7</sup>. Information on county level population density and population size was obtained from the 2000 Census of Population and Housing<sup>7</sup>. Latitude and longitude for ZIP code tabulation area was obtained from the 2000 Census Gazetteer File<sup>8</sup>. 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 Bureau<sup>9</sup>.

# **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 datasets<sup>10-13</sup>.

BMI was categorized into underweight (<18.50), normal weight (18.50-24.99), overweight (25.00-29.99), and obese ( $\geq$ 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 T<sub>0</sub>. Number of outpatient eGFR measurements represented the cumulative number of outpatient eGFR values from October 1, 1999 to T<sub>0</sub>. Number of hospitalizations was derived from the cumulative number of inpatient stays lasting a full day or longer from October 1, 1999 to T<sub>0</sub>. Population density and percent in poverty were assigned based on county of residence at T<sub>0</sub>.

## PM<sub>2.5</sub> exposure definition for NASA based data

We considered NASA's spaceborne satellite sensors as an additional source to capture ambient PM<sub>2.5</sub> exposure. NASA's SEDAC Global Annual PM2.5 Grids from MODIS, MISR and SeaWiFS Aerosol Optical Depth (AOD) provided the data on PM<sub>2.5</sub> estimates at the 10x10 km resolution<sup>14, 15</sup>. 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<sub>2.5</sub> grids and zip code's geographic area, resulting in surface area weighted PM<sub>2.5</sub> values for each zip code, was used to define exposure levels (as depicted in the figure below).



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

PAF was calculated using piecewise constant hazard models for disease incidence<sup>16, 17</sup>. The PAF for incidence of disease was obtained from the formula:

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

where D indicates disease, M mortality, n the number of individuals in analysis, J the number of intervals,  $a_1$ the survival time,  $\lambda_{ii}^{0}$  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<sub>2.5</sub> was 12 ug/m<sup>3</sup> for those with an exposure above 12 ug/m<sup>3</sup>, and the existing level of exposure for those at or under 12 ug/m<sup>3</sup> PAF was estimated using the annual average 2004 PM<sub>2.5</sub> data. Burden of disease, as the number of incident outcomes per year attributable to PM<sub>2.5</sub> exposure above the EPA standard of 12 ug/m<sup>3</sup>, was calculated using literature based estimates of outcome incident rates in the United States<sup>6, 18</sup> 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 assessed<sup>19</sup>. ABD was additionally calculated using a TMREL defined according to the Global Burden of Disease study methodologies<sup>20-22</sup>. This TMREL was assigned based on a uniform distribution of PM<sub>2.5</sub> from 2·4–5·9 µg/m<sup>3</sup> representing exposure values between the minimum and fifth percentiles of exposure distributions from outdoor air pollution cohort studies<sup>20-22</sup>. 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 achieve<sup>22</sup>. 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<sub>2.5</sub> quartiles<sup>23</sup> 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  $\mu$ g/m<sup>3</sup>, 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<sub>2.5</sub> 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 area<sup>24</sup>. 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)<sup>25</sup>. 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<sup>26, 27</sup>; 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<sub>2.5</sub>). 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<sub>0</sub>; 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<sub>2.5</sub> concentrations and the alternative renal outcome of rapid eGFR decline defined as eGFR slope <-5 ml/min/1.73m<sup>2</sup>/year, where odds of rapid eGFR decline was compared to stable eGFR decline (eGFR slope <0 to -1 ml/min per 1.73 m<sup>2</sup>/year) using a logistic regression model with the generalized estimating equation method to account for intra-county correlation <sup>13</sup>; g) examined the association of PM<sub>2.5</sub> 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<sub>2.5</sub> and risk of allcause mortality (as a positive control) using continuous and guartile exposure definitions; i) 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.\*)<sup>28</sup>, while additionally controlling for prior history of MI k) conducted sensitivity analyses for the competing risk of death<sup>29</sup>; I) 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  $\mu$ g/m<sup>3</sup>, 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  $\lambda_0$  is the baseline hazard,  $\beta_1$  the coefficient for PM2.5 exposure X for individual i,  $\beta_2$  the coefficient for city C (the city indicator), and  $\gamma$  the vector of coefficients for covariates Z for individual i.

For within-city models, PM<sub>2.5</sub> 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  $\lambda_0$  is the baseline hazard,  $\beta_B$  (the between city effect) the coefficient for city j's mean PM2.5 exposure

 $\bar{X}_j$ ,  $\beta_W$  (the within city effect) the coefficient for the difference between the individual i in city j's PM<sub>2.5</sub> exposure

Xij and the city j's mean PM<sub>2.5</sub> exposure  $\bar{X}_i$ , and  $\gamma$  the vector of coefficients for covariates Z for individual i.

# County Health Rankings<sup>26, 27</sup>:

County Health Rankings county level variable definitions and data sources.

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

| White   Estimates   population who are<br>Non-Hispanic White     % not proficient in<br>English   American Community<br>Survey, S-year<br>estimates   Percentage of the<br>population not<br>estimates   2008-2012     % Females   Census Population<br>Estimates   Percentage of the<br>population who are<br>ternale   2012     % Rural   Census Population<br>Estimates   Percentage of the<br>population living in a<br>rural area   2012     Drinking water<br>violations   Safe Drinking Water<br>Housing Affordability<br>Strategy   Population affected by<br>a water violation affected by<br>a water violation affected by<br>survey   FY 2012-2013     Driving alone to work   American Community<br>Survey   Percentage of<br>households with at<br>least 1 of 4 housing<br>problems   2006-2010     Driving alone to work   American Community<br>Survey   Percent opeople<br>work   2008-2012     Long commute -<br>driving alone   American Community<br>Survey   Percent of adults age<br>25-44 with some post<br>secondary education   2008-2012     Unemployment   Bureau of Labor<br>Statistics   Percent of children<br>and Poverty   Percent of children<br>to and Poverty   2012     Inadequate Social<br>Support   Small Area Income<br>and Poverty   Percent of children<br>to and Poverty   2012     Inadequate Social<br>Support   Smal Area Income<br>and Poverty  | % Non-Hispanic        | Census Population     | Percentage of the       | 2012         |
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| DentistsHRSA Area Resource<br>RileNumber of dentists<br>per 100,000<br>population2012Mental health<br>providersCMS, National<br>Provider IdentificationNumber of mental<br>health providers per<br>100,000 population2013Preventable hospital<br>staysMedicare/Dartmouth<br>InstituteDischarges for<br>ambulatory care2011   | pnysicians            | Rile                    | care physicians per          |             |
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| ProvidersProviders definitionPreventable hospitalMedicare/DartmouthDischarges for<br>ambulatory care2011   | providers             | Drovidor Identification | health providers per         | 2013        |
| Preventable hospital<br>staysMedicare/Dartmouth<br>InstituteDischarges for<br>ambulatory care2011  |                       |                         | 100 000 nonulation           |             |
| stays Institute ambulatory care  | Proventable beenital  | Medicare/Dartmouth      | Discharges for               | 2011        |
| institute ambulatory care  | stave                 | Institute               | ambulatory care              | 2011        |
| sensitive  |                       |                         | sensitive                    |             |

|                      |                         | conditions/Medicare      |           |
|----------------------|-------------------------|--------------------------|-----------|
| Diabetic monitoring  | Medicare/Dartmouth      | Percent of Diabetic      | 2011      |
| Diabetie morntoring  | Institute               | Medicare enrollees       | 2011      |
|                      | montato                 | receiving HbA1c test     |           |
| Mammography          | Medicare/Dartmouth      | Percent of female        | 2011      |
| screening            | Institute               | Medicare enrollees       |           |
| 5                    |                         | having at least 1        |           |
|                      |                         | mammogram in 2 yrs       |           |
|                      |                         | (age 67-69)              |           |
| Uninsured adults     | Small Area Health       | Percentage of the        | 2011      |
|                      | Insurance Estimates     | population ages 18 to    |           |
|                      |                         | 65 that has no health    |           |
|                      |                         | insurance coverage       |           |
| Uninsured children   | Small Area Health       | Percentage of the        | 2011      |
|                      | Insurance Estimates     | population under age     |           |
|                      |                         | 19 that has no health    |           |
|                      |                         | insurance coverage       |           |
| Health Care Costs    | Dartmouth Atlas of      | Price-adjusted           | 2011      |
|                      | Health Care             | Medicare                 |           |
|                      |                         | reimbursements (part     |           |
|                      |                         | A and B) per enrollee    |           |
| Could not see doctor | Behavioral Risk         | Percentage of the        | 2006-2012 |
| due to costs         | Factor Surveillance     | population who could     |           |
|                      | System                  | not see a doctor due     |           |
| Otherseitere         |                         | to costs                 | 0040      |
| Other primary care   | CINS, National          |                          | 2013      |
| providers            | Provider identification | primary care             |           |
|                      |                         | providers per the        |           |
|                      | Health O                |                          |           |
| Premature death      | National Center for     | Age-adjusted years of    | 2008-2010 |
|                      | Health Statistics       | potential life lost      | 2000 2010 |
|                      |                         | (YPLL) rate per          |           |
|                      |                         | 100.000                  |           |
| Poor or fair health  | Behavioral Risk         | Percent of adults that   | 2006-2012 |
|                      | Factor Surveillance     | report fair or poor      |           |
|                      | System                  | health (age-adjusted)    |           |
| Poor physical health | Behavioral Risk         | Average number of        | 2006-2012 |
| days                 | Factor Surveillance     | reported physically      |           |
|                      | System                  | unhealthy days per       |           |
|                      |                         | month                    |           |
| Poor mental health   | Behavioral Risk         | Average number of        | 2006-2012 |
| days                 | Factor Surveillance     | reported mentally        |           |
|                      | System                  | unhealthy days per       |           |
|                      |                         | month                    | 0005 0044 |
| Low birthweight      | National Center for     | Percent of births with   | 2005-2011 |
|                      |                         |                          |           |
| Diabataa             | National Cantor for     | (<2000)<br>Drovolopos of | 2010      |
| Diabeles             | Chronia Disesso         | diagnoood diabatas in    | 2010      |
|                      | Drovention and Health   |                          |           |
|                      |                         | a given county           |           |
|                      | Diabetes Translation    |                          |           |
| HIV prevalence rate  | National Center for     | Number of diagnoses      | 2010      |
|                      | HIV/AIDS. Viral         | cases of HIV in a        |           |

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

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