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# BMJ Open

## Association of short-term exposure to ambient PM2.5 with hospital admissions and 30-day readmissions in end-stage renal disease patients: population based retrospective cohort study

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2  
3 1 **Title**  
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5 2 Association of short-term exposure to ambient PM<sub>2.5</sub> with hospital admissions and 30-day  
6  
7 3 readmissions in end-stage renal disease patients: population based retrospective cohort study  
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32  
33 40 **Abstract**

34  
35 41 **Objectives:** To examine the effect of short-term exposure to ambient fine particulate matter  
36  
37 42 (PM<sub>2.5</sub>) on all-cause, cardiovascular, and respiratory related hospital admissions and  
38  
39 43 readmissions among patients receiving outpatient hemodialysis.  
40

41 44 **Design:** Retrospective cohort study.

42  
43 45 **Setting:** Inpatient hospitalization claims identified from the United States Renal Data System in  
44  
45 46 530 US counties.

46  
47 47 **Participants:** All patients receiving in-center hemodialysis between 2008 and 2014.

48  
49 48 **Primary and secondary outcome measures:** Risk of all-cause, cardiovascular, and  
50  
51 49 respiratory related hospital admissions and 30-day all-cause and cause-specific readmission  
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53 50 following an all-cause, cardiovascular, and respiratory related discharges. Readmission risk was  
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3 51 evaluated for early (1-7 days post-discharge) and late (8-30 days post-discharge) readmission  
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5 52 time-periods. Relative risk is expressed per 10  $\mu\text{g}/\text{m}^3$  of  $\text{PM}_{2.5}$ .  
6

7 53 **Results:** Same day ambient  $\text{PM}_{2.5}$  was associated with increased hospital admission risk for  
8  
9 54 cardiovascular causes (0.8%, 95%CI: [0.1, 1.5]). Greater  $\text{PM}_{2.5}$ -related associations were  
10  
11 55 observed with 30-day readmission risk. All-cause readmission risk associated with  $\text{PM}_{2.5}$  was  
12  
13 56 greater for early-readmissions compared to late-readmissions. Early-readmission risk was  
14  
15 57 increased by 1.4-1.7% following all-cause (1.4%, [0.5, 2.4]), cardiovascular (1.7%, [0.4, 3.1]),  
16  
17 58 and respiratory (1.6%, [0.2, 3.1]) discharges; while late-readmission risk increased by 0.3%  
18  
19 59 following all-cause and cardiovascular discharges.  $\text{PM}_{2.5}$ -related associations with readmission  
20  
21 60 risk were greatest for certain cause-specific readmissions ranging 1.8-7.6% for dysrhythmia and  
22  
23 61 conduction disorder, heart failure, COPD, other non-cardiac chest pain or respiratory syndrome,  
24  
25 62 and pneumonia. Following all-cause discharges, the cause-specific early-readmission risk was  
26  
27 63 increased by 6.1% (3.2, 9.2) for pneumonia, 4.6% (2.1, 7.1) for dysrhythmia and conduction  
28  
29 64 disorder, 3.6% (1.3, 5.9) for heart failure, and 2.7% (1.1, 4.2) for other non-cardiac chest pain or  
30  
31 65 respiratory syndrome related causes.  
32  
33

34 66 **Conclusions:** Daily ambient  $\text{PM}_{2.5}$  was associated with an increased risk of cardiovascular  
35  
36 67 admissions and 30-day readmissions following cardiopulmonary-related discharges in a  
37  
38 68 vulnerable ESRD population. In the first week following discharge, greater  $\text{PM}_{2.5}$ -related risk of  
39  
40 69 rehospitalization was identified for some diagnoses.  
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#### 45 71 **Strengths and limitations of this study**

- 46 72 • Hospitalization records for patients undergoing in-center hemodialysis between 2008  
47  
48 73 and 2014 were identified using the US Renal Data System (> 1.8 million inpatient  
49  
50 74 admissions).
- 51 75 • Fine resolution daily air pollution was linked to the location of the last dialysis visit.  
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3 76 • The time-stratified design in the admissions analysis reduced the potential confounding  
4  
5 77 by factors that vary slowly with time and those that are time-invariant.  
6  
7 78 • Using time-dependent risk factors in the Cox proportional hazard model allowed for  
8  
9 79 readmission risk estimates to reflect the risk associated with daily fluctuations in ambient  
10  
11 80 PM<sub>2.5</sub> and time-varying confounders.  
12  
13  
14 81 • This study uses ambient air quality near dialysis centers to estimate individual exposure  
15  
16 82 and diagnosis codes to classify cause-specific hospitalizations, which could contribute to  
17  
18 83 exposure and diagnosis misclassification.  
19  
20 84

## 85 Introduction

86 Ambient fine particulate matter (PM<sub>2.5</sub>) is a leading risk factor for all-cause mortality<sup>1-4</sup>,  
87 accounting for millions of premature deaths each year<sup>5</sup>. Daily variation in ambient PM<sub>2.5</sub> is also  
88 associated with increased rates of unplanned hospital admissions, urgent care visits, and  
89 medication usage<sup>6,7</sup>. Greater health impacts have been observed consistently in sensitive  
90 populations, including the elderly and individuals with chronic health conditions<sup>3,8-10</sup>; however,  
91 few studies to our knowledge have examined PM<sub>2.5</sub>-related health impacts on specific chronic  
92 health conditions, such as individuals living with chronic kidney disease (CKD).

94 CKD is a progressive condition that affects 8 to 16% of the population worldwide<sup>11-13</sup>, and in the  
95 final stage, end-stage renal disease (ESRD), many patients are transitioned to hemodialysis to  
96 prolong life. Patients receiving dialysis represent a particularly vulnerable population because of  
97 high rates of co-morbidities, including diabetes and cardiovascular disease, which may  
98 contribute to the greater likelihood of hospital admission and readmission following PM  
99 exposure. In the US, patients on hemodialysis average 1.7 inpatient admissions annually with a  
100 30-day readmission rate twice that of other Medicare beneficiaries<sup>14</sup>, contributing to a  
101 substantial economic impact<sup>15</sup>. In 2016, \$35.4 billion in Medicare fee-for-service costs were  
102 attributed to ESRD<sup>14</sup>, motivating health promotion and cost-containment efforts to slow the  
103 progression of CKD and reduce hospitalizations and readmissions<sup>16</sup>. While many current  
104 strategies to reduce hospitalizations focus on care processes and patient-level factors<sup>17-20</sup>,  
105 there is a knowledge gap on the role of modifiable environmental risk factors - specifically  
106 ambient PM<sub>2.5</sub><sup>2,21-23</sup>.

108 In this study, we examined the risk of daily hospitalization and subsequent 30-day readmission  
109 in relation to daily ambient PM<sub>2.5</sub> using data from the US Renal Data System (USRDS) over a 7-  
110 year period. We focused on all-cause, cardiovascular, and respiratory hospitalizations and



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3 111 estimated changes in risk for early (1 to 7 days post-discharge) and late (8 to 30 days post-  
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5 112 discharge) readmission accounting for the influence of different causal factors (i.e. acute and  
6  
7 113 chronic illness burden) that may influence early versus late-readmissions<sup>24 25</sup>.  
8  
9  
10 114

## 11 115 **Methods**

### 12 116 **Setting and study population**

13  
14 117 Using patient level data from the USRDS, we constructed an open cohort of individuals  
15  
16 118 receiving in-center hemodialysis between 2008 and 2014. USRDS is a national data registry for  
17  
18 119 dialysis services and includes records of patient demographic characteristics, hospitalizations,  
19  
20 120 and provider information on all patients receiving hemodialysis. Baseline demographic  
21  
22 121 characteristics (sex, birth date, race, and smoking status) recorded at the initiation of dialysis  
23  
24 122 were extracted from the Medical Evidence Form CMS-2728 for each patient. For every inpatient  
25  
26 123 hospital visit, we extracted the admission date, discharge date, discharge diagnoses codes, and  
27  
28 124 discharge status.  
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33 125  
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35 126 For the analysis of 30-day readmission risk, we considered only admissions where patients  
36  
37 127 were discharged alive. Each readmission was counted once as a readmission relative to the  
38  
39 128 prior index admissions and was then considered as a new index admission. Thus, each  
40  
41 129 admission could serve as both an index admission and readmission, consistent with previous  
42  
43 130 studies<sup>26</sup>. An admission that occurred on the same day as a discharge was combined with the  
44  
45 131 previous admission. These readmissions are likely to represent facility transfers for which we  
46  
47 132 were not able to obtain information. Admissions occurring within 30 days of the end of the study  
48  
49 133 period were excluded, as 30 days of follow-up data were not available. For both admissions and  
50  
51 134 readmissions, patients could be represented more than once if they were admitted multiple  
52  
53 135 times during the study period.  
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3 137 Health outcomes  
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5 138 The primary outcomes included daily counts of all-cause, respiratory, and cardiovascular-related  
6  
7 139 admissions and the time to readmission following the cause-specific discharges. All-cause and  
8  
9 140 cause-specific readmissions were examined separately. Readmissions were classified further  
10  
11 141 as early-readmissions, occurring within 1 to 7 days of an index hospitalization discharge, and  
12  
13 142 late-readmissions, occurring 8 to 30 days post-discharge.  
14  
15

16 143  
17  
18 144 International Classification of Diseases, 9<sup>th</sup> Revision (ICD-9) codes were used to identify cause-  
19  
20 145 specific hospitalizations. Cardiovascular-related diagnoses included hypertension (ICD-9 codes  
21  
22 146 401-405), myocardial infarction (410), ischemic heart disease (410-411, 413), pulmonary  
23  
24 147 embolism (415), dysrhythmia and conduction disorder (426-427), heart failure (428), and  
25  
26 148 peripheral arterial disease (444). Respiratory-related diagnoses included asthma (493), chronic  
27  
28 149 obstructive pulmonary disease (491-492, 496), pneumonia (480-486), and other non-cardiac  
29  
30 150 chest pain or respiratory syndrome (786).  
31  
32

33 151

34  
35 152 Environmental data  
36

37 153 Daily concentrations of fine particulate matter (PM<sub>2.5</sub>) were estimated using a previously  
38  
39 154 described exposure prediction model<sup>27 28</sup>. Briefly, this model estimates daily PM<sub>2.5</sub> on a 1 km  
40  
41 155 grid for the entire continental US by incorporating satellite aerosol optical depth measurements,  
42  
43 156 chemical transport model simulations, meteorology, land-use, and other variables. Gridded  
44  
45 157 PM<sub>2.5</sub> estimates were subsequently converted to population-weighted county-level estimates  
46  
47 158 using 2010 Census tract population values. To enable adjustment for potential confounding by  
48  
49 159 weather conditions, temperature and relative humidity data were obtained from the National  
50  
51 160 Centers for Environmental Information's Global Historical Climatology Network (Global Surface  
52  
53 161 Summary of the Day)<sup>29</sup> and using the Community Multiscale Air Quality model, respectively.  
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162 The study area was restricted to all counties containing at least one land surface station from  
163 the Global Historical Climatology Network (n = 530).

164  
165 Daily PM<sub>2.5</sub> was linked to patient hospitalizations based on the county of their last dialysis visit.  
166 Previous work has shown that patients in the USRDS cohort that receive in-center dialysis three  
167 times a week have a median travel distance of 5.7 miles to their initial dialysis center <sup>30 31</sup>.

168  
169 Study design and statistical analysis

170 *Daily county hospital admissions.* The relative risks of hospital admissions associated with daily  
171 PM<sub>2.5</sub> were estimated using a case-crossover design with conditional Poisson models for each  
172 of the three health outcomes separately (all-cause, cardiovascular, respiratory). Aggregated  
173 counts of daily admissions were time stratified by county-day, where each county served as its  
174 own control. For each county-day strata, PM<sub>2.5</sub> on the day of admission was compared with  
175 PM<sub>2.5</sub> concentrations on control days. Control days were defined as occurring on the same day  
176 of the week in the same month and year. This, by design, enabled us to control for differences  
177 in county characteristics, such as population size and risk characteristics, and the influence of  
178 day of the week, seasonal, and long-term time trends <sup>32</sup>.

179  
180 The relative risk of hospital admissions related to daily PM<sub>2.5</sub> for each health outcome was  
181 estimated using daily counts with respect to county-time strata, adjusted for meteorological  
182 conditions (temperature and humidity). Temperature and humidity effects were averaged over  
183 lag days 0, 1, and 2 and modeled using natural splines (df = 3) to allow for non-linear effects <sup>33</sup>.

184  
185 We evaluated immediate (same day) and delayed PM<sub>2.5</sub> effects on all-cause and cause-specific  
186 hospital admissions. Unconstrained distributed lag models were used to assess the delayed  
187 effects of short-term exposures to PM<sub>2.5</sub>. Delayed exposure up to 14 days were considered.

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5 189 *Early and late readmissions occurring within 30 days of discharge.* Cox proportional hazards  
6  
7 190 models were used to assess the relative risk of early (1 to 7 days post-discharge) and late (8 to  
8  
9 191 30 days post-discharge) readmission associated with daily PM<sub>2.5</sub> following all-cause and cause-  
10  
11 192 specific index hospitalizations. Early-readmission models were censored at 7 days and late-  
12  
13 193 readmission models at 30 days.

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18 195 Models for readmissions incorporated both time-dependent and time-independent risk factors.  
19  
20 196 Time-dependent variables included daily PM<sub>2.5</sub>, daily temperature, daily relative humidity, and  
21  
22 197 day-of-the-week. Time-independent factors included patient-specific and hospitalization event-  
23  
24 198 specific variables. Patient-specific variables included indicator of sex, race, baseline smoking  
25  
26 199 status, whether the patient had three or more previous hospital visits in the year prior, and age  
27  
28 200 at discharge. Event-specific variables included whether the discharge occurred on a holiday and  
29  
30 201 length of stay. Lastly, models were adjusted for patient-specific clusters to account for repeated  
31  
32 202 measures by individual.

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35 203  
36  
37 204 Daily county admission and readmission risks were expressed as the rate ratio (RR) per 10-  
38  
39 205 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>. The proportion hospital admissions and readmissions associated with  
40  
41 206 PM<sub>2.5</sub> is reported as the attributable fraction (AF), where  $AF = (RR-1) / RR$  <sup>34</sup>. All statistical  
42  
43 207 analyses were performed with R software (version 3.6.0) <sup>35</sup>.

44  
45 208

## 46 47 209 **Results**

48  
49 210 Characterization of clinical cohort and daily PM<sub>2.5</sub>

50  
51 211 Among 361,568 patients who were hospitalized during the study period, 10,274 were excluded  
52  
53 212 due to missing baseline demographic values, with 351,294 patients remaining. Demographic  
54  
55 213 descriptions are in Table 1. Patients had on average 2.97 hospital visits in the year prior to an

214 admission and more than 70% of patients had at least one hospital admission related to  
215 cardiovascular and respiratory causes (Table 2). The average daily county-level PM<sub>2.5</sub>  
216 concentration was 9.3 µg/m<sup>3</sup> (range: 0.05 to 155.16 µg/m<sup>3</sup>) (Table S1).

217

218 Description of clinical events, hospital admissions, and readmissions

219 In total, there were 1,801,966 hospital admissions, of which 1,493,795 recorded the patient as  
220 alive at discharge. Of admissions that were discharged alive, 11.9% were readmitted within 7  
221 days and 21.4% were readmitted 8 to 30 days post-discharge. The mean length of stay for all-  
222 cause, cardiovascular, and respiratory admissions was 7.0, 7.0, and 7.1 days, respectively  
223 (Table 2).

224

225 Associations between PM<sub>2.5</sub> and readmission

226 *Early-readmission.* Daily PM<sub>2.5</sub> was positively associated with increased risk for early-  
227 readmission following all-cause, cardiovascular, and respiratory related discharges. Same day  
228 (lag 0) PM<sub>2.5</sub> was associated with a 1.4% (95%CI: 0.5, 2.4), 1.7% (95%CI: 0.4, 3.1), and 1.6%  
229 (95%CI: 0.2, 3.1) increased risk of an early-readmission for any cause following all-cause,  
230 cardiovascular, and respiratory related discharges, respectively (Figure 1, Table S3).

231

232 PM<sub>2.5</sub> associated early-readmission risk was greater for certain cause-specific outcomes.

233 Following all-cause discharges, same day (lag 0) PM<sub>2.5</sub> was associated with increased early-  
234 readmission risk for dysrhythmia and conduction disorder (4.6% [2.1, 7.1]), heart failure (3.6%  
235 [1.3, 5.9]), pneumonia 6.1% [3.2, 9.2]), and other non-cardiac chest pain or respiratory  
236 syndrome (2.7% [1.1, 4.2]) causes. PM<sub>2.5</sub> associated early-readmission risk was greatest for  
237 pneumonia related readmissions following cardiovascular related discharges (7.6% [3.6, 11.7]).

238 Other cause-specific early-readmission risks following cardiovascular and respiratory related

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3 239 discharges were similar to estimates observed following discharge for any cause (Figure 2,  
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5 240 Table S4).

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9 242 An average AF at 10  $\mu\text{g}/\text{m}^3$  of  $\text{PM}_{2.5}$  at lag 0 was 1.4% (95%CI: 0.5, 2.4), 1.7% (95%CI: 0.3,  
10  
11 243 3.0), and 1.6% (95%CI: 0.2, 3.0) for an early-readmission following all-cause, cardiovascular,  
12  
13 244 and respiratory discharges, respectively (Figure 1). County AF ranged 0.5% to 2.3%, 0.6% to  
14  
15 245 2.7%, and 0.5% to 2.6% for an early-readmission following all-cause, cardiovascular, and  
16  
17 246 respiratory related discharges, respectively (Figure 2).

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22 248 *Late-readmission.* Daily  $\text{PM}_{2.5}$  was also associated with increased risk of late-readmission  
23  
24 249 following all-cause, cardiovascular, and respiratory related discharges, though the magnitude of  
25  
26 250 risk related to all-cause readmissions was smaller than that observed with early-readmission.  
27  
28 251 Same day  $\text{PM}_{2.5}$  was associated with a 0.3% (95%CI: 0.1, 0.5) and 0.3% (95%CI: 0.1, 0.6)  
29  
30 252 increased risk of a late all-cause readmission following all-cause and cardiovascular related  
31  
32 253 discharges, respectively (Figure 1, Table S3).

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36 255 Similar to observations made for early-readmissions,  $\text{PM}_{2.5}$  associated late-readmission risk was  
37  
38 256 greater for certain cause-specific outcomes. Following all-cause discharges, a 10  $\mu\text{g}/\text{m}^3$   
39  
40 257 increase in same day (lag 0)  $\text{PM}_{2.5}$  was associated with increased late-readmission risk for  
41  
42 258 dysrhythmia and conduction disorder (2.5% [1.5, 3.6]), heart failure (3.7% [2.7, 4.7]), COPD  
43  
44 259 (2.2% [0.4, 3.9]), pneumonia (4.6% [3.3, 5.8]), and other non-cardiac chest pain or respiratory  
45  
46 260 syndrome (3.5% [2.9, 4.1]). Other cause-specific early-readmission risks following  
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48 261 cardiovascular and respiratory related discharges were similar to estimates observed following  
49  
50 262 discharge for any cause (Figure 2, Table S4).

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3 264 The average AF at 10  $\mu\text{g}/\text{m}^3$  was 0.3% (95%CI: 0.1, 0.5) and 0.3% (95%CI: 0.1, 0.6) for a late-  
4  
5 265 readmission following all-cause and cardiovascular discharges, respectively (Figure 1). County  
6  
7 266 AF ranged 0.1% to 0.5% for a late-readmission following any cause (data not shown).  
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10 267

#### 11 268 Associations between $\text{PM}_{2.5}$ and daily admissions

12  
13  
14 269 Same day  $\text{PM}_{2.5}$  was associated with an increase in rate ratio of 0.3% (95%CI: -0.2, 0.9) for all-  
15  
16 270 cause admissions and 0.9% (95%CI: 0.2, 1.7) for cardiovascular admissions (Figure S2, Table  
17  
18 271 S2). We estimated 0.9% (95%CI: 0.1, 1.7) of cardiovascular admissions could be attributed to  
19  
20 272 10  $\mu\text{g}/\text{m}^3$  ambient  $\text{PM}_{2.5}$  (Figure 3). Across counties, exposures accounted for 0.3% to 1.5% of  
21  
22 273 cardiovascular admissions when evaluated at the average daily  $\text{PM}_{2.5}$  for each county (data not  
23  
24 274 shown).  
25  
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27 275

28  
29 276 No change in risk of all-cause and cardiovascular admissions was observed related to prior  
30  
31 277 exposure (lags 1-14). Similarly, no change in risk for respiratory admissions was observed with  
32  
33 278 same day exposure (lag 0) or prior exposure (lags 1-14) (Figure S2, Table S2).  
34  
35 279

## 36 37 280 Discussion

38  
39 281 In a nationwide cohort study of 351,294 patients with ESRD managed with hemodialysis, we  
40  
41 282 evaluated the association between 1.8 million inpatient admissions and nearly 0.5 million  
42  
43 283 corresponding 30-day readmissions and the variation in daily ambient  $\text{PM}_{2.5}$  in the US over 7  
44  
45 284 years, 2008-2014. Daily variation in  $\text{PM}_{2.5}$  was associated with increased risk of hospital  
46  
47 285 admission and even greater risk of rehospitalization. We found that the rehospitalization risk  
48  
49 286 related to readmission for any cause was 4.7-8.0 times greater for readmission in the first week  
50  
51 287 following discharge, compared to late-readmissions (8-30d after discharge). Following all-cause,  
52  
53 288 cardiovascular, and respiratory related discharges, the early-readmission risk for any cause was  
54  
55 289 increased by 1.4, 1.7, 1.6%, respectively per 10  $\mu\text{g}/\text{m}^3$  increase in daily  $\text{PM}_{2.5}$ . Importantly,  
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3 290 readmissions related to some cardiorespiratory diagnoses had the greatest PM<sub>2.5</sub> attributed  
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5 291 readmission risk that was observed to be elevated for both early and late-readmissions. The  
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7 292 early-readmission risk following all-cause discharges, was increased by 6.1%, 4.6%, and 3.6%  
8  
9 293 for pneumonia, dysrhythmia and conduction disorder, and heart failure related readmissions,  
10  
11 294 respectively. Most notably for readmissions related to pneumonia and dysrhythmia, the early-  
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13 295 readmission risk attributed to PM<sub>2.5</sub> was nearly twice as large as the late-readmission risk.  
14  
15 296 Overall, these results suggest that at 10 µg/m<sup>3</sup>, 1.4-1.7% of early-readmissions for any cause  
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17 297 were attributable to short-term exposure. In the context of the daily PM<sub>2.5</sub> National Ambient Air  
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19 298 Quality Standard (35 µg/m<sup>3</sup>), this attributable fraction would be 5-6%.  
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24 300 Our findings are consistent with previous studies that observed increased admission risks in  
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26 301 elderly populations <sup>6 9 36-40</sup> and patients with cardiovascular health complications <sup>7 41</sup>, and  
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28 302 increased readmission risk following cardiovascular related admissions <sup>7 41 42</sup>. Studies in the  
29  
30 303 Medicare population similarly observed a 1-2% increase in cardiovascular hospital admissions  
31  
32 304 associated with same-day PM<sub>2.5</sub> concentrations <sup>6 9 36 38</sup>. Risk appears to vary by diagnosis, as  
33  
34 305 the increased risk was slightly less (0.13%) for ST-elevation myocardial infarction related  
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36 306 admissions in a Chinese population <sup>7</sup> and greater (29%) for incident heart failure admissions in  
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38 307 an Australian population <sup>41</sup>. Increases in respiratory admissions (1-2%) have been noted in the  
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40 308 Medicare population <sup>6 9 36-38</sup>, but were not observed in this study. Prior studies provide evidence  
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42 309 that air pollution exposure is associated with adverse health outcomes including increased  
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44 310 infection rates, acute lung edema, and elevated concentrations of systematic inflammation  
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46 311 markers <sup>43-45</sup>. Despite known associations between PM exposure and adverse cardiovascular  
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48 312 and respiratory health outcomes, previous studies have not evaluated the impacts on hospital  
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50 313 readmissions among individuals with ESRD.  
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3 315 Few studies have examined PM<sub>2.5</sub>-related effects on readmissions, and those that have report  
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5 316 on the long-term (>1yr) risk following cardiovascular related admissions. Following  
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7 317 cardiovascular hospitalization, PM<sub>2.5</sub>-related rehospitalization risks were greater for cardiac  
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9 318 readmissions compared to our observations of all-cause readmissions (1.3-2.6% vs 0.3%)<sup>7 42</sup>.  
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11 319 Additionally, one study in an Australian population with very low ambient air pollution  
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13 320 concentrations (mean PM<sub>2.5</sub> = 2.9 µg/m<sup>3</sup>) found no relationship between PM<sub>2.5</sub> and the all-cause  
14  
15 321 readmissions after an incident heart failure hospitalization<sup>41</sup>. Short-term readmission risks were  
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17 322 greater in comparison to the long-term readmission risks, suggesting the week following a  
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19 323 discharge to be a window of heightened vulnerability. Prior work indicates that factors related to  
20  
21 324 index hospitalizations and acute illness burden were predictive of an early-readmission<sup>24 25</sup>.  
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24 325 This may indicate that hospital readmissions related to acute illness burdens may be more  
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26 326 susceptible to PM<sub>2.5</sub> exposure.  
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31 328 Our study contributes to the currently limited literature on the association between air pollution  
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33 329 and health impacts among hemodialysis patients and shines a light on the vulnerability in this  
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35 330 clinical population related to ambient airborne particulate matter. The 30-day rehospitalization  
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37 331 rate is 35% in this population, which is twice that of older Medicare beneficiaries without a  
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39 332 kidney disease diagnosis<sup>14</sup>. As many as 70% of readmissions are thought to be unnecessary<sup>46</sup>,  
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41 333 prompting efforts to improve outcomes. Economic healthcare costs associated with short-term  
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43 334 increases in PM<sub>2.5</sub> are considerable; annual inpatient and post-acute care costs related to a 10  
44  
45 335 µg/m<sup>3</sup> in daily PM<sub>2.5</sub> ranges \$30-70 million for cardiovascular and respiratory related diseases<sup>47</sup>.  
46  
47 336 PM<sub>2.5</sub> is a modifiable risk factor and reductions in short-term exposures could contribute to  
48  
49 337 reduced healthcare costs. Our findings suggest that short-term increases in PM<sub>2.5</sub> contribute to  
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51 338 healthcare usage through unplanned admissions and readmissions.  
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56 340 Strengths and Limitations  
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3 341 This study included a nearly complete cohort of US patients undergoing in-center hemodialysis.  
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5 342 To our knowledge this is the largest analysis of short-term exposure to air pollution in the US in  
6  
7 343 this highly vulnerable population. The USRDS registry provides a complete registry of all  
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9 344 hospitalizations and contains detailed information regarding demographics, dialysis,  
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11 345 hospitalization, rehospitalization, and co-morbid conditions. Secondly, ambient PM<sub>2.5</sub> was  
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13 346 estimated using a prediction model with highly resolved spatial and temporal resolution with  
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15 347 proven accuracy<sup>27 28</sup>. Thirdly, the time-stratified design allowed for county matching that  
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17 348 reduced the potential confounding by factors that very slowly with time and those that are time-  
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19 349 invariant. Fourthly, the use of time-dependent risk factors in the Cox proportional hazard model  
20  
21 350 allowed for readmission risk estimates to reflect the risk associated with daily fluctuations in  
22  
23 351 ambient PM<sub>2.5</sub> and time-varying confounders.  
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28 352  
29 353 This study also had some limitations. Firstly, there was the potential for exposure  
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31 354 misclassification as the location of the last dialysis visit was used to estimate individual level  
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33 355 exposures. PM<sub>2.5</sub> around dialysis centers could differ from concentrations around hospitals and  
34  
35 356 patient residences. However, given that patients generally reside less than 6 miles from their  
36  
37 357 initial dialysis center, differences in temporal variation of exposure should be small and not likely  
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39 358 to contribute a systematic bias favoring an association between ambient PM<sub>2.5</sub> and clinical  
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41 359 events<sup>30 31</sup>. Secondly, diagnosis misclassification was possible but was not likely to confound  
42  
43 360 the relationship because it is not likely to vary on the same temporal scale as PM<sub>2.5</sub>. Thirdly,  
44  
45 361 there is the possibility that some unmeasured time variant factors may have confounded our  
46  
47 362 estimates (smoking status, medication usage, behaviors). Data availability restricted the  
48  
49 363 consideration of some patient level confounders, such as smoking status, to values recorded at  
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51 364 baseline. Lastly, generalization of the results is limited to the Medicare population with ESRD  
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53 365 managed with hemodialysis treatments. Future studies are needed to understand PM<sub>2.5</sub>-related  
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3 366 impacts on specific health conditions, and if health impacts vary based on race, socioeconomic  
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5 367 indicators, or other individual and population factors.  
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7 368

9 369 **Conclusion**

11 370 In conclusion, this United States wide cohort study identified increased risk in patients receiving

13 371 in-center hemodialysis associated with short-term increases in ambient air particle pollution.

15 372 Elevated PM<sub>2.5</sub> concentrations were found to be associated with increased inpatient hospital

17 373 admissions related to cardiovascular causes, and an increased likelihood of hospital

19 374 readmission following cardiovascular and respiratory related hospitalizations. Medicare

21 375 spending for beneficiaries with ESRD is high. Traditional efforts to reduce the burden of disease

23 376 focus on patient factors; however, these data suggest that air particle pollution is a factor that

25 377 contributes to increased risks for hospital admission and subsequent readmission. To reduce

27 378 PM<sub>2.5</sub>-related morbidities, we echo the recommendations made in the Million Hearts initiative,

29 379 that healthcare systems, insurers, physicians, and health care professionals should

31 380 incorporate health risks related to ambient PM into patient care.  
32

33 381

35 382 **Disclaimer**

37 383 The research described in this article has been reviewed by the Center for Public Health and the

39 384 Environment, U.S. Environmental Protection Agency, and approved for publication. Approval

41 385 does not signify that the contents necessarily reflect the views and policies of the Agency, nor

43 386 does the mention of trade names of commercial products constitute endorsement or

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3 392 Schwartz and Qian Di. The interpretation and reporting of these data are the responsibility of the  
4  
5 393 author(s) and in no way should be seen as an official policy or interpretation of the U.S.  
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7 394 government.  
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### 11 396 **Contributors**

13 397 LHW, AGR conceived and designed the study. TJW, WEC, and AVK provided subject expert  
14  
15 398 input into the study design and interpretation of evidence. AVK, QD, and CWC provided access  
16  
17 399 to the data for the study; LHW managed and analyzed the data and AGR oversaw the analysis.  
18  
19 400 LHW and AGR wrote the first draft of the manuscript. LHW, YX, AVK, CWC, TJW, WEC, and  
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21 401 AGR critically contributed to the manuscript and approved the final draft. LHW and AGR are the  
22  
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41 409

### 43 410 **Competing Interests**

45 411 All authors have completed the ICMJE uniform disclosure form at  
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53 415 appear to have influenced the submitted work.  
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3 417 **Ethical approval**  
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5 418 This study was reviewed by the institutional review board at the University of North Carolina at  
6  
7 419 Chapel Hill and determined to be exempt based on the study design involving secondary data  
8  
9 420 analysis.  
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14 422 **Data sharing**

15  
16 423 Data access to USRDS data sets is through an internal data use agreement with the University  
17  
18 424 of North Carolina at Chapel Hill's Cecil G. Sheps Center. PM<sub>2.5</sub> data was obtained through  
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21  
22 426 (Tsinghua University). For general data sharing inquiries, contact [rappold.ana@epa.gov](mailto:rappold.ana@epa.gov) or  
23  
24 427 [wyatt.lauren@epa.gov](mailto:wyatt.lauren@epa.gov).  
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27  
28 429 **Transparency**

29  
30 430 The lead and corresponding authors (LHW and AGR) affirm that the manuscript is an honest,  
31  
32 431 accurate, and transparent account of the study being reported; that no important aspects of the  
33  
34 432 study have been omitted; and that any discrepancies from the study as planned (and, if  
35  
36 433 relevant, registered) have been explained.  
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41 435 **Patient and Public Involvement**

42  
43 436 This study utilized a deidentified database, thus contact with patients was not possible.  
44

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49 439 I Ana G Rappold The Corresponding Author of this article contained within the original  
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32 457 of my co-authors are.\*

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601 **Table 1.** Baseline Demographic Characteristics of the Study Population Between 2008 and  
 602 2014 by Hospital Admission Category.

Characteristic	No. (%)		
	All-cause N = 351,294	Cardiovascular n = 262,385	Respiratory n = 247,829
Age (yr), mean (SD)	64.69 (14.70)	65.58 (14.53)	65.61 (14.48)
Male sex (%)	190,716 (54.3)	140,206 (53.4)	132,288 (53.4)
Race			
White	209,921 (59.8)	155,405 (59.2)	147,204 (59.4)
Black	122,943 (35.0)	93,325 (35.6)	87,831 (35.4)
Other	18,430 (5.2)	13,655 (5.2)	12,794 (5.2)
Smoking status at initiation (no)	330,837 (94.2)	246,634 (94.0)	232,396 (93.8)

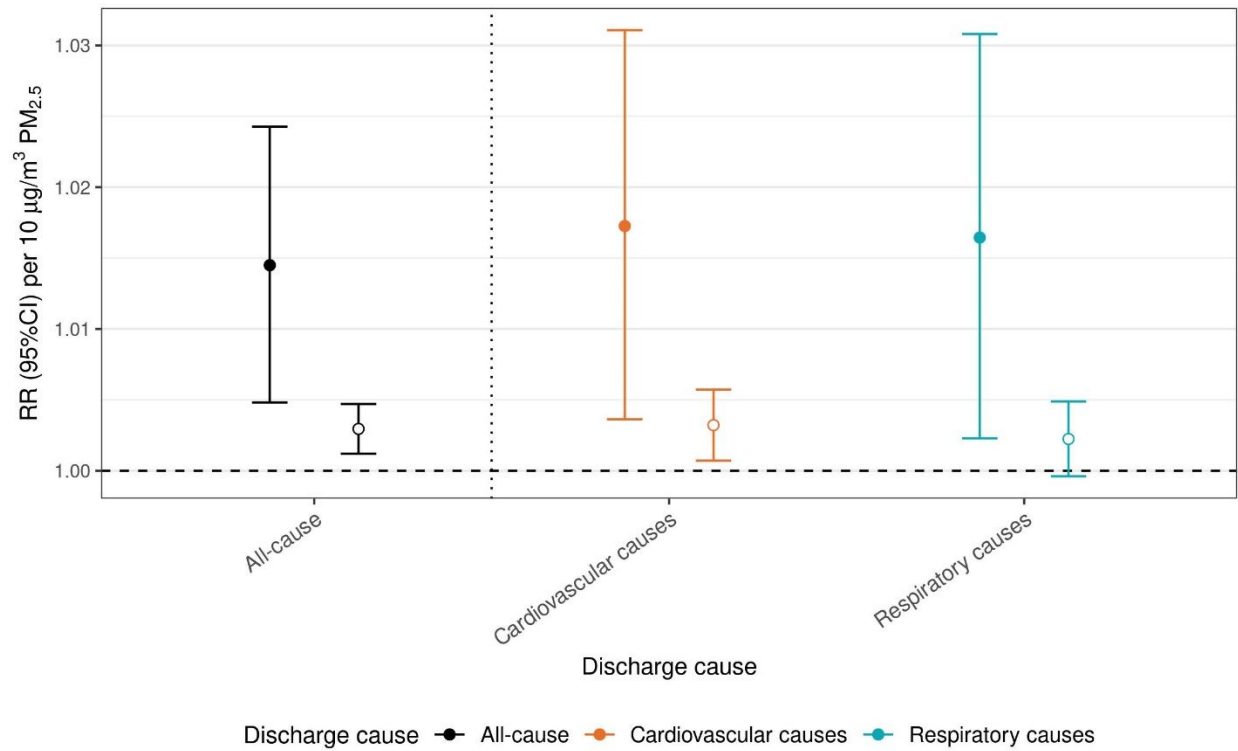
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604 **Table 2.** Hospital Admission Characteristics Among the Study Population Between 2008 and  
605 2014.

Outcome	Number of Events (Number of Unique Patients)		
	All-cause	Cardiovascular	Respiratory
Admissions	1,801,966 (351,294)	832,255 (262,385)	766,447 (247,829)
Discharged alive	1,493,795 (312,521)	685,680 (229,780)	637,250 (217,221)
Early-readmission (1-7d)	177,552 (91,944)	83,533 (52,622)	78,723 (49,576)
Late-readmission (8-30d)	319,058 (130,935)	150,576 (81,149)	142,139 (76,722)
Length of stay, d			
Mean (SD)	6.98 (10.68)	7.05 (10.34)	7.07 (10.38)
Median (IQR)	4 (2-7)	4 (2-8)	4 (2-8)
Hospital visits in prior year			
3+ visits	637,503 (123,949)	307,891 (93,399)	292,803 (89,905)
Mean (SD)	2.97 (3.80)	3.14 (3.95)	3.21 (3.89)
Median (IQR)	2 (1-4)	2 (1-4)	2 (1-4)

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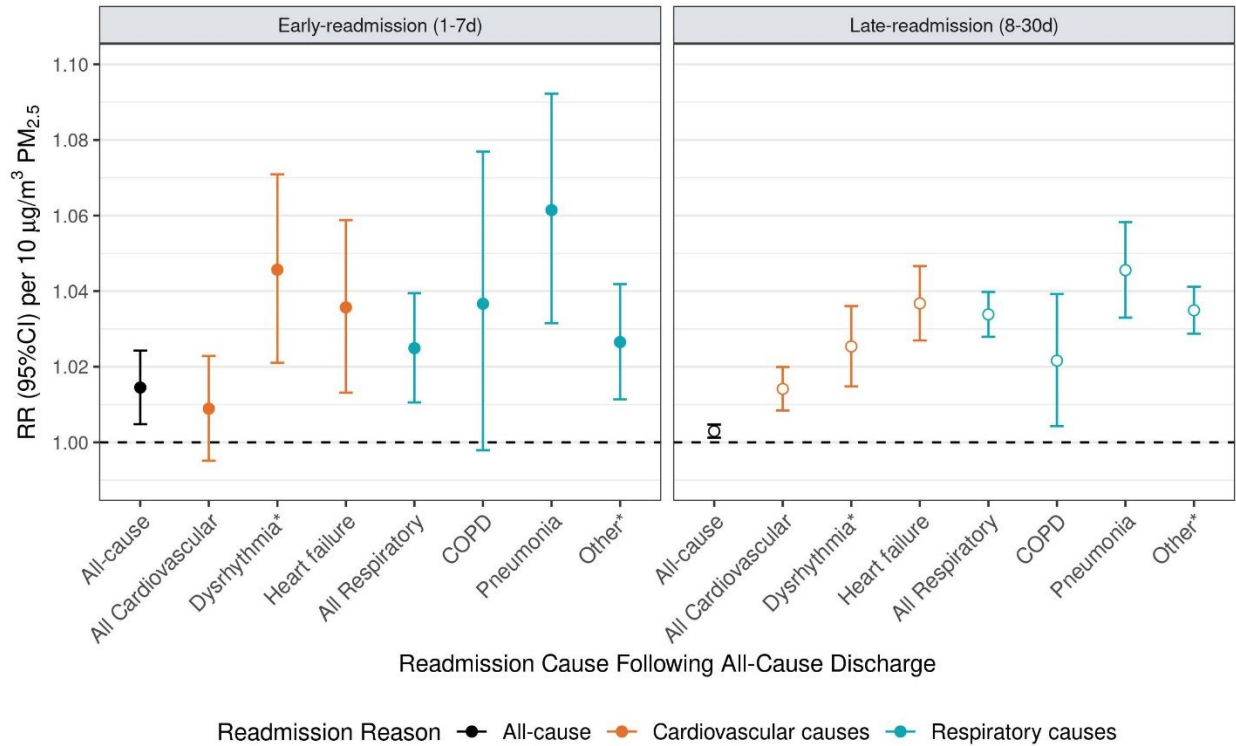
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609 **Figure 1.** The relative risk (RR, 95%CI) for an all-cause early and late-readmission following all-  
 610 cause and cause-specific discharges. Discharges are color coded: all-cause discharges are  
 611 indicated in black, cardiovascular causes in orange, and respiratory causes in blue. Early-  
 612 readmissions are indicated with filled in circles, late-readmissions with open circles. RR is  
 613 expressed per 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ .

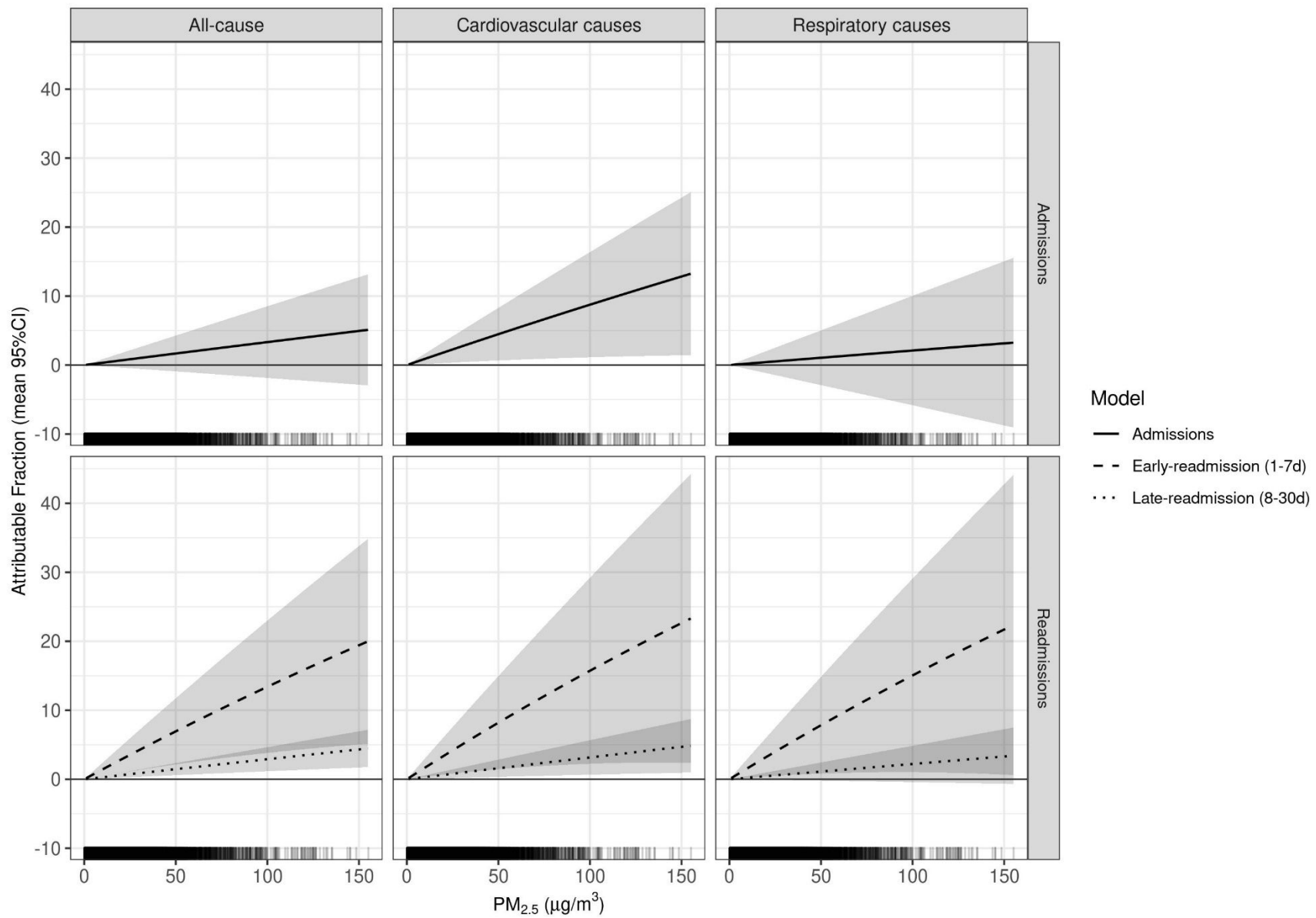
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**Figure 2.** The relative risk (RR, 95%CI) of cause-specific early and late-readmission following all-cause discharge. Readmission causes are color coded: all-cause readmissions are indicated in black, cardiovascular causes in orange, and respiratory causes in blue. RR is expressed per 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>.

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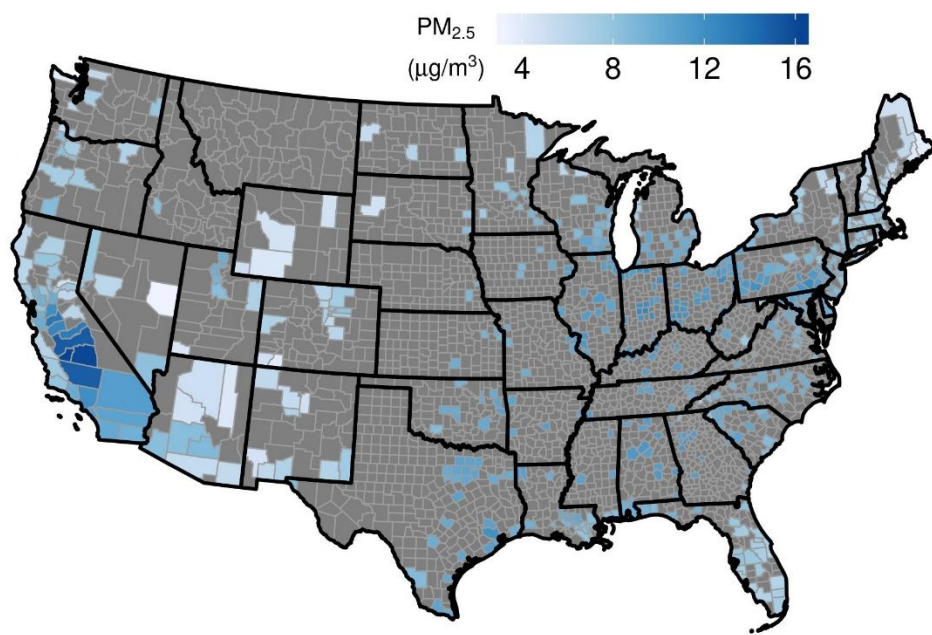
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3 622 **Figure 3.** Mean proportion (95%CI) of all-cause and cause-specific hospital admissions, early readmissions (1-7d), and late  
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5 623 readmissions (8-30d) with respect to PM<sub>2.5</sub> (µg/m<sup>3</sup>). Hash marks above the x-axis represent the density of daily county PM<sub>2.5</sub>.  
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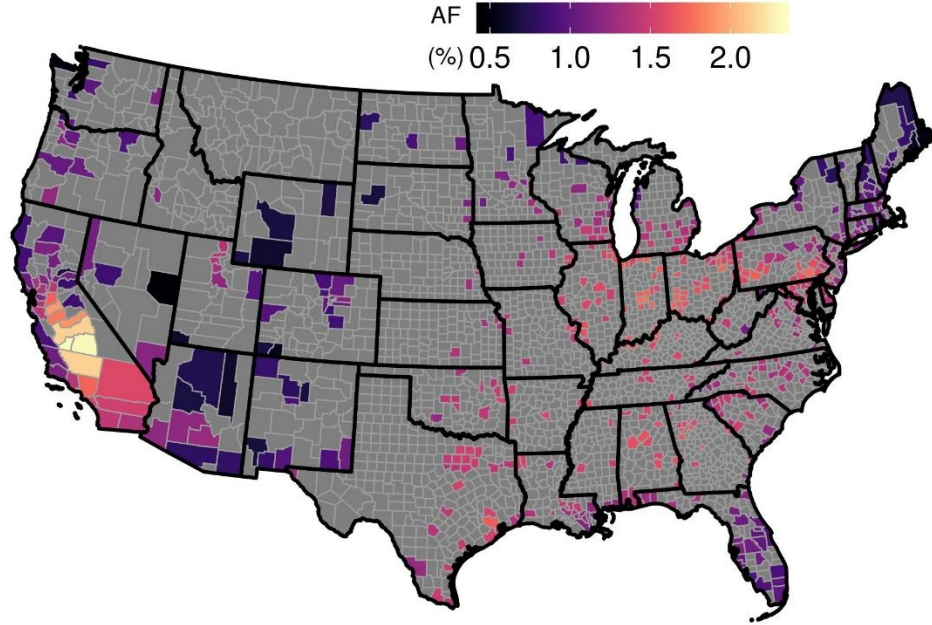


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A) Daily county average PM<sub>2.5</sub> (7yr average)



B) Exposure attributable fraction for early-readmission following an all-cause discharge



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3 626 **Figure 4.** Average daily county PM<sub>2.5</sub> (µg/m<sup>3</sup>) between 2008 and 2014 (A) and the attributable  
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5 627 fraction for early-readmission following an all-cause discharge based on the average PM<sub>2.5</sub> (B)  
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7 628 for the 530 counties included in the study.  
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629 **Supplemental Materials**

630

631 **Table S1.** Summary statistics of PM<sub>2.5</sub> and meteorological variables across 530 counties.

Variable	Mean ± SD	Minimum	Maximum
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	9.29 ± 5.39	0.05	155.16
Temperature (°F)	56.37 ± 18.50	-37.30	104.74
Relative humidity (%)	65.24 ± 16.24	0	100

632

633 **Table S2.** Relative risk (RR ± 95% CI) of all-cause and cause-specific daily county admission634 rates associated with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> for exposure lags 0-14 days

Endpoint	Lag	RR (95% CI)	N
All-cause	0	1.003 (0.998, 1.009)	1,801,966
All-cause	1	0.997 (0.990, 1.003)	1,801,966
All-cause	2	0.999 (0.992, 1.005)	1,801,966
All-cause	3	0.996 (0.990, 1.002)	1,801,966
All-cause	4	1.002 (0.996, 1.008)	1,801,966
All-cause	5	1.001 (0.995, 1.007)	1,801,966
All-cause	6	1.001 (0.995, 1.008)	1,801,966
All-cause	7	1.000 (0.993, 1.006)	1,801,966
All-cause	8	1.004 (0.997, 1.010)	1,801,966
All-cause	9	1.004 (0.998, 1.010)	1,801,966
All-cause	10	0.999 (0.993, 1.005)	1,801,966
All-cause	11	0.996 (0.989, 1.002)	1,801,966
All-cause	12	1.002 (0.996, 1.009)	1,801,966
All-cause	13	0.995 (0.989, 1.001)	1,801,966

All-cause	14	1.000 (0.994, 1.005)	1,801,966
CVD broad definition	0	1.009 (1.002, 1.017)	832,255
CVD broad definition	1	0.995 (0.986, 1.004)	832,255
CVD broad definition	2	0.998 (0.988, 1.007)	832,255
CVD broad definition	3	0.993 (0.984, 1.002)	832,255
CVD broad definition	4	1.003 (0.994, 1.012)	832,255
CVD broad definition	5	1.004 (0.994, 1.013)	832,255
CVD broad definition	6	0.999 (0.990, 1.008)	832,255
CVD broad definition	7	1.005 (0.995, 1.014)	832,255
CVD broad definition	8	1.002 (0.993, 1.011)	832,255
CVD broad definition	9	1.009 (1.000, 1.018)	832,255
CVD broad definition	10	0.992 (0.983, 1.001)	832,255
CVD broad definition	11	0.999 (0.990, 1.008)	832,255
CVD broad definition	12	0.999 (0.990, 1.008)	832,255
CVD broad definition	13	0.996 (0.987, 1.005)	832,255
CVD broad definition	14	1.002 (0.994, 1.009)	832,255
Respiratory broad definition	0	1.002 (0.994, 1.010)	766,447
Respiratory broad definition	1	0.998 (0.989, 1.008)	766,447
Respiratory broad definition	2	0.995 (0.985, 1.004)	766,447
Respiratory broad definition	3	0.995 (0.985, 1.004)	766,447
Respiratory broad definition	4	0.999 (0.989, 1.008)	766,447
Respiratory broad definition	5	1.009 (1.000, 1.019)	766,447
Respiratory broad definition	6	0.999 (0.990, 1.009)	766,447
Respiratory broad definition	7	0.999 (0.989, 1.009)	766,447
Respiratory broad definition	8	1.005 (0.996, 1.015)	766,447

Respiratory broad definition	9	1.008 (0.999, 1.018)	766,447
Respiratory broad definition	10	0.995 (0.985, 1.004)	766,447
Respiratory broad definition	11	0.997 (0.988, 1.007)	766,447
Respiratory broad definition	12	1.002 (0.992, 1.011)	766,447
Respiratory broad definition	13	0.997 (0.987, 1.006)	766,447
Respiratory broad definition	14	1.001 (0.993, 1.009)	766,447

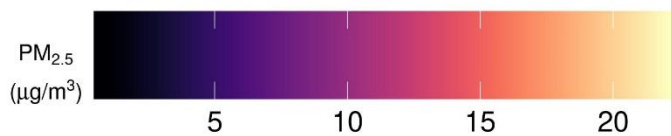
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636 **Table S3.** The relative risk (RR, 95%CI) for an all-cause early and late-readmission following637 all-cause and cause-specific discharges. RR is expressed per 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ .

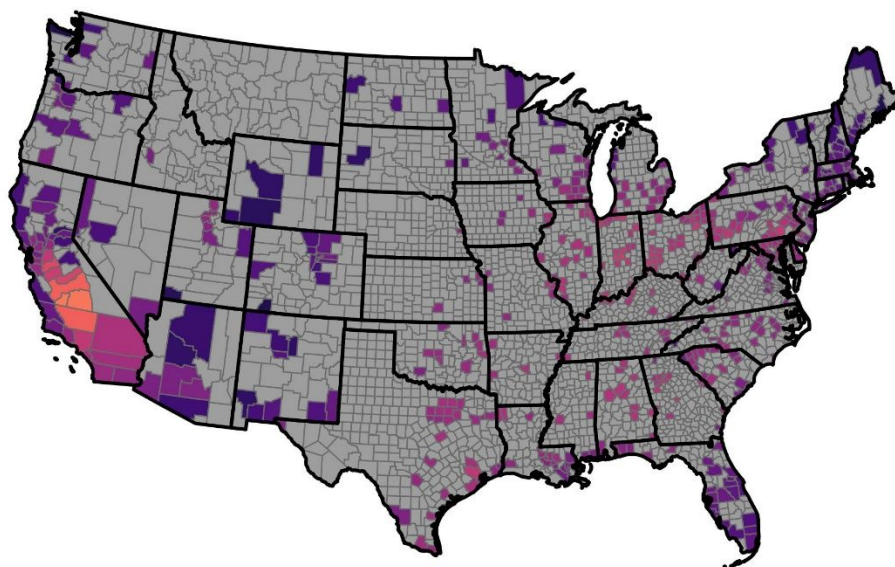
Discharge cause	Model	RR (95% CI)	N
All-cause	Early-readmission (1-7d)	1.014 (1.005, 1.024)	177,552
All-cause	Late-readmission (8-30d)	1.003 (1.001, 1.005)	319,058
CVD broad definition	Early-readmission (1-7d)	1.017 (1.004, 1.031)	83,533
CVD broad definition	Late-readmission (8-30d)	1.003 (1.001, 1.006)	150,576
Respiratory broad definition	Early-readmission (1-7d)	1.016 (1.002, 1.031)	78,723
Respiratory broad definition	Late-readmission (8-30d)	1.002 (0.999, 1.005)	142,139

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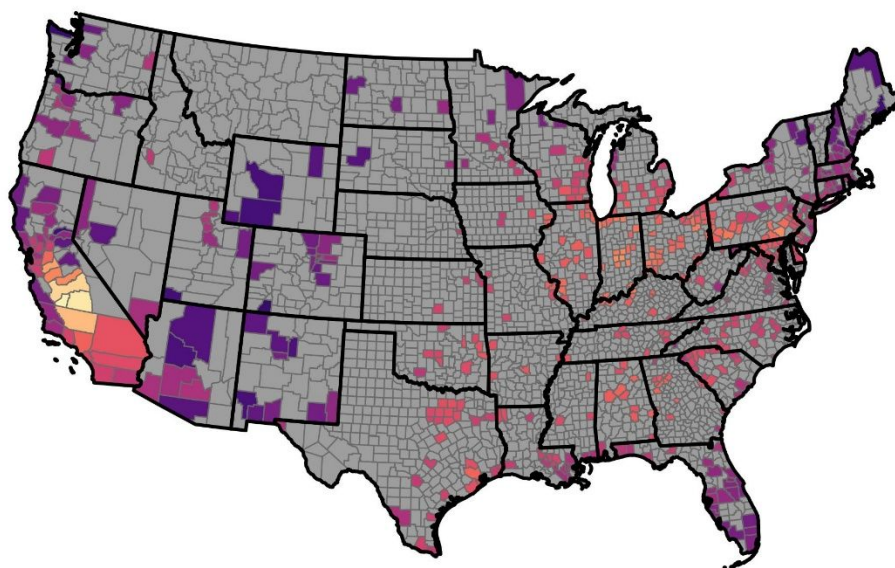
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A) Long-term county PM<sub>2.5</sub> (7yr average)

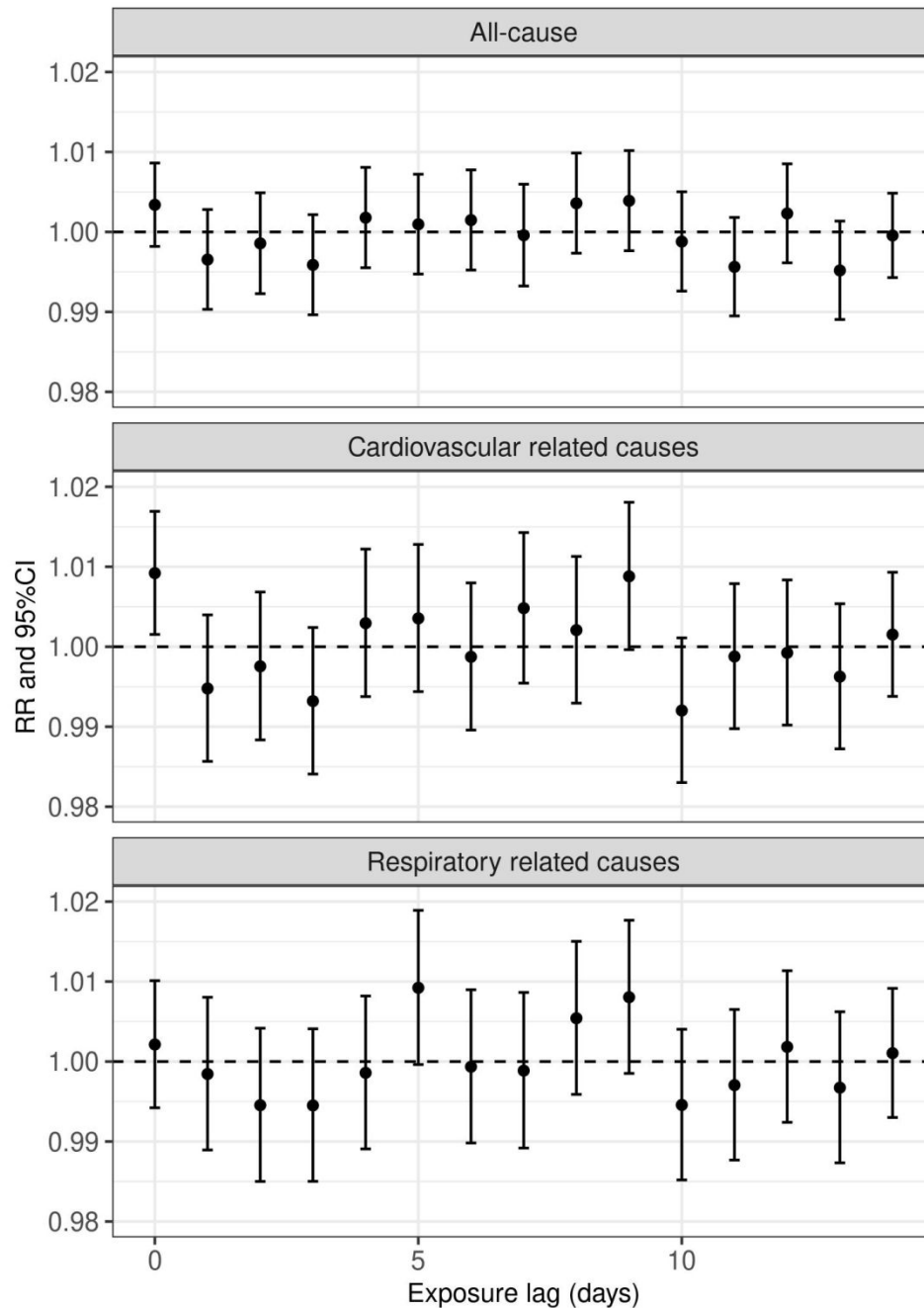


B) 20% of county days are above PM<sub>2.5</sub> (80th percentile)



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3 641 **Figure S1.** County PM<sub>2.5</sub> levels for the 530 counties included in the study. PM<sub>2.5</sub> levels shown  
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5 642 include the A) long-term average and B) 80th percentile (indicating that 20% of county days are  
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7 643 at or above this PM<sub>2.5</sub> level) for the years 2008-2014.  
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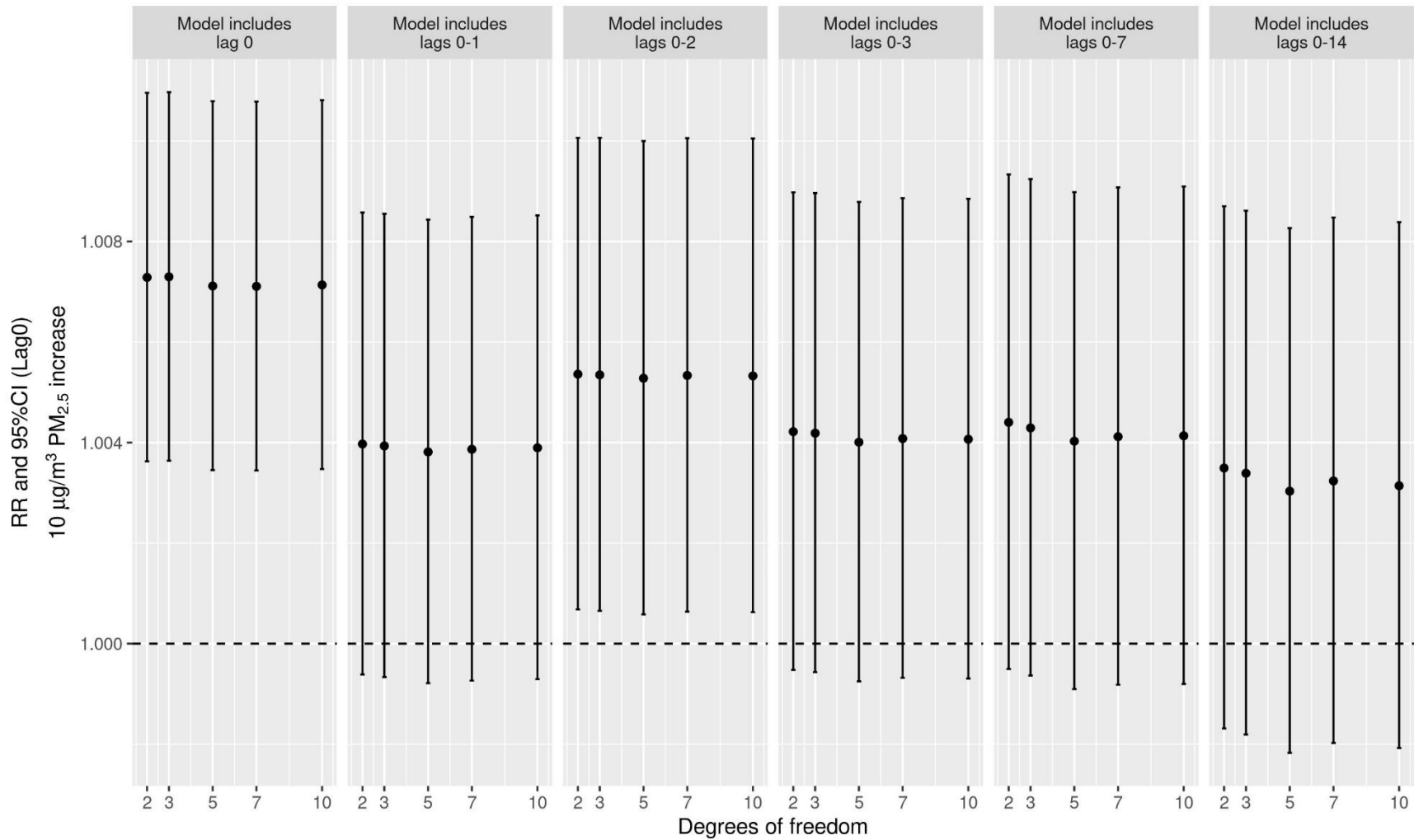
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3 646 **Figure S2.** Relative risk (RR  $\pm$  95%CI) for daily county admission rates for all-cause  
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5 647 hospitalization associated with a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  for exposure lags 0-14 days using  
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7 648 an unconstrained distributed lag model (Table S1).  
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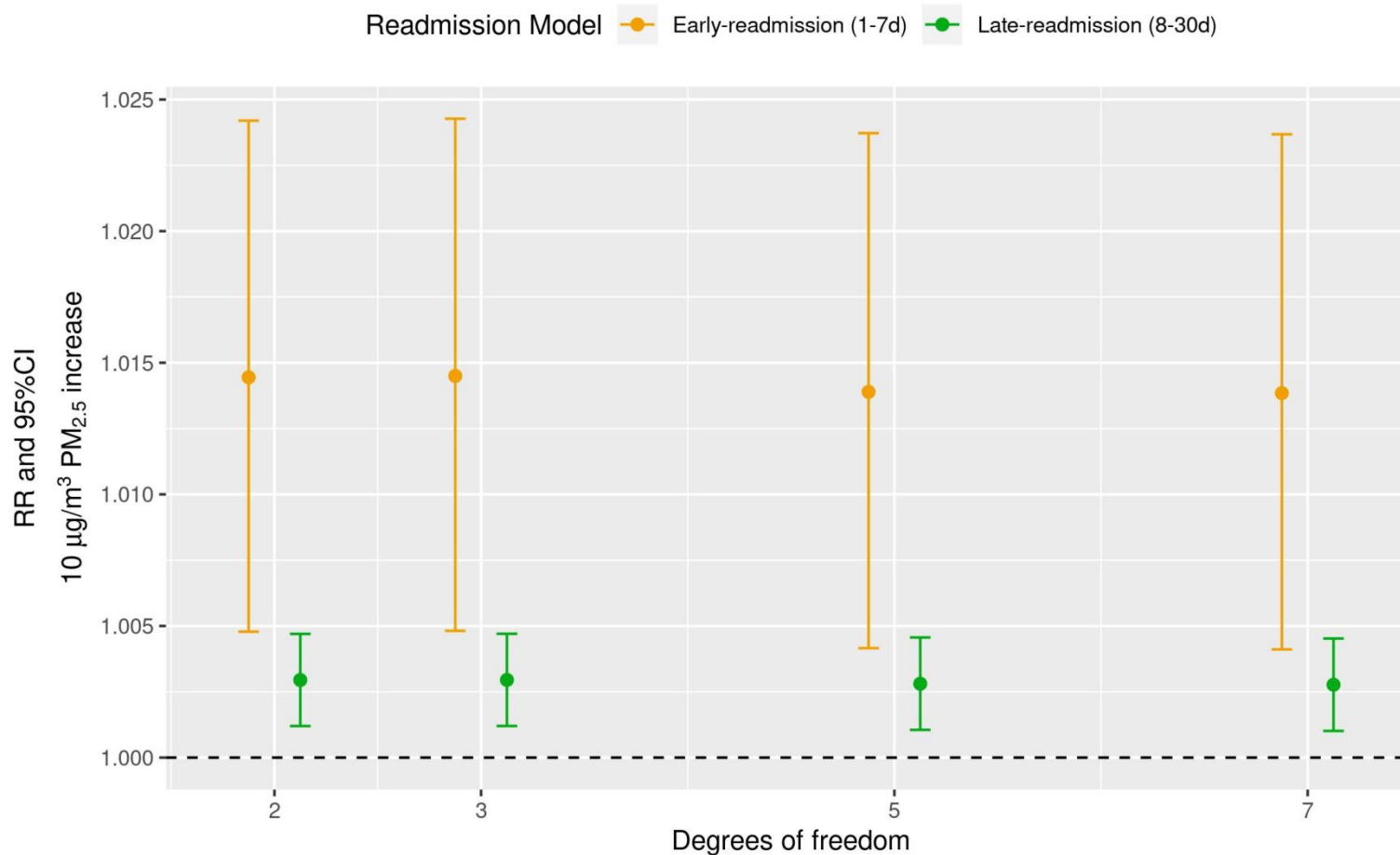
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 652 **Figure S3.** Sensitivity analysis for all-cause admissions models showing the impact on the lag 0 estimate from changing the number  
 653 of lags considered (grouped figures), and the number of degrees of freedom (x-axis) for the temperature and relative humidity  
 654 variables. Relative risk (RR ± 95%CI) of all-cause daily county admission rates associated with a 10 µg/m³ increase in PM<sub>2.5</sub> on lag 0.

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656

657 **Figure S4.** Sensitivity analysis for all-cause readmission models showing the impact on the lag 0 estimate from changing the number  
 658 of degrees of freedom (x-axis) for the temperature and relative humidity variables. Relative risk (RR ± 95%CI) of all-cause daily  
 659 county admission rates associated with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> on lag 0.

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3 **1 Supplemental Materials for**

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5 **2 Association of short-term ambient PM<sub>2.5</sub> with hospital admissions and 30-day readmissions in**  
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7 **3 end-stage renal disease patients: population based retrospective cohort study**  
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10 **4**

11 **5 Table S1.** Summary statistics of PM<sub>2.5</sub> and meteorological variables across 530 counties.  
12

Variable	Mean ± SD	Minimum	Maximum
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	9.29 ± 5.39	0.05	155.16
Temperature (°F)	56.37 ± 18.50	-37.30	104.74
Relative humidity (%)	65.24 ± 16.24	0	100

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22 **6**  
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24 **7 Table S2.** Relative risk (RR ± 95% CI) of all-cause and cause-specific daily county admission  
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26 **8 rates associated with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> for exposure lags 0-14 days**  
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Endpoint	Lag	RR (95% CI)
All-cause	0	1.003 (0.998, 1.009)
All-cause	1	0.997 (0.990, 1.003)
All-cause	2	0.999 (0.992, 1.005)
All-cause	3	0.996 (0.990, 1.002)
All-cause	4	1.002 (0.996, 1.008)
All-cause	5	1.001 (0.995, 1.007)
All-cause	6	1.001 (0.995, 1.008)
All-cause	7	1.000 (0.993, 1.006)
All-cause	8	1.004 (0.997, 1.010)
All-cause	9	1.004 (0.998, 1.010)
All-cause	10	0.999 (0.993, 1.005)
All-cause	11	0.996 (0.989, 1.002)

All-cause	12	1.002 (0.996, 1.009)
All-cause	13	0.995 (0.989, 1.001)
All-cause	14	1.000 (0.994, 1.005)
CVD broad definition	0	1.009 (1.002, 1.017)
CVD broad definition	1	0.995 (0.986, 1.004)
CVD broad definition	2	0.998 (0.988, 1.007)
CVD broad definition	3	0.993 (0.984, 1.002)
CVD broad definition	4	1.003 (0.994, 1.012)
CVD broad definition	5	1.004 (0.994, 1.013)
CVD broad definition	6	0.999 (0.990, 1.008)
CVD broad definition	7	1.005 (0.995, 1.014)
CVD broad definition	8	1.002 (0.993, 1.011)
CVD broad definition	9	1.009 (1.000, 1.018)
CVD broad definition	10	0.992 (0.983, 1.001)
CVD broad definition	11	0.999 (0.990, 1.008)
CVD broad definition	12	0.999 (0.990, 1.008)
CVD broad definition	13	0.996 (0.987, 1.005)
CVD broad definition	14	1.002 (0.994, 1.009)
Respiratory broad definition	0	1.002 (0.994, 1.010)
Respiratory broad definition	1	0.998 (0.989, 1.008)
Respiratory broad definition	2	0.995 (0.985, 1.004)
Respiratory broad definition	3	0.995 (0.985, 1.004)
Respiratory broad definition	4	0.999 (0.989, 1.008)
Respiratory broad definition	5	1.009 (1.000, 1.019)
Respiratory broad definition	6	0.999 (0.990, 1.009)

Respiratory broad definition	7	0.999 (0.989, 1.009)
Respiratory broad definition	8	1.005 (0.996, 1.015)
Respiratory broad definition	9	1.008 (0.999, 1.018)
Respiratory broad definition	10	0.995 (0.985, 1.004)
Respiratory broad definition	11	0.997 (0.988, 1.007)
Respiratory broad definition	12	1.002 (0.992, 1.011)
Respiratory broad definition	13	0.997 (0.987, 1.006)
Respiratory broad definition	14	1.001 (0.993, 1.009)

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10 **Table S3.** Relative risk (RR  $\pm$  95% CI) for early and late-readmissions following all-cause and  
 11 cause-specific discharges. RR is associated with a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ .

Discharge Cause	Model	RR (95% CI)
All-cause	Early-readmission (1-7d)	1.014 (1.005, 1.024)
All-cause	Late-readmission (8-30d)	1.003 (1.001, 1.005)
CVD broad definition	Early-readmission (1-7d)	1.017 (1.004, 1.031)
CVD broad definition	Late-readmission (8-30d)	1.003 (1.001, 1.006)
Respiratory broad definition	Early-readmission (1-7d)	1.016 (1.002, 1.031)
Respiratory broad definition	Late-readmission (8-30d)	1.002 (0.999, 1.005)

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13 **Table S4.** Relative risk (RR  $\pm$  95% CI) for early and late all-cause and cause specific readmissions following all-cause,  
 14 cardiovascular, and respiratory discharges. RR is associated with a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ .

Discharge Cause	Readmission cause	Model	RR (95% CI)
All-cause	All-cause	Early-readmission (1-7d)	1.014 (1.005, 1.024)
All-cause	All-cause	Late-readmission (8-30d)	1.003 (1.001, 1.005)
All-cause	CVD broad definition	Early-readmission (1-7d)	1.009 (0.995, 1.023)
All-cause	CVD broad definition	Late-readmission (8-30d)	1.014 (1.008, 1.020)
All-cause	Dysrhythmia and conduction disorder	Early-readmission (1-7d)	1.046 (1.021, 1.071)
All-cause	Dysrhythmia and conduction disorder	Late-readmission (8-30d)	1.025 (1.015, 1.036)
All-cause	Heart failure	Early-readmission (1-7d)	1.036 (1.013, 1.059)
All-cause	Heart failure	Late-readmission (8-30d)	1.037 (1.027, 1.047)
All-cause	Hypertension	Early-readmission (1-7d)	1.007 (0.990, 1.024)
All-cause	Hypertension	Late-readmission (8-30d)	1.006 (0.999, 1.014)
All-cause	Ischemic heart disease	Early-readmission (1-7d)	0.974 (0.934, 1.016)
All-cause	Ischemic heart disease	Late-readmission (8-30d)	1.016 (0.998, 1.035)
All-cause	Myocardial infarction	Early-readmission (1-7d)	0.962 (0.913, 1.014)
All-cause	Myocardial infarction	Late-readmission (8-30d)	0.999 (0.976, 1.022)
All-cause	Peripheral arterial disease	Early-readmission (1-7d)	0.902 (0.752, 1.083)
All-cause	Peripheral arterial disease	Late-readmission (8-30d)	0.975 (0.903, 1.054)
All-cause	Pulmonary embolism	Early-readmission (1-7d)	1.047 (0.932, 1.177)
All-cause	Pulmonary embolism	Late-readmission (8-30d)	1.032 (0.973, 1.094)
All-cause	Asthma	Early-readmission (1-7d)	1.098 (0.988, 1.222)
All-cause	Asthma	Late-readmission (8-30d)	1.013 (0.971, 1.058)
All-cause	COPD	Early-readmission (1-7d)	1.037 (0.998, 1.077)
All-cause	COPD	Late-readmission (8-30d)	1.022 (1.004, 1.039)
All-cause	Other non-cardiac chest pain or resp syndrome	Early-readmission (1-7d)	1.027 (1.011, 1.042)
All-cause	Other non-cardiac chest pain or resp syndrome	Late-readmission (8-30d)	1.035 (1.029, 1.041)
All-cause	Pneumonia	Early-readmission (1-7d)	1.061 (1.032, 1.092)
All-cause	Pneumonia	Late-readmission (8-30d)	1.046 (1.033, 1.058)

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3	All-cause	Respiratory broad definition	Early-readmission (1-7d) 1.025 (1.011, 1.039)
4	All-cause	Respiratory broad definition	Late-readmission (8-30d) 1.034 (1.028, 1.040)
5	CVD broad definition	All-cause	Early-readmission (1-7d) 1.017 (1.004, 1.031)
6	CVD broad definition	All-cause	Late-readmission (8-30d) 1.003 (1.001, 1.006)
7	CVD broad definition	CVD broad definition	Early-readmission (1-7d) 1.006 (0.989, 1.024)
8	CVD broad definition	CVD broad definition	Late-readmission (8-30d) 1.013 (1.005, 1.020)
9	CVD broad definition	Dysrhythmia and conduction disorder	Early-readmission (1-7d) 1.042 (1.010, 1.074)
10	CVD broad definition	Dysrhythmia and conduction disorder	Late-readmission (8-30d) 1.027 (1.013, 1.041)
11	CVD broad definition	Heart failure	Early-readmission (1-7d) 1.027 (1.000, 1.056)
12	CVD broad definition	Heart failure	Late-readmission (8-30d) 1.031 (1.019, 1.043)
13	CVD broad definition	Hypertension	Early-readmission (1-7d) 1.006 (0.985, 1.028)
14	CVD broad definition	Hypertension	Late-readmission (8-30d) 1.002 (0.993, 1.011)
15	CVD broad definition	Ischemic heart disease	Early-readmission (1-7d) 1.015 (0.964, 1.070)
16	CVD broad definition	Ischemic heart disease	Late-readmission (8-30d) 1.017 (0.993, 1.041)
17	CVD broad definition	Myocardial infarction	Early-readmission (1-7d) 0.991 (0.927, 1.058)
18	CVD broad definition	Myocardial infarction	Late-readmission (8-30d) 1.002 (0.972, 1.032)
19	CVD broad definition	Peripheral arterial disease	Early-readmission (1-7d) 0.914 (0.688, 1.215)
20	CVD broad definition	Peripheral arterial disease	Late-readmission (8-30d) 1.029 (0.922, 1.148)
21	CVD broad definition	Pulmonary embolism	Early-readmission (1-7d) 1.129 (0.984, 1.296)
22	CVD broad definition	Pulmonary embolism	Late-readmission (8-30d) 1.004 (0.928, 1.085)
23	CVD broad definition	Asthma	Early-readmission (1-7d) 1.085 (0.947, 1.242)
24	CVD broad definition	Asthma	Late-readmission (8-30d) 1.006 (0.949, 1.066)
25	CVD broad definition	COPD	Early-readmission (1-7d) 1.032 (0.982, 1.085)
26	CVD broad definition	COPD	Late-readmission (8-30d) 1.026 (1.003, 1.049)
27	CVD broad definition	Other non-cardiac chest pain or resp syndrome	Early-readmission (1-7d) 1.025 (1.005, 1.045)
28	CVD broad definition	Other non-cardiac chest pain or resp syndrome	Late-readmission (8-30d) 1.036 (1.027, 1.044)
29	CVD broad definition	Pneumonia	Early-readmission (1-7d) 1.076 (1.036, 1.117)
30	CVD broad definition	Pneumonia	Late-readmission (8-30d) 1.041 (1.024, 1.058)
31	CVD broad definition	Respiratory broad definition	Early-readmission (1-7d) 1.026 (1.007, 1.045)
32	CVD broad definition	Respiratory broad definition	Late-readmission (8-30d) 1.034 (1.026, 1.042)
33	Respiratory broad definition	All-cause	Early-readmission (1-7d) 1.016 (1.002, 1.031)
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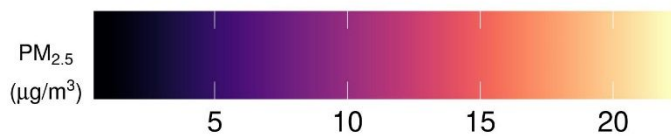
Respiratory broad definition	All-cause	Late-readmission (8-30d)	1.002 (1.000, 1.005)
Respiratory broad definition	CVD broad definition	Early-readmission (1-7d)	1.007 (0.988, 1.026)
Respiratory broad definition	CVD broad definition	Late-readmission (8-30d)	1.013 (1.005, 1.021)
Respiratory broad definition	Dysrhythmia and conduction disorder	Early-readmission (1-7d)	1.042 (1.008, 1.077)
Respiratory broad definition	Dysrhythmia and conduction disorder	Late-readmission (8-30d)	1.018 (1.004, 1.033)
Respiratory broad definition	Heart failure	Early-readmission (1-7d)	1.016 (0.987, 1.045)
Respiratory broad definition	Heart failure	Late-readmission (8-30d)	1.028 (1.015, 1.041)
Respiratory broad definition	Hypertension	Early-readmission (1-7d)	1.014 (0.991, 1.039)
Respiratory broad definition	Hypertension	Late-readmission (8-30d)	1.007 (0.997, 1.017)
Respiratory broad definition	Ischemic heart disease	Early-readmission (1-7d)	0.971 (0.918, 1.028)
Respiratory broad definition	Ischemic heart disease	Late-readmission (8-30d)	0.998 (0.973, 1.023)
Respiratory broad definition	Myocardial infarction	Early-readmission (1-7d)	0.940 (0.874, 1.011)
Respiratory broad definition	Myocardial infarction	Late-readmission (8-30d)	0.979 (0.948, 1.011)
Respiratory broad definition	Peripheral arterial disease	Early-readmission (1-7d)	0.844 (0.596, 1.197)
Respiratory broad definition	Peripheral arterial disease	Late-readmission (8-30d)	1.050 (0.935, 1.179)
Respiratory broad definition	Pulmonary embolism	Early-readmission (1-7d)	1.071 (0.910, 1.260)
Respiratory broad definition	Pulmonary embolism	Late-readmission (8-30d)	1.027 (0.941, 1.120)
Respiratory broad definition	Asthma	Early-readmission (1-7d)	1.068 (0.932, 1.224)
Respiratory broad definition	Asthma	Late-readmission (8-30d)	0.973 (0.918, 1.031)
Respiratory broad definition	COPD	Early-readmission (1-7d)	1.039 (0.991, 1.090)
Respiratory broad definition	COPD	Late-readmission (8-30d)	1.015 (0.994, 1.037)
Respiratory broad definition	Other non-cardiac chest pain or resp syndrome	Early-readmission (1-7d)	1.028 (1.008, 1.048)
Respiratory broad definition	Other non-cardiac chest pain or resp syndrome	Late-readmission (8-30d)	1.022 (1.014, 1.030)
Respiratory broad definition	Pneumonia	Early-readmission (1-7d)	1.044 (1.006, 1.084)
Respiratory broad definition	Pneumonia	Late-readmission (8-30d)	1.046 (1.029, 1.063)
Respiratory broad definition	Respiratory broad definition	Early-readmission (1-7d)	1.025 (1.006, 1.044)
Respiratory broad definition	Respiratory broad definition	Late-readmission (8-30d)	1.022 (1.014, 1.030)



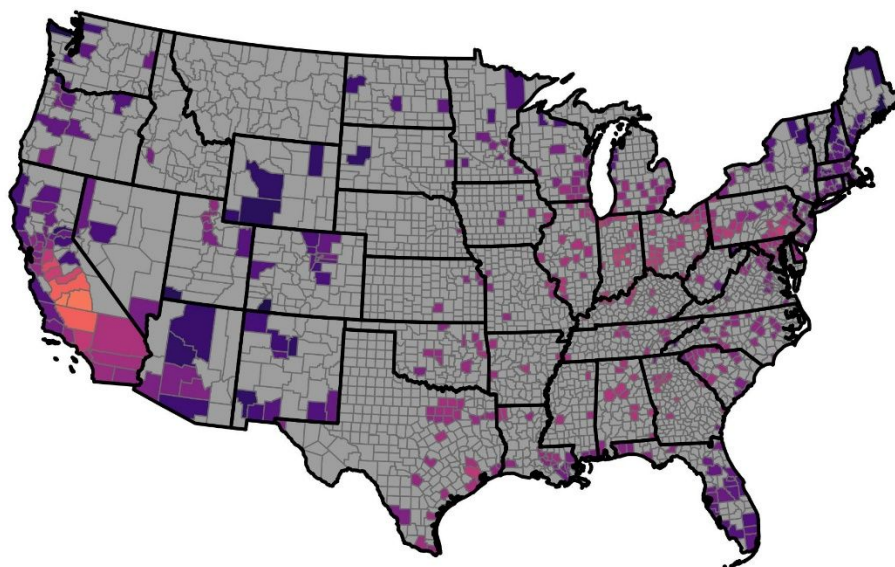
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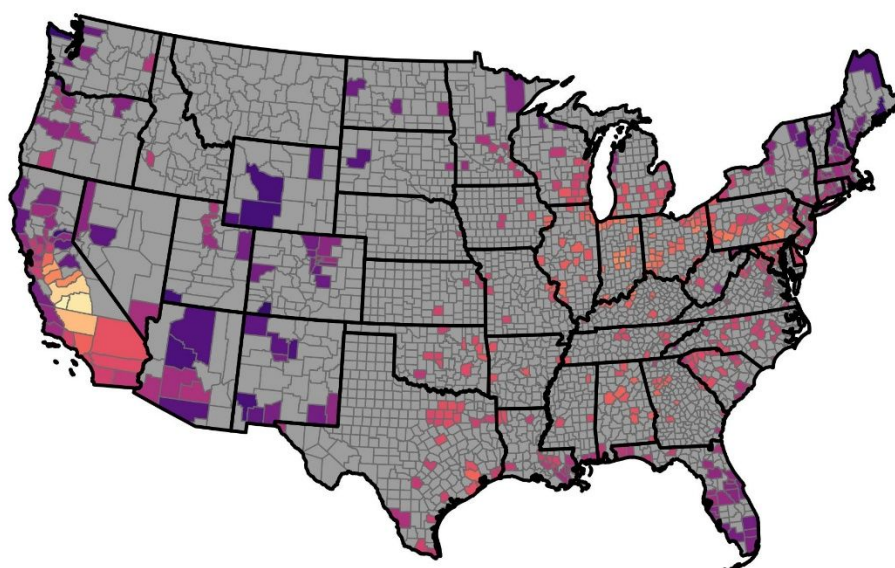

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A) Long-term county PM<sub>2.5</sub> (7yr average)

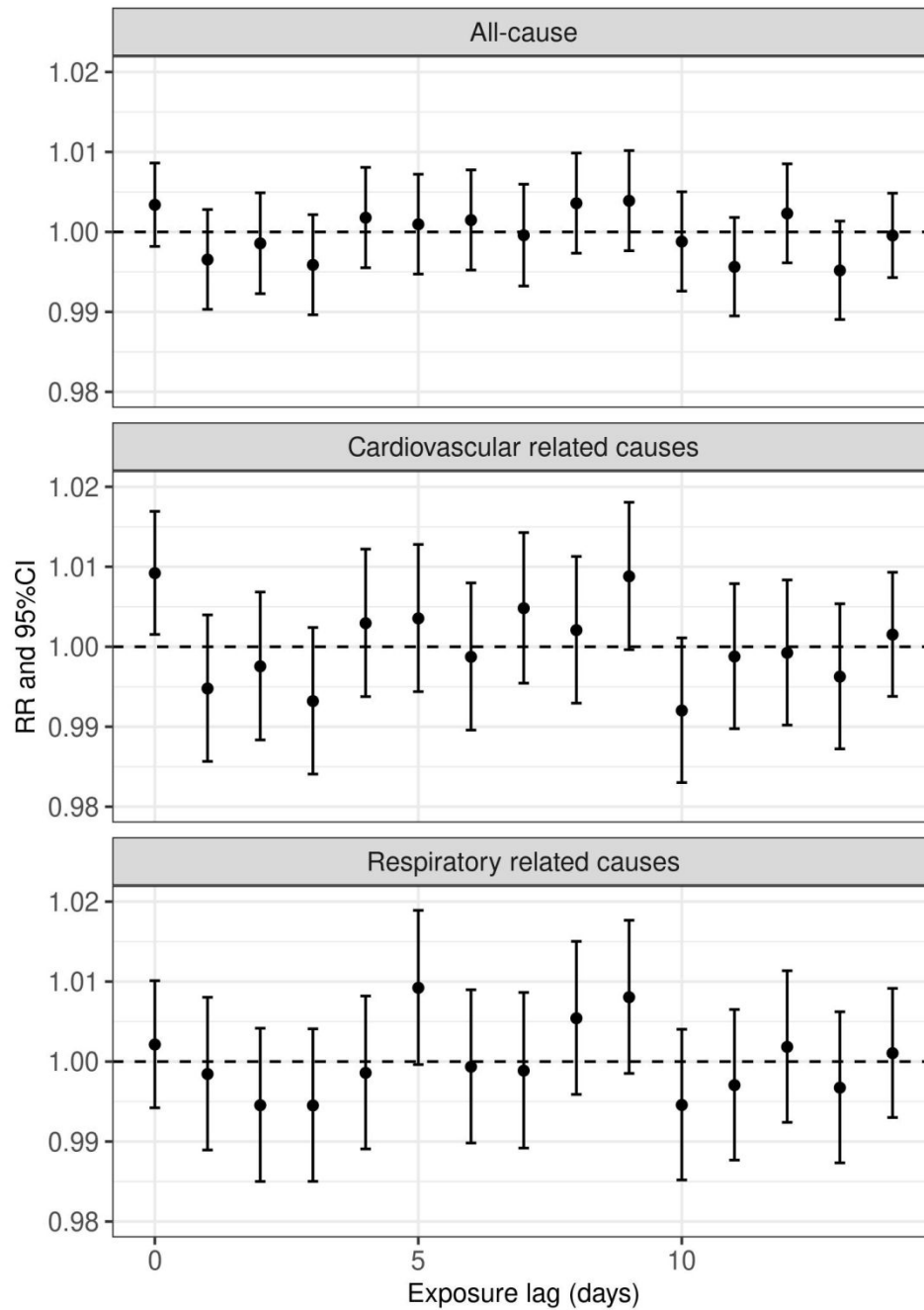


B) 20% of county days are above PM<sub>2.5</sub> (80th percentile)



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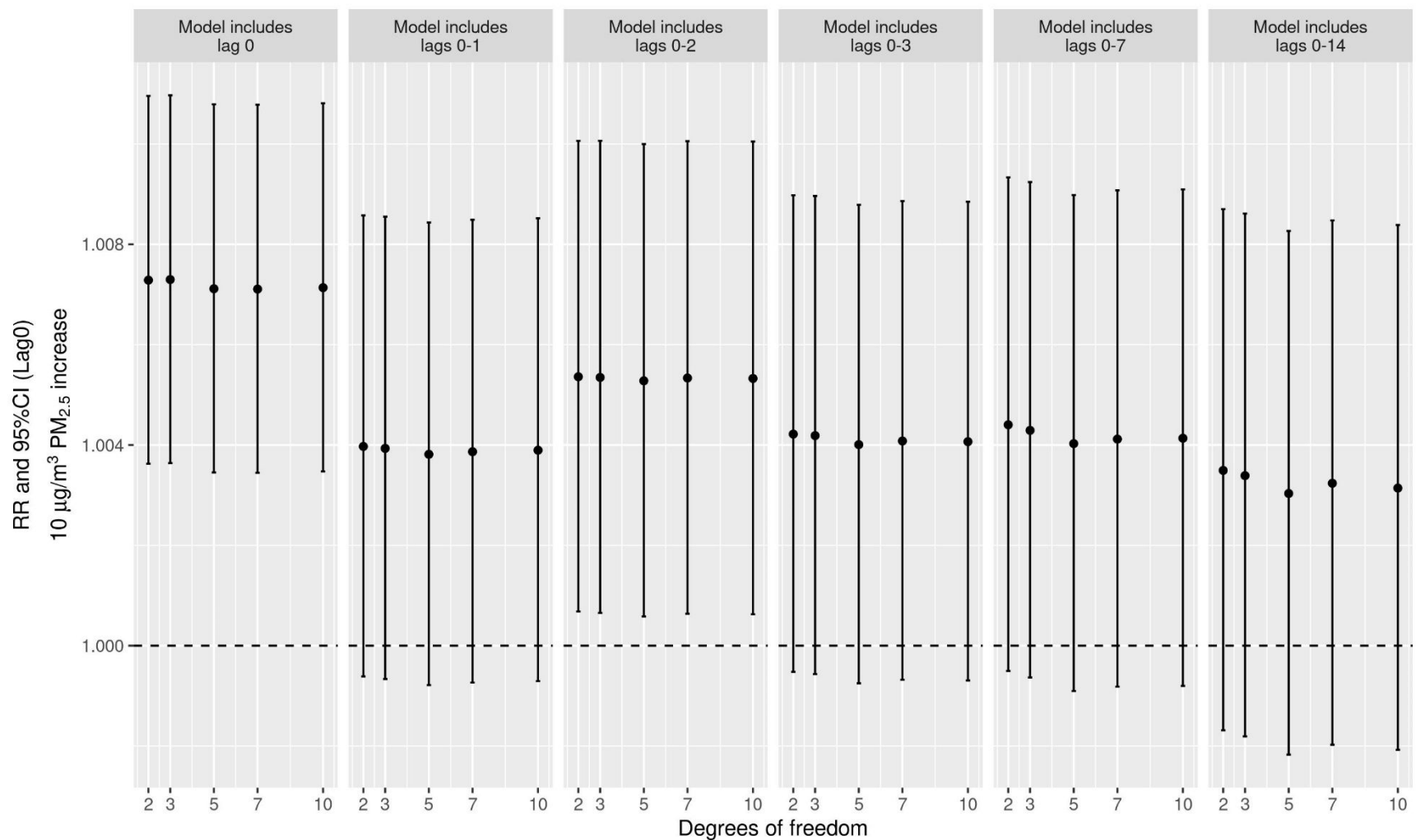
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3 18 **Figure S1.** County PM<sub>2.5</sub> levels for the 530 counties included in the study. PM<sub>2.5</sub> levels shown  
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5 19 include the A) long-term average and B) 80th percentile (indicating that 20% of county days are  
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7 20 at or above this PM<sub>2.5</sub> level) for the years 2008-2014.  
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3 23 **Figure S2.** Relative risk (RR  $\pm$  95%CI) for daily county admission rates for all-cause  
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5 24 hospitalization associated with a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  for exposure lags 0-14 days using  
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7 25 an unconstrained distributed lag model (Table S1).  
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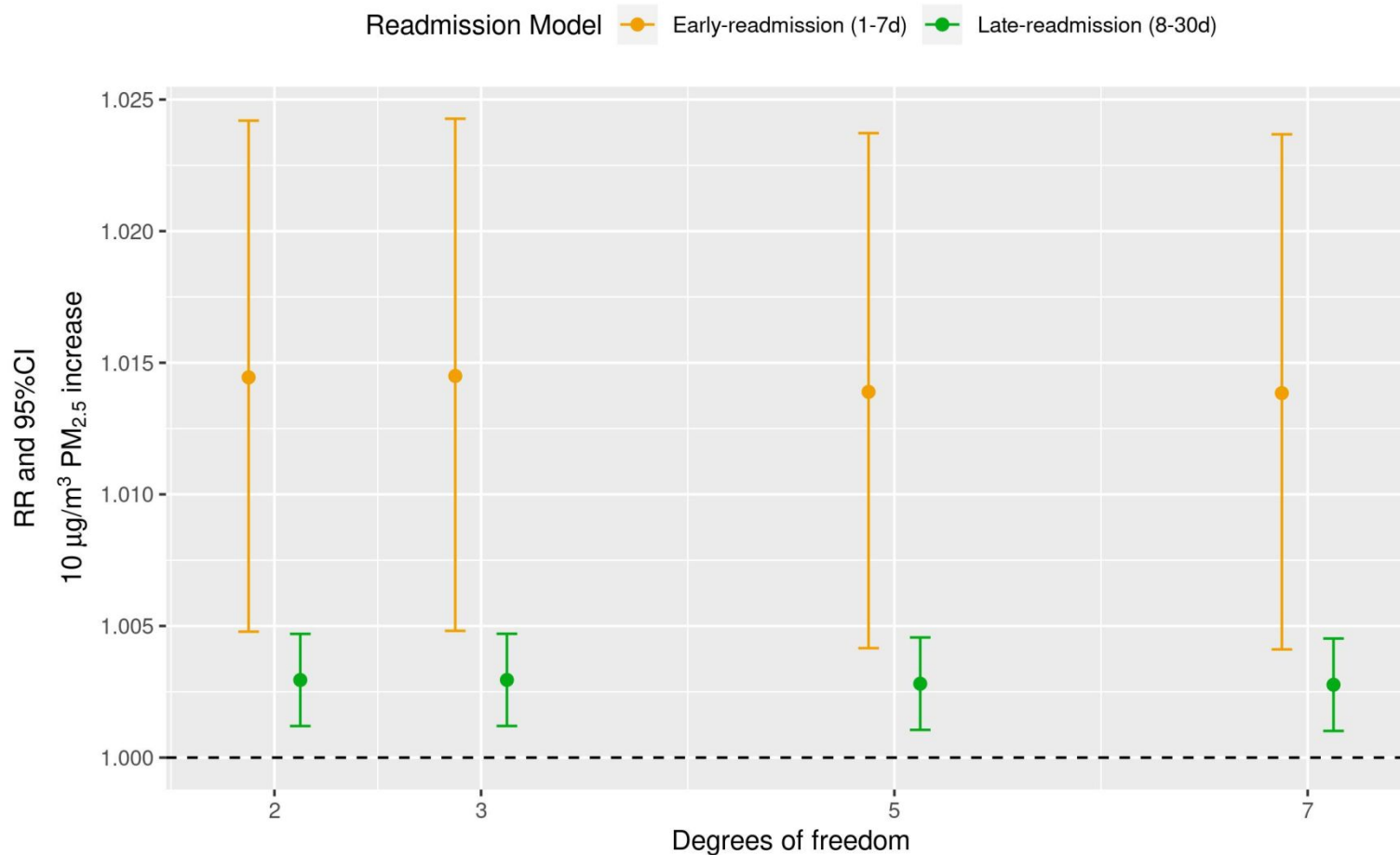
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29 **Figure S3.** Sensitivity analysis for all-cause admissions models showing the impact on the lag 0 estimate from changing the number  
 30 of lags considered (grouped figures), and the number of degrees of freedom (x-axis) for the temperature and relative humidity  
 31 variables. Relative risk (RR ± 95%CI) of all-cause daily county admission rates associated with a 10 µg/m³ increase in PM<sub>2.5</sub> on lag 0.

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34 **Figure S4.** Sensitivity analysis for all-cause readmission models showing the impact on the lag 0 estimate from changing the number  
 35 of degrees of freedom (x-axis) for the temperature and relative humidity variables. Relative risk (RR ± 95%CI) of all-cause daily  
 36 county admission rates associated with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> on lag 0.

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7-9
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	8-9
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9-10
Outcome data	15*	Report numbers of outcome events or summary measures over time	10

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-12
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
10				
11	<b>Discussion</b>			
12				
13	Key results	18	Summarise key results with reference to study objectives	12-13
14				
15	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
16				
17	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-16
18				
19				
20	Generalisability	21	Discuss the generalisability (external validity) of the study results	16
21				
22	<b>Other information</b>			
23	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17
24				
25				

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.



# BMJ Open

## Association of short-term exposure to ambient PM2.5 with hospital admissions and 30-day readmissions in end-stage renal disease patients: population based retrospective cohort study

Journal:	<i>BMJ Open</i>
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<b>Primary Subject Heading</b>:	Epidemiology
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Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, NEPHROLOGY

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3 1 **Title**  
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5 2 Association of short-term exposure to ambient PM<sub>2.5</sub> with hospital admissions and 30-day  
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7 3 readmissions in end-stage renal disease patients: population based retrospective cohort study  
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26 37 Manuscript word count: 3439  
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28 38 Abstract word count: 285  
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33 40 **Abstract**

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35 41 **Objectives:** To examine the effect of short-term exposure to ambient fine particulate matter  
36  
37 42 (PM<sub>2.5</sub>) on all-cause, cardiovascular, and respiratory related hospital admissions and  
38  
39 43 readmissions among patients receiving outpatient hemodialysis.  
40

41 44 **Design:** Retrospective cohort study.  
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43 45 **Setting:** Inpatient hospitalization claims identified from the United States Renal Data System in  
44  
45 46 530 US counties.  
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47 47 **Participants:** All patients receiving in-center hemodialysis between 2008 and 2014.  
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49 48 **Primary and secondary outcome measures:** Risk of all-cause, cardiovascular, and  
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51 49 respiratory related hospital admissions and 30-day all-cause and cause-specific readmission  
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53 50 following an all-cause, cardiovascular, and respiratory related discharges. Readmission risk was  
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3 51 evaluated for early (1-7 days post-discharge) and late (8-30 days post-discharge) readmission  
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5 52 time-periods. Relative risk is expressed per 10  $\mu\text{g}/\text{m}^3$  of  $\text{PM}_{2.5}$ .  
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7 53 **Results:** Same day ambient  $\text{PM}_{2.5}$  was associated with increased hospital admission risk for  
8  
9 54 cardiovascular causes (0.9%, 95%CI: [0.2, 1.7]). Greater  $\text{PM}_{2.5}$ -related associations were  
10  
11 55 observed with 30-day readmission risk. Early-readmission risk was increased by 1.6-1.8%  
12  
13 56 following all-cause (1.6%, [0.6, 2.6]), cardiovascular (1.8%, [0.4, 3.2]), and respiratory (1.8%,  
14  
15 [0.4, 3.2]) discharges; while late-readmission risk increased by 1.2-1.3% following all-cause and  
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17 57 cardiovascular discharges.  $\text{PM}_{2.5}$ -related associations with readmission risk were greatest for  
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19 58 certain cause-specific readmissions ranging 4.0-6.5% for dysrhythmia and conduction disorder,  
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21 59 heart failure, COPD, other non-cardiac chest pain or respiratory syndrome, and pneumonia.  
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23 60 Following all-cause discharges, the cause-specific early-readmission risk was increased by  
24  
25 61 6.5% (3.5, 9.6) for pneumonia, 4.8% (2.3, 7.4) for dysrhythmia and conduction disorder, 3.7%  
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27 62 (1.4, 6.0) for heart failure, and 2.7% (1.2, 4.2) for other non-cardiac chest pain or respiratory  
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29 63 syndrome related causes.  
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31 64

32 65 **Conclusions:** Daily ambient  $\text{PM}_{2.5}$  was associated with an increased risk of cardiovascular  
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34 66 admissions and 30-day readmissions following cardiopulmonary-related discharges in a  
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36 67 vulnerable ESRD population. In the first week following discharge, greater  $\text{PM}_{2.5}$ -related risk of  
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38 68 rehospitalization was identified for some diagnoses.  
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#### 43 70 **Strengths and limitations of this study**

- 44 71 • Nearly complete representation of hospitalization records (> 1.8 million inpatient  
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46 72 admissions), identified using the US Renal Data System, of patients undergoing in-  
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48 73 center hemodialysis between 2008 and 2014.
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50 74 • Location of last dialysis visit was linked with daily population-weighted air pollution.
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52 75 • Admission risk estimated using time and county stratified design to control for county-  
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54 76 level time trends.
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3 77 • Cox proportional hazard model with time-varying exposure was used to estimate  
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5 78 readmission risk associated with daily fluctuations in ambient PM<sub>2.5</sub> controlled for time-  
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7 79 varying confounders.  
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10 80 • Potential diagnosis misclassification from using diagnosis codes to classify cause-  
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12 81 specific hospitalizations and exposure misclassification related to PM<sub>2.5</sub> exposure not  
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14 82 captured by ambient air quality near dialysis centers.  
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## 84 Introduction

85 Ambient fine particulate matter (PM<sub>2.5</sub>) is a leading risk factor for all-cause mortality<sup>1-4</sup>,  
86 accounting for millions of premature deaths each year<sup>5</sup>. Daily variation in ambient PM<sub>2.5</sub> is also  
87 associated with increased rates of unplanned hospital admissions, urgent care visits, and  
88 medication usage<sup>6,7</sup>. Greater health impacts have been observed consistently in sensitive  
89 populations, including the elderly and individuals with chronic health conditions such as chronic  
90 kidney disease (CKD)<sup>3,8-11</sup>. Additionally, PM<sub>2.5</sub> exposure during wildfire periods has been shown  
91 to increase the risk of mortality among patients managing their end stage renal disease with  
92 hemodialysis<sup>12</sup>. However, the role of short-term PM<sub>2.5</sub> exposure at ambient levels on  
93 progression of disease and cause-specific morbidities has not been characterized.

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95 CKD is a progressive condition that affects 8 to 16% of the population worldwide<sup>13-15</sup>, and in the  
96 final stage, end-stage renal disease (ESRD), many patients are transitioned to hemodialysis to  
97 prolong life. Patients receiving dialysis represent a particularly vulnerable population because of  
98 high rates of co-morbidities, including diabetes and cardiovascular disease, which may  
99 contribute to the greater likelihood of hospital admission and readmission following PM  
100 exposure. In the US, patients on hemodialysis average 1.7 inpatient admissions annually with a  
101 30-day readmission rate twice that of other Medicare beneficiaries<sup>16</sup>, contributing to a  
102 substantial economic impact<sup>17</sup>. In 2016, \$35.4 billion in Medicare fee-for-service costs were  
103 attributed to ESRD<sup>16</sup>, motivating health promotion and cost-containment efforts to slow the  
104 progression of CKD and reduce hospitalizations and readmissions<sup>18</sup>. While many current  
105 strategies to reduce hospitalizations focus on care processes and patient-level factors<sup>19-22</sup>,  
106 there is a knowledge gap on the role of modifiable environmental risk factors - specifically  
107 ambient PM<sub>2.5</sub><sup>2,23-25</sup>.

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3 109 In this study, we examined the risk of daily hospitalization and subsequent 30-day readmission  
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5 110 in relation to daily ambient PM<sub>2.5</sub> using data from the US Renal Data System (USRDS) over a 7-  
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7 111 year period. We focused on all-cause, cardiovascular, and respiratory hospitalizations and  
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9 112 estimated changes in risk for early (1 to 7 days post-discharge) and late (8 to 30 days post-  
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11 113 discharge) readmission accounting for the influence of different causal factors (i.e. acute and  
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13 114 chronic illness burden) that may influence early versus late-readmissions <sup>26 27</sup>.  
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## 17 18 116 **Methods**

### 19 20 117 **Setting and study population**

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22 118 Using patient level data from the USRDS, we constructed an open cohort of individuals  
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24 119 receiving in-center hemodialysis between 2008 and 2014. USRDS is a national data registry for  
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26 120 dialysis services and includes records of patient demographic characteristics, hospitalizations,  
27  
28 121 and provider information on all patients receiving hemodialysis. Baseline demographic  
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30 122 characteristics (sex, birth date, race, and smoking status) recorded at the initiation of dialysis  
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32 123 were extracted from the Medical Evidence Form CMS-2728 for each patient. For every inpatient  
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34 124 hospital visit, we extracted the admission date, discharge date, discharge diagnoses codes, and  
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36 125 discharge status.  
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41 127 For the analysis of 30-day readmission risk, we considered only admissions where patients  
42  
43 128 were discharged alive. Each readmission was counted once as a readmission relative to the  
44  
45 129 prior index admissions and was then considered as a new index admission. Thus, each  
46  
47 130 admission could serve as both an index admission and readmission, consistent with previous  
48  
49 131 studies <sup>28</sup>. An admission that occurred on the same day as a discharge was combined with the  
50  
51 132 previous admission. These readmissions are likely to represent facility transfers for which we  
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53 133 were not able to obtain information. Discharges occurring within 30 days of the end of the study  
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55 134 period were excluded, as 30 days of follow-up data were not available. For both admissions and



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3 135 readmissions, patients could be represented more than once if they were admitted multiple  
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5 136 times during the study period.  
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9 138 Health outcomes

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11 139 The primary outcomes included daily counts of all-cause, respiratory, and cardiovascular-related  
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13 140 admissions and the time to readmission following the cause-specific discharges. All-cause and  
14  
15 141 cause-specific readmissions were examined separately. Readmissions were classified further  
16  
17 142 as early-readmissions, occurring within 1 to 7 days of an index hospitalization discharge, and  
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19 143 late-readmissions, occurring 8 to 30 days post-discharge.  
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24 145 International Classification of Diseases, 9<sup>th</sup> Revision (ICD-9) codes were used to identify cause-  
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26 146 specific hospitalizations. Cardiovascular-related diagnoses included hypertension (ICD-9 codes  
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28 147 401-405), myocardial infarction (410), ischemic heart disease (410-411, 413), pulmonary  
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30 148 embolism (415), dysrhythmia and conduction disorder (426-427), heart failure (428), and  
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32 149 peripheral arterial disease (444). Respiratory-related diagnoses included asthma (493), chronic  
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34 150 obstructive pulmonary disease (491-492, 496), pneumonia (480-486), and other non-cardiac  
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36 151 chest pain or respiratory syndrome (786).  
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41 153 Environmental data

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43 154 Daily concentrations of fine particulate matter (PM<sub>2.5</sub>) were estimated using a previously  
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45 155 described exposure prediction model<sup>29 30</sup>. Briefly, this model estimates daily PM<sub>2.5</sub> on a 1 km  
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47 156 grid for the entire continental US by incorporating satellite aerosol optical depth measurements,  
48  
49 157 chemical transport model simulations, meteorology, land-use, and other variables. Gridded  
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51 158 PM<sub>2.5</sub> estimates were subsequently converted to population-weighted county-level estimates  
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53 159 using 2010 Census tract population values. To enable adjustment for potential confounding by  
54  
55 160 weather conditions, temperature and relative humidity data were obtained from the National  
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3 161 Centers for Environmental Information's Global Historical Climatology Network (Global Surface  
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5 162 Summary of the Day)<sup>31</sup> and using the Community Multiscale Air Quality model, respectively.  
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7 163 The study area was restricted to all counties containing at least one land surface station from  
8  
9 164 the Global Historical Climatology Network (n = 530).  
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11 165  
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13 166 Daily PM<sub>2.5</sub> was linked to patient hospitalizations based on the county of their last dialysis visit.  
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15 167 Previous work has shown that patients in the USRDS cohort that receive in-center dialysis three  
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17 168 times a week have a median travel distance of 5.7 miles to their initial dialysis center<sup>32 33</sup>.  
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#### 20 169 21 22 170 Study design and statistical analysis

23  
24 171 *Daily county hospital admissions.* The relative risks of hospital admissions associated with daily  
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26 172 PM<sub>2.5</sub> were estimated using a case-crossover design with conditional Poisson models for each  
27  
28 173 of the three health outcomes separately (all-cause, cardiovascular, respiratory). Aggregated  
29  
30 174 counts of daily admissions were time stratified by county-day, where each county served as its  
31  
32 175 own control. For each county-day strata, PM<sub>2.5</sub> on the day of admission was compared with  
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34 176 PM<sub>2.5</sub> concentrations on control days. Control days were defined as occurring on the same day  
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36 177 of the week in the same month and year. This, by design, enabled us to control for differences  
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38 178 in county characteristics, such as population size and risk characteristics, and the influence of  
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40 179 day of the week, seasonal, and long-term time trends<sup>34</sup>.  
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43 180  
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45 181 The relative risk of hospital admissions related to daily PM<sub>2.5</sub> for each health outcome was  
46  
47 182 estimated using daily counts with respect to county-time strata, adjusted for meteorological  
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49 183 conditions (temperature and humidity). Temperature and humidity effects were averaged over  
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51 184 lag days 0, 1, and 2 and modeled using natural splines (df = 3) to allow for non-linear effects<sup>35</sup>.  
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3 186 We evaluated immediate (same day) and delayed PM<sub>2.5</sub> effects on all-cause and cause-specific  
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5 187 hospital admissions. Unconstrained distributed lag models were used to assess the delayed  
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7 188 effects of short-term exposures to PM<sub>2.5</sub>. Delayed exposure up to 14 days and models stratified  
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9 189 on county socioeconomic status were considered. To assess the impact of county  
10  
11 190 socioeconomic level, we used the percent of individuals below poverty from the 2010 US  
12  
13 191 Census. Associations were assessed for counties both above and below the median poverty  
14  
15 192 level (12.5%).

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18 193 *Early and late readmissions occurring within 30 days of discharge.* Cox proportional hazards  
19  
20 194 models were used to assess the relative risk of early (1 to 7 days post-discharge) and late (8 to  
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22 195 30 days post-discharge) readmission associated with daily PM<sub>2.5</sub> following all-cause and cause-  
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24 196 specific index hospitalizations. Early-readmission models were censored at 7 days and late-  
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26 197 readmission models at 30 days.

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30 199 Models for readmissions incorporated both time-dependent and time-independent risk factors.  
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32 200 Time-dependent variables included daily PM<sub>2.5</sub>, daily temperature, daily relative humidity, and  
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34 201 day-of-the-week. Time-independent factors included patient-specific, hospitalization event-  
35  
36 202 specific, and county socioeconomic variables. Patient-specific variables included indicator of  
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38 203 sex, race, baseline smoking status, whether the patient had three or more previous hospital  
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40 204 visits in the year prior, and age at discharge. Event-specific variables included whether the  
41  
42 205 discharge occurred on a holiday and length of stay. To adjust for county socioeconomic level,  
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44 206 the percent of individuals below poverty was included as a covariate. Models were also adjusted  
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46 207 for patient-specific clusters to account for repeated measures by individual. Lastly, models were  
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48 208 adjusted for the competing cause of death by including death as an additional censoring criteria.  
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50 209 The presented models represent the cause-specific readmission hazard. Non-linear PM<sub>2.5</sub>  
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52 210 associations were also explored.  
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3 212 Daily county admission and readmission risks were expressed as the rate ratio (RR) per 10-  
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5 213  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ . The proportion hospital admissions and readmissions associated with  
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7 214  $\text{PM}_{2.5}$  is reported as the attributable fraction (AF), where  $\text{AF} = (\text{RR}-1) / \text{RR}$  <sup>36</sup>. All statistical  
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9 215 analyses were performed with R software (version 3.6.0) <sup>37</sup>.  
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## 217 **Results**

### 218 Characterization of clinical cohort and daily $\text{PM}_{2.5}$

219 Among 361,568 patients who were hospitalized during the study period, 10,274 were excluded  
20  
21 due to missing baseline demographic values, with 351,294 patients remaining. Demographic  
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23 descriptions are in Table 1. Patients had on average 2.97 hospital visits in the year prior to an  
24  
25 admission and more than 70% of patients had at least one hospital admission related to  
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27 cardiovascular and respiratory causes (Table 2). The average daily county-level  $\text{PM}_{2.5}$   
28  
29 concentration was  $9.3 \mu\text{g}/\text{m}^3$  (range: 0.05 to  $155.16 \mu\text{g}/\text{m}^3$ ) (Table S1). The highest daily  
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31 county-level  $\text{PM}_{2.5}$  was observed in California (Figure S1, Supplementary file).  
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### 227 Description of clinical events, hospital admissions, and readmissions

36  
37 228 In total, there were 1,801,966 hospital admissions, of which 1,493,795 recorded the patient as  
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39 229 alive at discharge. Of admissions that were discharged alive, 11.8% were readmitted within 7  
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41 230 days and 21.3% were readmitted 8 to 30 days post-discharge. The mean length of stay for all-  
42  
43 231 cause, cardiovascular, and respiratory admissions was 7.0, 7.0, and 7.1 days, respectively  
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45 232 (Table 2).  
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### 234 Associations between $\text{PM}_{2.5}$ and readmission

51  
52 235 *Early-readmission.* Daily  $\text{PM}_{2.5}$  was positively associated with increased risk for early-  
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54 236 readmission following all-cause, cardiovascular, and respiratory related discharges. Same day  
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56 237 (lag 0)  $\text{PM}_{2.5}$  was associated with a 1.6% (95%CI: 0.6, 2.6), 1.8% (95%CI: 0.4, 3.2), and 1.8%

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3 238 (95%CI: 0.4, 3.2) increased risk of an early-readmission for any cause following all-cause,  
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5 239 cardiovascular, and respiratory related discharges, respectively (Figure 1, Table S2).  
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9 241 PM<sub>2.5</sub> associated early-readmission risk was greater for certain cause-specific outcomes.  
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11 242 Following all-cause discharges, same day (lag 0) PM<sub>2.5</sub> was associated with increased early-  
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13 243 readmission risk for dysrhythmia and conduction disorder (4.8% [2.3, 7.4]), heart failure (3.7%  
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15 244 [1.4, 6.0]), pneumonia 6.5% [3.5, 9.6]), and other non-cardiac chest pain or respiratory  
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17 245 syndrome (2.7% [1.2, 4.2]) causes. PM<sub>2.5</sub> associated early-readmission risk was greatest for  
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19 246 pneumonia related readmissions following cardiovascular related discharges (7.5% [3.5, 11.7]).  
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21 247 Other cause-specific early-readmission risks following cardiovascular and respiratory related  
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23 248 discharges were similar to estimates observed following discharge for any cause (Figure 2,  
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25 249 Table S2).  
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28 250  
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30 251 An average AF at 10 µg/m<sup>3</sup> of PM<sub>2.5</sub> at lag 0 was 1.5% (95%CI: 0.6, 2.5), 1.7% (95%CI: 0.4,  
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32 252 3.1), and 1.7% (95%CI: 0.3, 3.2) for an early-readmission for any cause following all-cause,  
33  
34 253 cardiovascular, and respiratory discharges, respectively (Figure 3). County AF ranged 0.5-2.5%,  
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36 254 0.6-2.8%, and 0.6-2.8% for an early-readmission following all-cause, cardiovascular, and  
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38 255 respiratory related discharges, respectively (Figure 4).  
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43 257 *Late-readmission.* Daily PM<sub>2.5</sub> was also associated with increased risk of late-readmission  
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45 258 following all-cause, cardiovascular, and respiratory related discharges and the magnitude of risk  
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47 259 related to all-cause readmissions was similar to that observed with early-readmission. Same  
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49 260 day PM<sub>2.5</sub> was associated with a 1.3% (95%CI: 0.6, 2.0), 1.2% (95%CI: 0.3, 2.2), and 1.0%  
50  
51 261 (95%CI: 0.01, 2.0) increased risk of a late all-cause readmission following all-cause,  
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53 262 cardiovascular, and respiratory related discharges, respectively (Figure 1, Table S2).  
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264 Similar to observations made for early-readmissions, PM<sub>2.5</sub> associated late-readmission risk was  
265 greater for certain cause-specific outcomes. Following all-cause discharges, a 10 µg/m<sup>3</sup>  
266 increase in same day (lag 0) PM<sub>2.5</sub> was associated with increased late-readmission risk for  
267 dysrhythmia and conduction disorder (3.1% [1.3, 5.0]), heart failure (4.1% [2.5, 5.8]), COPD  
268 (4.6% [1.7, 7.6]), pneumonia (5.9% [3.7, 8.2]), and other non-cardiac chest pain or respiratory  
269 syndrome (3.0% [1.9, 4.1]) (Figure 2, Table S2).

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271 The average AF at 10 µg/m<sup>3</sup> was 0.1% (95%CI: 0.5, 1.8) and 1.0% (95%CI: 0.1, 2.0) for a late-  
272 readmission following all-cause and cardiovascular discharges, respectively (Figure 3). County  
273 AF ranged 0.3-1.9% for a late-readmission following any cause (data not shown).

274

275 Associations between PM<sub>2.5</sub> and daily admissions

276 Same day PM<sub>2.5</sub> was associated with an increase in rate ratio of 0.3% (95%CI: -0.2, 0.9) for all-  
277 cause admissions and 0.9% (95%CI: 0.2, 1.7) for cardiovascular admissions (Figure S2, Table  
278 S3, Supplementary file). We estimated 0.9% (95%CI: 0.1, 1.7) of cardiovascular admissions  
279 could be attributed to 10 µg/m<sup>3</sup> ambient PM<sub>2.5</sub> (Figure 3). Across counties, exposures accounted  
280 for 0.3% to 1.5% of cardiovascular admissions when evaluated at the average daily PM<sub>2.5</sub> for  
281 each county (data not shown).

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283 No change in risk of all-cause and cardiovascular admissions was observed related to prior  
284 exposure (lags 1-14). Similarly, no change in risk for respiratory admissions was observed with  
285 same day exposure (lag 0) or prior exposure (lags 1-14) (Figure S2, Table S3, Supplementary  
286 file). The model with a dose-specific association for PM<sub>2.5</sub> (non-linear dose-response function)  
287 did not improve model fit. Models stratified on median percent below poverty were similar  
288 (Figure S2, Table S3, Supplementary file). In a sensitivity analysis, changing the number of

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3 289 degrees of freedom considered for temperature and relative humidity had a negligible effect  
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5 290 (Figure S3, Figure S4, Supplementary file).  
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## 9 292 **Discussion**

11 293 In a nationwide cohort study of 351,294 patients with ESRD managed with hemodialysis, we  
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13 294 evaluated the association between 1.8 million inpatient admissions and nearly 0.5 million  
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15 295 corresponding 30-day readmissions and the variation in daily ambient PM<sub>2.5</sub> in the US over 7  
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17 296 years, 2008-2014. Daily variation in PM<sub>2.5</sub> was associated with increased risk of hospital  
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19 297 admission and even greater risk of rehospitalization. Following all-cause, cardiovascular, and  
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21 298 respiratory related discharges, the early-readmission risk for any cause was increased by 1.6,  
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23 299 1.8, 1.8%, respectively per 10 µg/m<sup>3</sup> increase in daily PM<sub>2.5</sub>. Importantly, readmissions related  
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25 300 to some cardiorespiratory diagnoses had the greatest PM<sub>2.5</sub> attributed readmission risk that was  
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27 301 observed to be elevated for both early and late-readmissions. The early-readmission risk  
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29 302 following all-cause discharges, was increased by 6.5, 4.8, 3.7, and 2.7% for pneumonia,  
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31 303 dysrhythmia and conduction disorder, heart failure, and other non-cardiac chest pain or  
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33 304 respiratory syndrome related readmissions, respectively. Overall, these results suggest that at  
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35 305 10 µg/m<sup>3</sup>, 1.5-1.7% of early-readmissions for any cause were attributable to short-term  
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37 306 exposure. In the context of the daily PM<sub>2.5</sub> National Ambient Air Quality Standard (35 µg/m<sup>3</sup>),  
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39 307 this attributable fraction would be 5.3-6.0%.  
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45 309 Our findings are consistent with previous studies that observed increased admission risks in  
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47 310 elderly populations <sup>6 9 38-42</sup> and patients with cardiovascular health complications <sup>7 43</sup>, and  
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49 311 increased readmission risk following cardiovascular related admissions <sup>7 43 44</sup>. Studies in the  
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51 312 Medicare population similarly observed a 1-2% increase in cardiovascular hospital admissions  
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53 313 associated with same-day PM<sub>2.5</sub> concentrations <sup>6 9 38 40</sup>. Risk appears to vary by diagnosis, as  
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55 314 the increased risk was slightly less (0.13%) for ST-elevation myocardial infarction related  
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3 315 admissions in a Chinese population <sup>7</sup> and greater (29%) for incident heart failure admissions in  
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5 316 an Australian population <sup>43</sup>. Increases in respiratory admissions (1-2%) have been noted in the  
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7 317 Medicare population <sup>6 9 38-40</sup>, but were not observed in this study. Prior studies provide evidence  
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9 318 that air pollution exposure is associated with adverse health outcomes including increased  
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11 319 infection rates, acute lung edema, and elevated concentrations of systematic inflammation  
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13 320 markers <sup>45-47</sup>. Despite known associations between PM exposure and adverse cardiovascular  
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15 321 and respiratory health outcomes, previous studies have not evaluated the impacts on hospital  
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17 322 readmissions among individuals with ESRD.  
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22 324 Few studies have examined PM<sub>2.5</sub>-related effects on readmissions, and those that have report  
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24 325 on the long-term (>1yr) risk following cardiovascular related admissions. Following  
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26 326 cardiovascular hospitalization, greater PM<sub>2.5</sub>-related rehospitalization risk was observed for  
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28 327 some cardiac and respiratory readmissions (dysrhythmia, pneumonia) compared to our  
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30 328 observations of all-cause readmissions (4.3-7.5% vs 1.6%).  
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32 329 Studies in other populations, have noted similar same-day cardiovascular related readmission  
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34 330 risks of 5.5-7.7% and 2.6% associated with PM<sub>2.5</sub> <sup>7</sup> and PM<sub>10</sub> <sup>44</sup>, respectively. Additionally, one  
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36 331 study in an Australian population with very low ambient air pollution concentrations (mean PM<sub>2.5</sub>  
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38 332 = 2.9 µg/m<sup>3</sup>) found no relationship between PM<sub>2.5</sub> and all-cause readmissions after an incident  
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40 333 heart failure hospitalization <sup>43</sup>. In some instances, short-term readmission risks were greater in  
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42 334 comparison to the long-term readmission risks, suggesting the week following a discharge to be  
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44 335 a window of heightened vulnerability. Prior work indicates that factors related to index  
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46 336 hospitalizations and acute illness burden are predictive of an early-readmission <sup>26 27</sup>. This may  
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48 337 indicate that hospital readmissions related to certain acute illness burdens may be more  
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50 338 susceptible to PM<sub>2.5</sub> exposure.  
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3 340 Our study contributes to the currently limited literature on the association between air pollution  
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5 341 and health impacts among hemodialysis patients and shines a light on the vulnerability in this  
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7 342 clinical population related to ambient airborne particulate matter. The 30-day rehospitalization  
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9 343 rate is 33% in this population, which is twice that of older Medicare beneficiaries without a  
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11 344 kidney disease diagnosis <sup>16</sup>. As many as 70% of readmissions are thought to be unnecessary <sup>48</sup>,  
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13 345 prompting efforts to improve outcomes. Economic healthcare costs associated with short-term  
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15 346 increases in PM<sub>2.5</sub> are considerable; annual inpatient and post-acute care costs related to a 10  
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17 347 µg/m<sup>3</sup> in daily PM<sub>2.5</sub> ranges \$30-70 million for cardiovascular and respiratory related diseases <sup>49</sup>.  
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19 348 PM<sub>2.5</sub> is a modifiable risk factor and reductions in short-term exposures could contribute to  
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21 349 reduced healthcare costs. Our findings suggest that short-term increases in PM<sub>2.5</sub> contribute to  
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23 350 healthcare usage through unplanned admissions and readmissions.  
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28 352 Additionally, the findings of the study may have a broader public health implication. In the  
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30 353 conceptual framework for public health action, ambient airborne particulate matter fits well into  
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32 354 the base of a 5-tiered pyramid as a socioeconomic or social determinant of health <sup>50</sup>.  
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34 355 Interventions that address the base of the pyramid may provide the greatest potential impact  
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36 356 given the widespread population exposure of such a determinant of health like ambient airborne  
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38 357 particulate matter. Mitigation strategies would need to include policy initiatives to curb the  
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40 358 expulsion of airborne pollutants, as well as education of persons, patients, hospital staff, and  
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42 359 others. Areas with the higher concentrations of ambient airborne particulate matter may see the  
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44 360 greatest benefit from mitigation strategies.  
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49 362 Strengths and Limitations  
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51 363 This study included a nearly complete cohort of US patients undergoing in-center hemodialysis.  
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53 364 To our knowledge this is the largest analysis of short-term exposure to air pollution in the US in  
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55 365 this highly vulnerable population. The USRDS registry provides a complete registry of all  
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3 366 hospitalizations and contains detailed information regarding demographics, dialysis,  
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5 367 hospitalization, rehospitalization, and co-morbid conditions. Secondly, ambient PM<sub>2.5</sub> was  
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7 368 estimated using a prediction model with highly resolved spatial and temporal resolution with  
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9 369 proven accuracy<sup>29 30</sup>. Thirdly, the time-stratified design allowed for county matching that  
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11 370 reduced the potential confounding by factors that vary slowly with time and those that are time-  
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13 371 invariant. Fourthly, the use of time-dependent risk factors in the Cox proportional hazard model  
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15 372 allowed for readmission risk estimates to reflect the risk associated with daily fluctuations in  
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17 373 ambient PM<sub>2.5</sub> and time-varying confounders.  
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22 375 This study also had some limitations. Firstly, there was the potential for exposure  
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24 376 misclassification as the location of the last dialysis visit was used to estimate individual level  
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26 377 exposures. PM<sub>2.5</sub> around dialysis centers could differ from concentrations around hospitals and  
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28 378 patient residences. However, given that patients generally reside less than 6 miles from their  
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30 379 initial dialysis center, differences in temporal variation of exposure should be small and not likely  
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32 380 to contribute a systematic bias favoring an association between ambient PM<sub>2.5</sub> and clinical  
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34 381 events<sup>32 33</sup>. Secondly, diagnosis misclassification was possible but was not likely to confound  
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36 382 the relationship because it is not likely to vary on the same temporal scale as PM<sub>2.5</sub>. Thirdly,  
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38 383 there is the possibility that some unmeasured time variant factors may have confounded our  
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40 384 estimates (smoking status, medication usage, behaviors, lipid levels, C-reactive protein levels,  
41  
42 385 etc.). Data availability restricted the consideration of some patient level confounders, such as  
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44 386 smoking status, to values recorded at baseline. We used a time stratified design to control for  
45  
46 387 time-varying confounding for time scales larger than a month, such as the number of patients  
47  
48 388 enrolled in the USRDS. At scales smaller than a month, the control of person time was not  
49  
50 389 possible. Lastly, generalization of the results is limited to the Medicare population with ESRD  
51  
52 390 managed with hemodialysis treatment. Future studies are needed to understand PM<sub>2.5</sub>-related  
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3 391 impacts on specific health conditions, and if health impacts vary based on race, socioeconomic  
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5 392 indicators, or other individual and population factors.  
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9 394 **Conclusion**

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11 395 In conclusion, this United States wide cohort study identified increased risk in patients receiving  
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13 396 in-center hemodialysis associated with short-term increases in ambient air particle pollution.  
14  
15 397 Elevated PM<sub>2.5</sub> concentrations were found to be associated with increased inpatient hospital  
16  
17 398 admissions related to cardiovascular causes, and an increased likelihood of hospital  
18  
19 399 readmission following cardiovascular and respiratory related hospitalizations. Medicare  
20  
21 400 spending for beneficiaries with ESRD is high. Traditional efforts to reduce the burden of disease  
22  
23 401 focus on patient factors; however, these data suggest that air particle pollution is a factor that  
24  
25 402 contributes to increased risks for hospital admission and subsequent readmission. To reduce  
26  
27 403 PM<sub>2.5</sub>-related morbidities, we echo the recommendations made in the Million Hearts initiative,  
28  
29 404 that healthcare systems, insurers, physicians, and health care professionals should  
30  
31 405 incorporate health risks related to ambient PM into patient care.  
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37 407 **Disclaimer**

38  
39 408 The research described in this article has been reviewed by the Center for Public Health and the  
40  
41 409 Environment, U.S. Environmental Protection Agency, and approved for publication. Approval  
42  
43 410 does not signify that the contents necessarily reflect the views and policies of the Agency, nor  
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45 411 does the mention of trade names of commercial products constitute endorsement or  
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47 412 recommendation for use.  
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3 417 Schwartz and Qian Di. The interpretation and reporting of these data are the responsibility of the  
4  
5 418 author(s) and in no way should be seen as an official policy or interpretation of the U.S.  
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7 419 government.  
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9 420

### 11 421 **Contributors**

12  
13 422 LHW, AGR conceived and designed the study. TJW, WEC, and AVK provided subject expert  
14  
15 423 input into the study design and interpretation of evidence. AVK, QD, and CWC provided access  
16  
17 424 to the data for the study; LHW managed and analyzed the data and AGR oversaw the analysis.  
18  
19 425 LHW and AGR wrote the first draft of the manuscript. LHW, YX, AVK, CWC, TJW, WEC, and  
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41 434

### 43 435 **Competing Interests**

44  
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56 441

### 442 **Ethical approval**

443 This study was reviewed by the institutional review board at the University of North Carolina at  
444 Chapel Hill and determined to be exempt based on the study design involving secondary data  
445 analysis (IRB Number: 20-0984).

446

### 447 **Data sharing**

448 Data access to USRDS data sets is through an internal data use agreement with the University  
449 of North Carolina at Chapel Hill's Cecil G. Sheps Center. PM<sub>2.5</sub> data was obtained through  
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451 (Tsinghua University). For general data sharing inquiries, contact [rappold.ana@epa.gov](mailto:rappold.ana@epa.gov) or  
452 [wyatt.lauren@epa.gov](mailto:wyatt.lauren@epa.gov).

453

### 454 **Transparency**

455 The lead and corresponding authors (LHW and AGR) affirm that the manuscript is an honest,  
456 accurate, and transparent account of the study being reported; that no important aspects of the  
457 study have been omitted; and that any discrepancies from the study as planned (and, if  
458 relevant, registered) have been explained.

459

### 460 **Patient and Public Involvement**

461 This study utilized a deidentified database, thus contact with patients was not possible.

462

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32 482 of my co-authors are.\*

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For peer review only

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3 635 **Figure 1.** The relative risk (RR, 95%CI) for an all-cause early and late-readmission following all-  
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5 636 cause and cause-specific discharges. Discharges are color coded: all-cause discharges are  
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7 637 indicated in black, cardiovascular causes in orange, and respiratory causes in blue. Early-  
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9 638 readmissions are indicated with filled in circles, late-readmissions with open circles. RR is  
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11 639 expressed per 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ .  
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14 640  
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16 641 **Figure 2.** The relative risk (RR, 95%CI) of cause-specific early and late-readmission following  
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18 642 all-cause discharge. Readmission causes are color coded: all-cause readmissions are indicated  
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20 643 in black, cardiovascular causes in orange, and respiratory causes in blue. RR is expressed per  
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22 644 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ .  
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25 645  
26 646 **Figure 3.** Mean proportion (95%CI) of all-cause and cause-specific hospital admissions, early  
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28 647 readmissions (1-7d), and late readmissions (8-30d) with respect to  $\text{PM}_{2.5}$  ( $\mu\text{g}/\text{m}^3$ ). Hash marks  
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30 648 above the x-axis represent the density of daily county  $\text{PM}_{2.5}$ . The 95% CI under 15.9  $\mu\text{g}/\text{m}^3$  is  
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32 649 shaded darker to indicate where 90 percent of the data falls.  
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37 651 **Figure 4.** Average daily county  $\text{PM}_{2.5}$  ( $\mu\text{g}/\text{m}^3$ ) between 2008 and 2014 (A) and the attributable  
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39 652 fraction for early-readmission following an all-cause discharge based on the average  $\text{PM}_{2.5}$  (B)  
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41 653 for the 530 counties included in the study.  
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655 **Table 1.** Baseline Demographic Characteristics of the Study Population Between 2008 and  
 656 2014 by Hospital Admission Category.

Characteristic	No. (%)		
	All-cause N = 351,294	Cardiovascular n = 262,385	Respiratory n = 247,829
Age (yr), mean (SD)	64.69 (14.70)	65.58 (14.53)	65.61 (14.48)
Male sex (%)	190,716 (54.3)	140,206 (53.4)	132,288 (53.4)
Race			
White	209,921 (59.8)	155,405 (59.2)	147,204 (59.4)
Black	122,943 (35.0)	93,325 (35.6)	87,831 (35.4)
Other	18,430 (5.2)	13,655 (5.2)	12,794 (5.2)
Smoking status at initiation (no)	330,837 (94.2)	246,634 (94.0)	232,396 (93.8)

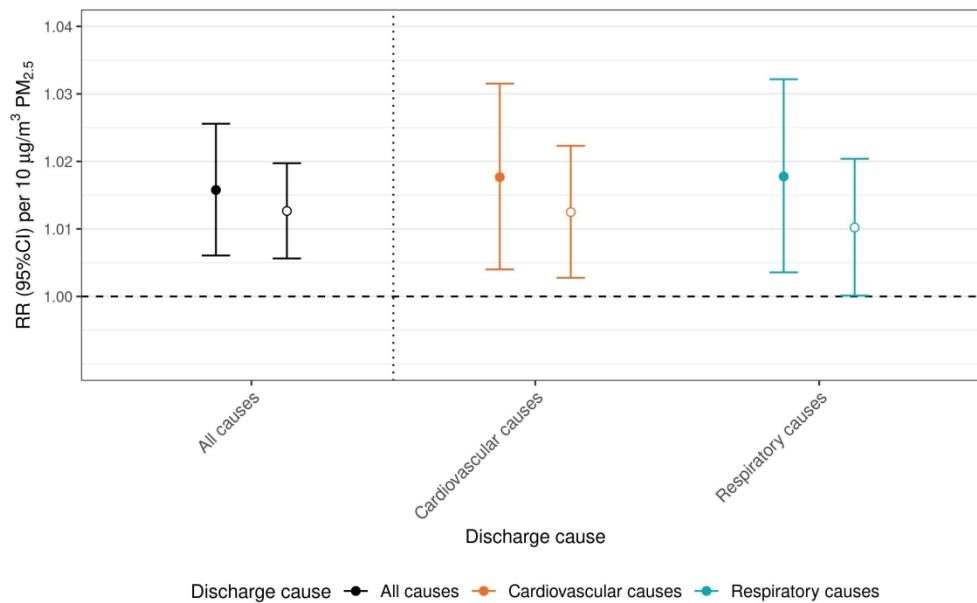
657

658 **Table 2.** Hospital Admission Characteristics Among the Study Population Between 2008 and  
659 2014.

Outcome	Number of Events (Number of Unique Patients)		
	All-cause	Cardiovascular	Respiratory
Admissions	1,801,966 (351,294)	832,255 (262,385)	766,447 (247,829)
Discharged alive	1,493,795 (312,521)	685,680 (229,780)	637,250 (217,221)
Early-readmission (1-7d)	176,822 (91,508)	83,193 (52,374)	78,392 (49,343)
Late-readmission (8-30d)	317,948 (130, 454)	150,080 (80,851)	141,656 (76,444)
Length of stay, d			
Mean (SD)	6.98 (10.68)	7.05 (10.34)	7.07 (10.38)
Median (IQR)	4 (2-7)	4 (2-8)	4 (2-8)
Hospital visits in prior year			
3+ visits	637,503 (123,949)	307,891 (93,399)	292,803 (89,905)
Mean (SD)	2.97 (3.80)	3.14 (3.95)	3.21 (3.89)
Median (IQR)	2 (1-4)	2 (1-4)	2 (1-4)

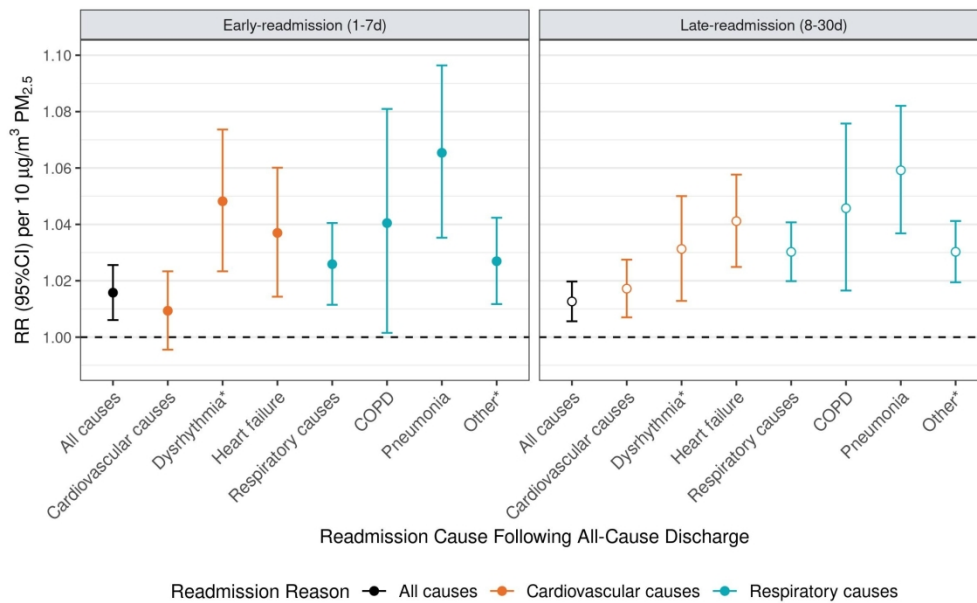
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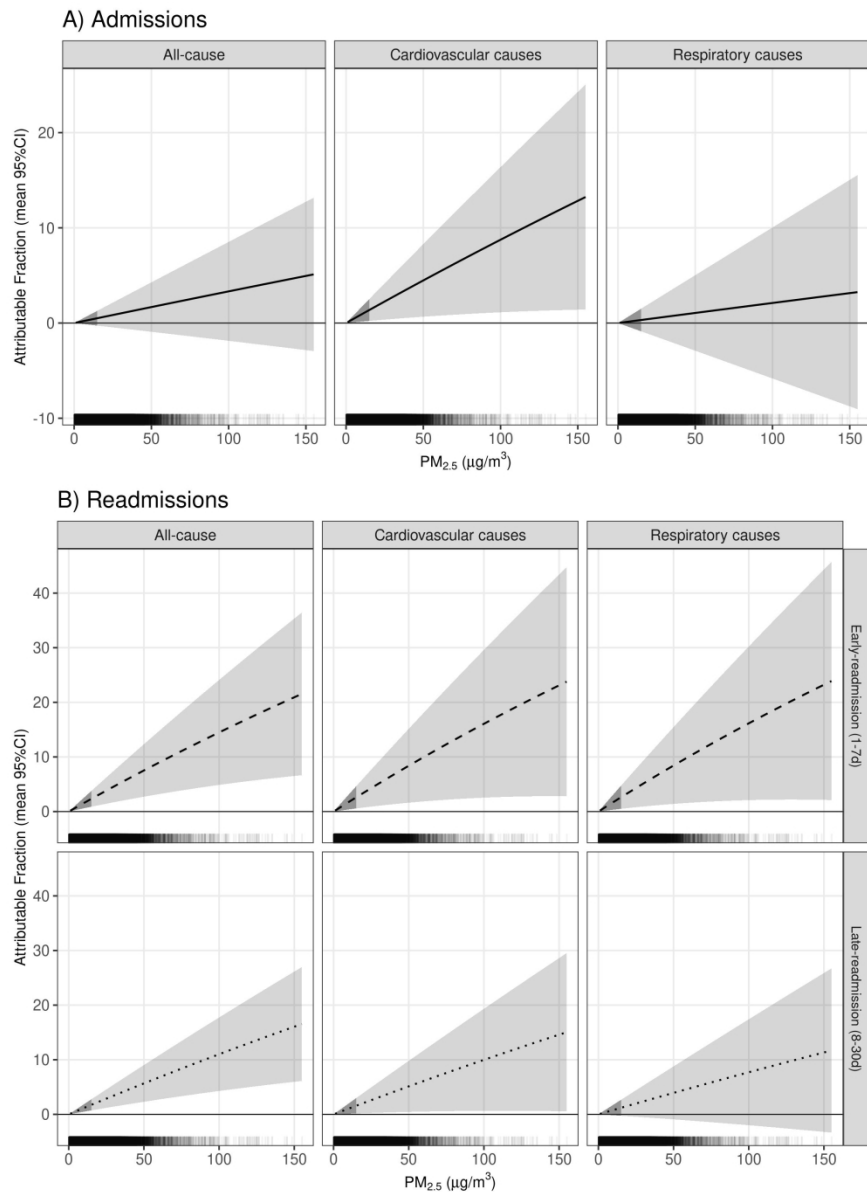
The relative risk (RR, 95%CI) for an all-cause early and late-readmission following all-cause and cause-specific discharges. Discharges are color coded: all-cause discharges are indicated in black, cardiovascular causes in orange, and respiratory causes in blue. Early-readmissions are indicated with filled in circles, late-readmissions with open circles. RR is expressed per 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>.

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The relative risk (RR, 95%CI) of cause-specific early and late-readmission following all-cause discharge. Readmission causes are color coded: all-cause readmissions are indicated in black, cardiovascular causes in orange, and respiratory causes in blue. RR is expressed per 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>.

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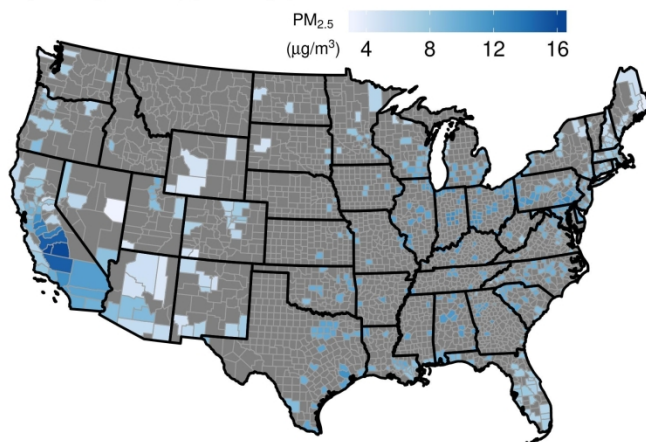


45 Mean proportion (95%CI) of all-cause and cause-specific hospital admissions, early readmissions (1-7d),  
 46 and late readmissions (8-30d) with respect to PM<sub>2.5</sub> (µg/m<sup>3</sup>). Hash marks above the x-axis represent the  
 47 density of daily county PM<sub>2.5</sub>. The 95% CI under 15.9 µg/m<sup>3</sup> is shaded darker to indicate where 90 percent  
 48 of the data falls.

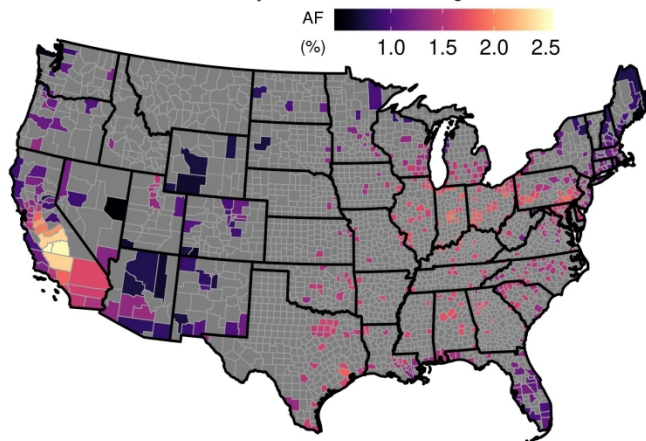
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A) Daily county average PM<sub>2.5</sub> (7yr average)



B) Exposure attributable fraction for early-readmission following an all-cause discharge



Average daily county PM<sub>2.5</sub> (µg/m<sup>3</sup>) between 2008 and 2014 (A) and the attributable fraction for early-readmission following an all-cause discharge based on the average PM<sub>2.5</sub> (B) for the 530 counties included in the study.

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1 **Supplemental Materials**

3 **Table S1.** Summary statistics of PM<sub>2.5</sub> and meteorological variables across 530 counties.

Variable	Mean ± SD	Minimum	Maximum
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	9.29 ± 5.39	0.05	155.16
Temperature (°F)	56.37 ± 18.50	-37.30	104.74
Relative humidity (%)	65.24 ± 16.24	0	100

4

**Table S2.** The relative risk (RR, 95%CI) for an all-cause, cardiovascular, and respiratory related early and late-readmission following all-cause and cause-specific discharges. RR is expressed per 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ . Models presented include the main model presented in the paper (model 1) where  $\text{PM}_{2.5}$  is considered as a linear variable and a model that considers  $\text{PM}_{2.5}$  as a non-linear variable (model 2).

Readmission model	Discharge cause	Readmission cause	Model 1 PM linear RR (95%CI)	Model 2 PM non-linear RR (95%CI)
Early-readmission (1-7d)	All Causes	All Causes	1.016 (1.006, 1.026)	1.089 (1.016, 1.168)
Early-readmission (1-7d)	All Causes	All Cardiovascular	1.009 (0.996, 1.023)	0.984 (0.892, 1.085)
Early-readmission (1-7d)	All Causes	Dysrhythmia*	1.048 (1.023, 1.074)	0.898 (0.754, 1.070)
Early-readmission (1-7d)	All Causes	Heart failure	1.037 (1.014, 1.060)	1.065 (0.906, 1.252)
Early-readmission (1-7d)	All Causes	Hypertension	1.007 (0.990, 1.025)	1.011 (0.895, 1.141)
Early-readmission (1-7d)	All Causes	Ischemic heart disease	0.970 (0.929, 1.012)	0.910 (0.678, 1.222)
Early-readmission (1-7d)	All Causes	Myocardial infarction	0.955 (0.906, 1.007)	0.940 (0.651, 1.358)
Early-readmission (1-7d)	All Causes	Peripheral arterial disease	0.900 (0.748, 1.083)	0.389 (0.121, 1.254)
Early-readmission (1-7d)	All Causes	All Respiratory	1.026 (1.011, 1.040)	1.082 (0.977, 1.199)
Early-readmission (1-7d)	All Causes	Asthma	1.102 (0.992, 1.226)	0.464 (0.240, 0.900)
Early-readmission (1-7d)	All Causes	COPD	1.040 (1.002, 1.081)	1.021 (0.763, 1.366)
Early-readmission (1-7d)	All Causes	Other*	1.027 (1.012, 1.042)	1.093 (0.981, 1.218)
Early-readmission (1-7d)	All Causes	Pneumonia	1.065 (1.035, 1.096)	1.263 (1.012, 1.576)
Early-readmission (1-7d)	All Causes	Pulmonary embolism	1.047 (0.930, 1.179)	0.911 (0.371, 2.233)
Early-readmission (1-7d)	All Cardiovascular	All Causes	1.018 (1.004, 1.032)	1.034 (0.933, 1.145)
Early-readmission (1-7d)	All Cardiovascular	All Cardiovascular	1.006 (0.989, 1.024)	0.938 (0.823, 1.070)
Early-readmission (1-7d)	All Cardiovascular	Dysrhythmia*	1.043 (1.012, 1.076)	1.006 (0.793, 1.278)
Early-readmission (1-7d)	All Cardiovascular	Heart failure	1.027 (0.999, 1.056)	0.994 (0.810, 1.221)
Early-readmission (1-7d)	All Cardiovascular	Hypertension	1.006 (0.985, 1.028)	0.911 (0.776, 1.069)
Early-readmission (1-7d)	All Cardiovascular	Ischemic heart disease	1.014 (0.963, 1.069)	0.888 (0.603, 1.309)
Early-readmission (1-7d)	All Cardiovascular	Myocardial infarction	0.987 (0.924, 1.054)	0.901 (0.557, 1.459)
Early-readmission (1-7d)	All Cardiovascular	Peripheral arterial disease	0.924 (0.693, 1.230)	0.195 (0.044, 0.875)

1	Early-readmission (1-7d)	All Cardiovascular	All Respiratory	1.025 (1.006, 1.045)	1.015 (0.882, 1.169)
2	Early-readmission (1-7d)	All Cardiovascular	Asthma	1.086 (0.948, 1.243)	0.335 (0.144, 0.781)
3	Early-readmission (1-7d)	All Cardiovascular	COPD	1.035 (0.985, 1.087)	0.877 (0.604, 1.275)
4	Early-readmission (1-7d)	All Cardiovascular	Other*	1.025 (1.005, 1.045)	1.067 (0.919, 1.238)
5	Early-readmission (1-7d)	All Cardiovascular	Pneumonia	1.075 (1.035, 1.117)	1.124 (0.831, 1.521)
6	Early-readmission (1-7d)	All Cardiovascular	Pulmonary embolism	1.134 (0.986, 1.303)	1.879 (0.544, 6.491)
7	Early-readmission (1-7d)	All Respiratory	All Causes	1.018 (1.004, 1.032)	1.041 (0.939, 1.154)
8	Early-readmission (1-7d)	All Respiratory	All Cardiovascular	1.007 (0.988, 1.026)	1.011 (0.880, 1.161)
9	Early-readmission (1-7d)	All Respiratory	Dysrhythmia*	1.045 (1.011, 1.080)	0.936 (0.731, 1.198)
10	Early-readmission (1-7d)	All Respiratory	Heart failure	1.017 (0.988, 1.047)	0.989 (0.802, 1.220)
11	Early-readmission (1-7d)	All Respiratory	Hypertension	1.014 (0.990, 1.038)	1.056 (0.885, 1.260)
12	Early-readmission (1-7d)	All Respiratory	Ischemic heart disease	0.971 (0.918, 1.028)	0.783 (0.534, 1.149)
13	Early-readmission (1-7d)	All Respiratory	Myocardial infarction	0.938 (0.872, 1.009)	0.682 (0.422, 1.102)
14	Early-readmission (1-7d)	All Respiratory	Peripheral arterial disease	0.857 (0.603, 1.219)	0.189 (0.035, 1.004)
15	Early-readmission (1-7d)	All Respiratory	All Respiratory	1.025 (1.006, 1.044)	1.087 (0.947, 1.248)
16	Early-readmission (1-7d)	All Respiratory	Asthma	1.074 (0.938, 1.230)	0.407 (0.180, 0.920)
17	Early-readmission (1-7d)	All Respiratory	COPD	1.041 (0.993, 1.092)	0.856 (0.600, 1.223)
18	Early-readmission (1-7d)	All Respiratory	Other*	1.028 (1.008, 1.048)	1.114 (0.963, 1.289)
19	Early-readmission (1-7d)	All Respiratory	Pneumonia	1.049 (1.011, 1.089)	1.185 (0.890, 1.578)
20	Early-readmission (1-7d)	All Respiratory	Pulmonary embolism	1.075 (0.913, 1.265)	0.921 (0.265, 3.202)
21	Late-readmission (8-30d)	All Causes	All Causes	1.013 (1.006, 1.020)	1.024 (0.974, 1.077)
22	Late-readmission (8-30d)	All Causes	All Cardiovascular	1.017 (1.007, 1.027)	1.071 (0.995, 1.153)
23	Late-readmission (8-30d)	All Causes	Dysrhythmia*	1.031 (1.013, 1.050)	1.103 (0.961, 1.266)
24	Late-readmission (8-30d)	All Causes	Heart failure	1.041 (1.025, 1.058)	1.027 (0.915, 1.154)
25	Late-readmission (8-30d)	All Causes	Hypertension	1.010 (0.998, 1.023)	1.036 (0.947, 1.135)
26	Late-readmission (8-30d)	All Causes	Ischemic heart disease	1.008 (0.975, 1.042)	0.858 (0.676, 1.089)
27	Late-readmission (8-30d)	All Causes	Myocardial infarction	0.974 (0.933, 1.017)	0.722 (0.538, 0.968)
28	Late-readmission (8-30d)	All Causes	Peripheral arterial disease	1.003 (0.873, 1.153)	1.367 (0.511, 3.653)
29	Late-readmission (8-30d)	All Causes	All Respiratory	1.030 (1.020, 1.041)	1.083 (1.004, 1.169)
30	Late-readmission (8-30d)	All Causes	Asthma	1.071 (0.998, 1.150)	1.327 (0.739, 2.382)
31	Late-readmission (8-30d)	All Causes	COPD	1.046 (1.017, 1.076)	1.001 (0.813, 1.232)
32	Late-readmission (8-30d)	All Causes	Other*	1.030 (1.019, 1.041)	1.113 (1.028, 1.206)

Late-readmission (8-30d)	All Causes	Pneumonia	1.059 (1.037, 1.082)	1.104 (0.940, 1.297)
Late-readmission (8-30d)	All Causes	Pulmonary embolism	1.063 (0.959, 1.178)	1.774 (0.742, 4.240)
Late-readmission (8-30d)	All Cardiovascular	All Causes	1.012 (1.003, 1.022)	1.030 (0.956, 1.109)
Late-readmission (8-30d)	All Cardiovascular	All Cardiovascular	1.016 (1.003, 1.029)	1.048 (0.950, 1.157)
Late-readmission (8-30d)	All Cardiovascular	Dysrhythmia*	1.035 (1.012, 1.058)	1.058 (0.884, 1.266)
Late-readmission (8-30d)	All Cardiovascular	Heart failure	1.035 (1.015, 1.055)	1.055 (0.907, 1.227)
Late-readmission (8-30d)	All Cardiovascular	Hypertension	1.007 (0.991, 1.023)	1.002 (0.889, 1.129)
Late-readmission (8-30d)	All Cardiovascular	Ischemic heart disease	0.977 (0.936, 1.020)	0.740 (0.542, 1.010)
Late-readmission (8-30d)	All Cardiovascular	Myocardial infarction	0.946 (0.894, 1.002)	0.593 (0.405, 0.868)
Late-readmission (8-30d)	All Cardiovascular	Peripheral arterial disease	1.013 (0.815, 1.258)	1.084 (0.257, 4.566)
Late-readmission (8-30d)	All Cardiovascular	All Respiratory	1.028 (1.015, 1.042)	1.086 (0.978, 1.206)
Late-readmission (8-30d)	All Cardiovascular	Asthma	1.057 (0.963, 1.160)	1.424 (0.654, 3.097)
Late-readmission (8-30d)	All Cardiovascular	COPD	1.047 (1.011, 1.084)	0.840 (0.645, 1.094)
Late-readmission (8-30d)	All Cardiovascular	Other*	1.028 (1.014, 1.042)	1.130 (1.012, 1.262)
Late-readmission (8-30d)	All Cardiovascular	Pneumonia	1.052 (1.023, 1.082)	1.203 (0.963, 1.504)
Late-readmission (8-30d)	All Cardiovascular	Pulmonary embolism	1.036 (0.909, 1.181)	1.251 (0.389, 4.020)
Late-readmission (8-30d)	All Respiratory	All Causes	1.010 (1.000, 1.020)	1.039 (0.963, 1.120)
Late-readmission (8-30d)	All Respiratory	All Cardiovascular	1.020 (1.006, 1.034)	1.076 (0.970, 1.194)
Late-readmission (8-30d)	All Respiratory	Dysrhythmia*	1.037 (1.012, 1.062)	1.053 (0.869, 1.277)
Late-readmission (8-30d)	All Respiratory	Heart failure	1.034 (1.013, 1.055)	1.130 (0.968, 1.319)
Late-readmission (8-30d)	All Respiratory	Hypertension	1.013 (0.996, 1.030)	1.040 (0.914, 1.184)
Late-readmission (8-30d)	All Respiratory	Ischemic heart disease	0.975 (0.932, 1.002)	0.759 (0.553, 1.040)
Late-readmission (8-30d)	All Respiratory	Myocardial infarction	0.948 (0.893, 1.006)	0.710 (0.472, 1.069)
Late-readmission (8-30d)	All Respiratory	Peripheral arterial disease	1.102 (0.894, 1.359)	1.895 (0.351, 10.226)
Late-readmission (8-30d)	All Respiratory	All Respiratory	1.019 (1.005, 1.032)	1.078 (0.974, 1.193)
Late-readmission (8-30d)	All Respiratory	Asthma	0.996 (0.905, 1.095)	1.200 (0.579, 2.489)
Late-readmission (8-30d)	All Respiratory	COPD	1.026 (0.991, 1.063)	0.887 (0.691, 1.138)
Late-readmission (8-30d)	All Respiratory	Other*	1.019 (1.005, 1.033)	1.119 (1.005, 1.246)
Late-readmission (8-30d)	All Respiratory	Pneumonia	1.062 (1.033, 1.092)	1.178 (0.947, 1.465)
Late-readmission (8-30d)	All Respiratory	Pulmonary embolism	1.070 (0.915, 1.252)	1.848 (0.599, 5.701)

**Table S3.** Relative risk (RR ± 95% CI) of all-cause and cause-specific daily county admission rates associated with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> for exposure lags 0-14 days. Models presented include the main model presented in the paper (model 1) where PM<sub>2.5</sub> is considered as a linear variable and a model that considers PM<sub>2.5</sub> as a non-linear variable (model 2). Additionally, the main model was stratified on the median of percent of individuals below poverty with respect to county (12.5% below poverty), with model 3 representing the model with counties with high % below poverty and model 4 representing counties with low % below poverty.

		Model 1, PM linear	Model 2, PM non-linear	Model 3, PM linear high % poverty	Model 4, PM linear low % poverty
Endpoint	Lag	RR (95%CI)	RR (95%CI)	RR (95%CI)	RR (95%CI)
All-cause	0	1.003 (0.998, 1.009)	0.998 (1.009, 0.996)	1.009 (0.996, 0.978)	0.996 (0.978, 1.015)
All-cause	1	0.997 (0.99, 1.003)	0.99 (1.003, 0.988)	1.003 (0.988, 0.968)	0.988 (0.968, 1.008)
All-cause	2	0.999 (0.992, 1.005)	0.992 (1.005, 0.998)	1.005 (0.998, 0.978)	0.998 (0.978, 1.018)
All-cause	3	0.996 (0.99, 1.002)	0.99 (1.002, 1.011)	1.002 (1.011, 0.991)	1.011 (0.991, 1.032)
All-cause	4	1.002 (0.996, 1.008)	0.996 (1.008, 1.006)	1.008 (1.006, 0.986)	1.006 (0.986, 1.027)
All-cause	5	1.001 (0.995, 1.007)	0.995 (1.007, 0.977)	1.007 (0.977, 0.957)	0.977 (0.957, 0.997)
All-cause	6	1.001 (0.995, 1.008)	0.995 (1.008, 0.988)	1.008 (0.988, 0.968)	0.988 (0.968, 1.009)
All-cause	7	1 (0.993, 1.006)	0.993 (1.006, 0.982)	1.006 (0.982, 0.961)	0.982 (0.961, 1.003)
All-cause	8	1.004 (0.997, 1.01)	0.997 (1.01, 1.001)	1.01 (1.001, 0.981)	1.001 (0.981, 1.022)
All-cause	9	1.004 (0.998, 1.01)	0.998 (1.01, 0.985)	1.01 (0.985, 0.965)	0.985 (0.965, 1.006)
All-cause	10	0.999 (0.993, 1.005)	0.993 (1.005, 1.02)	1.005 (1.02, 1)	1.02 (1, 1.042)
All-cause	11	0.996 (0.989, 1.002)	0.989 (1.002, 0.998)	1.002 (0.998, 0.978)	0.998 (0.978, 1.019)
All-cause	12	1.002 (0.996, 1.009)	0.996 (1.009, 1.006)	1.009 (1.006, 0.986)	1.006 (0.986, 1.028)
All-cause	13	0.995 (0.989, 1.001)	0.989 (1.001, 0.979)	1.001 (0.979, 0.959)	0.979 (0.959, 0.999)
All-cause	14	1 (0.994, 1.005)	0.994 (1.005, 0.987)	1.005 (0.987, 0.968)	0.987 (0.968, 1.006)
Cardiovascular related causes	0	1.009 (1.002, 1.017)	1.002 (1.017, 0.994)	1.017 (0.994, 0.967)	0.994 (0.967, 1.022)
Cardiovascular related causes	1	0.995 (0.986, 1.004)	0.986 (1.004, 0.978)	1.004 (0.978, 0.949)	0.978 (0.949, 1.007)

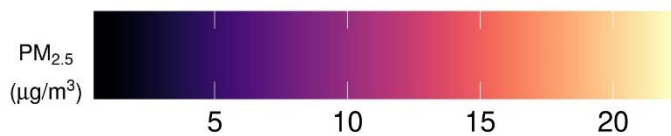
Cardiovascular related causes	2	0.998 (0.988, 1.007)	0.988 (1.007, 0.997)	1.007 (0.997, 0.968)	0.997 (0.968, 1.028)
Cardiovascular related causes	3	0.993 (0.984, 1.002)	0.984 (1.002, 1)	1.002 (1, 0.97)	1 (0.97, 1.03)
Cardiovascular related causes	4	1.003 (0.994, 1.012)	0.994 (1.012, 1.029)	1.012 (1.029, 0.999)	1.029 (0.999, 1.06)
Cardiovascular related causes	5	1.004 (0.994, 1.013)	0.994 (1.013, 0.976)	1.013 (0.976, 0.947)	0.976 (0.947, 1.006)
Cardiovascular related causes	6	0.999 (0.99, 1.008)	0.99 (1.008, 0.991)	1.008 (0.991, 0.962)	0.991 (0.962, 1.022)
Cardiovascular related causes	7	1.005 (0.995, 1.014)	0.995 (1.014, 0.979)	1.014 (0.979, 0.949)	0.979 (0.949, 1.01)
Cardiovascular related causes	8	1.002 (0.993, 1.011)	0.993 (1.011, 0.999)	1.011 (0.999, 0.969)	0.999 (0.969, 1.03)
Cardiovascular related causes	9	1.009 (1, 1.018)	1 (1.018, 0.992)	1.018 (0.992, 0.963)	0.992 (0.963, 1.023)
Cardiovascular related causes	10	0.992 (0.983, 1.001)	0.983 (1.001, 0.996)	1.001 (0.996, 0.966)	0.996 (0.966, 1.026)
Cardiovascular related causes	11	0.999 (0.99, 1.008)	0.99 (1.008, 1.017)	1.008 (1.017, 0.987)	1.017 (0.987, 1.048)
Cardiovascular related causes	12	0.999 (0.99, 1.008)	0.99 (1.008, 1.004)	1.008 (1.004, 0.974)	1.004 (0.974, 1.035)
Cardiovascular related causes	13	0.996 (0.987, 1.005)	0.987 (1.005, 0.969)	1.005 (0.969, 0.94)	0.969 (0.94, 0.999)
Cardiovascular related causes	14	1.002 (0.994, 1.009)	0.994 (1.009, 1.007)	1.009 (1.007, 0.978)	1.007 (0.978, 1.036)
Respiratory related causes	0	1.002 (0.994, 1.01)	0.994 (1.01, 0.998)	1.01 (0.998, 0.97)	0.998 (0.97, 1.027)
Respiratory related causes	1	0.998 (0.989, 1.008)	0.989 (1.008, 0.977)	1.008 (0.977, 0.948)	0.977 (0.948, 1.008)
Respiratory related causes	2	0.995 (0.985, 1.004)	0.985 (1.004, 1.007)	1.004 (1.007, 0.976)	1.007 (0.976, 1.039)
Respiratory related causes	3	0.995 (0.985, 1.004)	0.985 (1.004, 1.006)	1.004 (1.006, 0.975)	1.006 (0.975, 1.038)
Respiratory related causes	4	0.999 (0.989, 1.008)	0.989 (1.008, 0.997)	1.008 (0.997, 0.967)	0.997 (0.967, 1.029)

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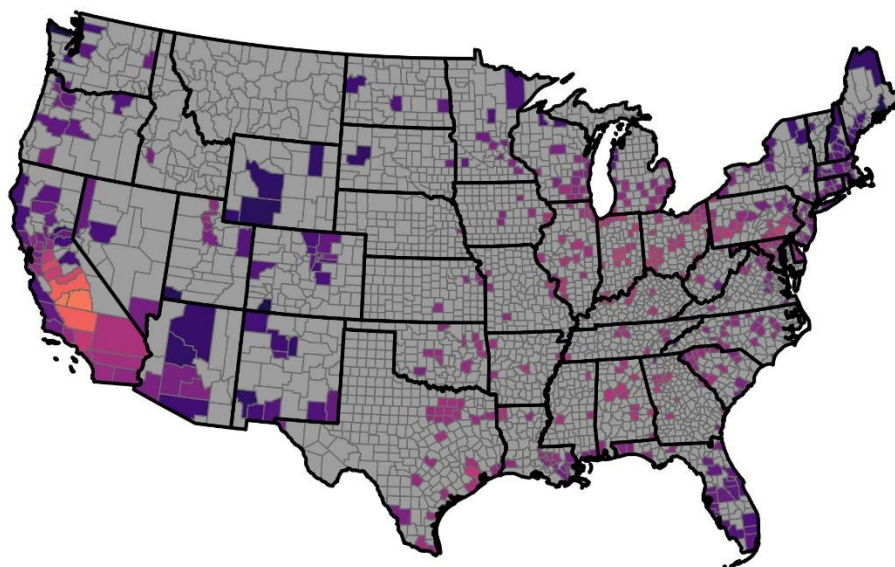
Respiratory related causes	5	1.009 (1, 1.019)	1 (1.019, 0.993)	1.019 (0.993, 0.962)	0.993 (0.962, 1.024)
Respiratory related causes	6	0.999 (0.99, 1.009)	0.99 (1.009, 0.974)	1.009 (0.974, 0.944)	0.974 (0.944, 1.005)
Respiratory related causes	7	0.999 (0.989, 1.009)	0.989 (1.009, 0.984)	1.009 (0.984, 0.952)	0.984 (0.952, 1.017)
Respiratory related causes	8	1.005 (0.996, 1.015)	0.996 (1.015, 1.011)	1.015 (1.011, 0.98)	1.011 (0.98, 1.043)
Respiratory related causes	9	1.008 (0.999, 1.018)	0.999 (1.018, 0.979)	1.018 (0.979, 0.948)	0.979 (0.948, 1.01)
Respiratory related causes	10	0.995 (0.985, 1.004)	0.985 (1.004, 0.994)	1.004 (0.994, 0.963)	0.994 (0.963, 1.026)
Respiratory related causes	11	0.997 (0.988, 1.007)	0.988 (1.007, 1.013)	1.007 (1.013, 0.981)	1.013 (0.981, 1.046)
Respiratory related causes	12	1.002 (0.992, 1.011)	0.992 (1.011, 0.998)	1.011 (0.998, 0.967)	0.998 (0.967, 1.03)
Respiratory related causes	13	0.997 (0.987, 1.006)	0.987 (1.006, 0.979)	1.006 (0.979, 0.948)	0.979 (0.948, 1.011)
Respiratory related causes	14	1.001 (0.993, 1.009)	0.993 (1.009, 0.995)	1.009 (0.995, 0.966)	0.995 (0.966, 1.025)

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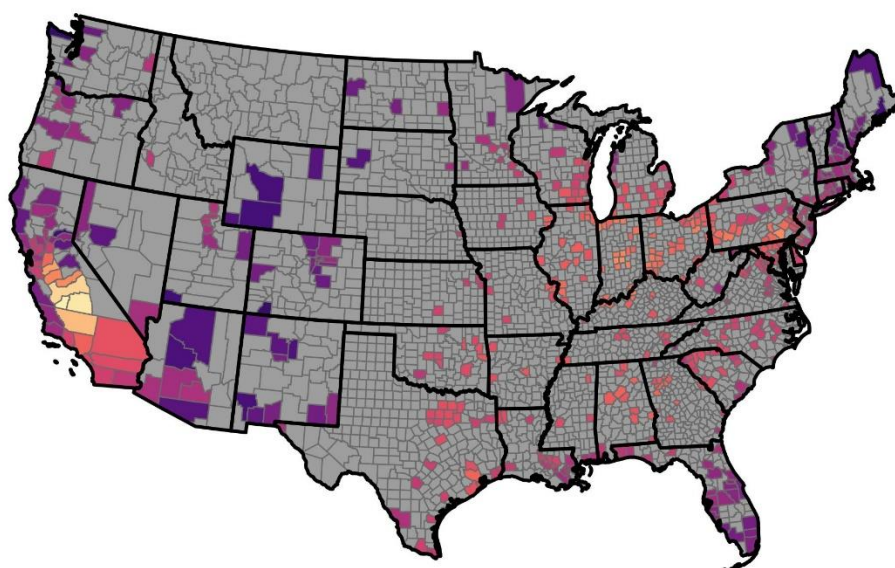




A) Long-term county PM<sub>2.5</sub> (7yr average)



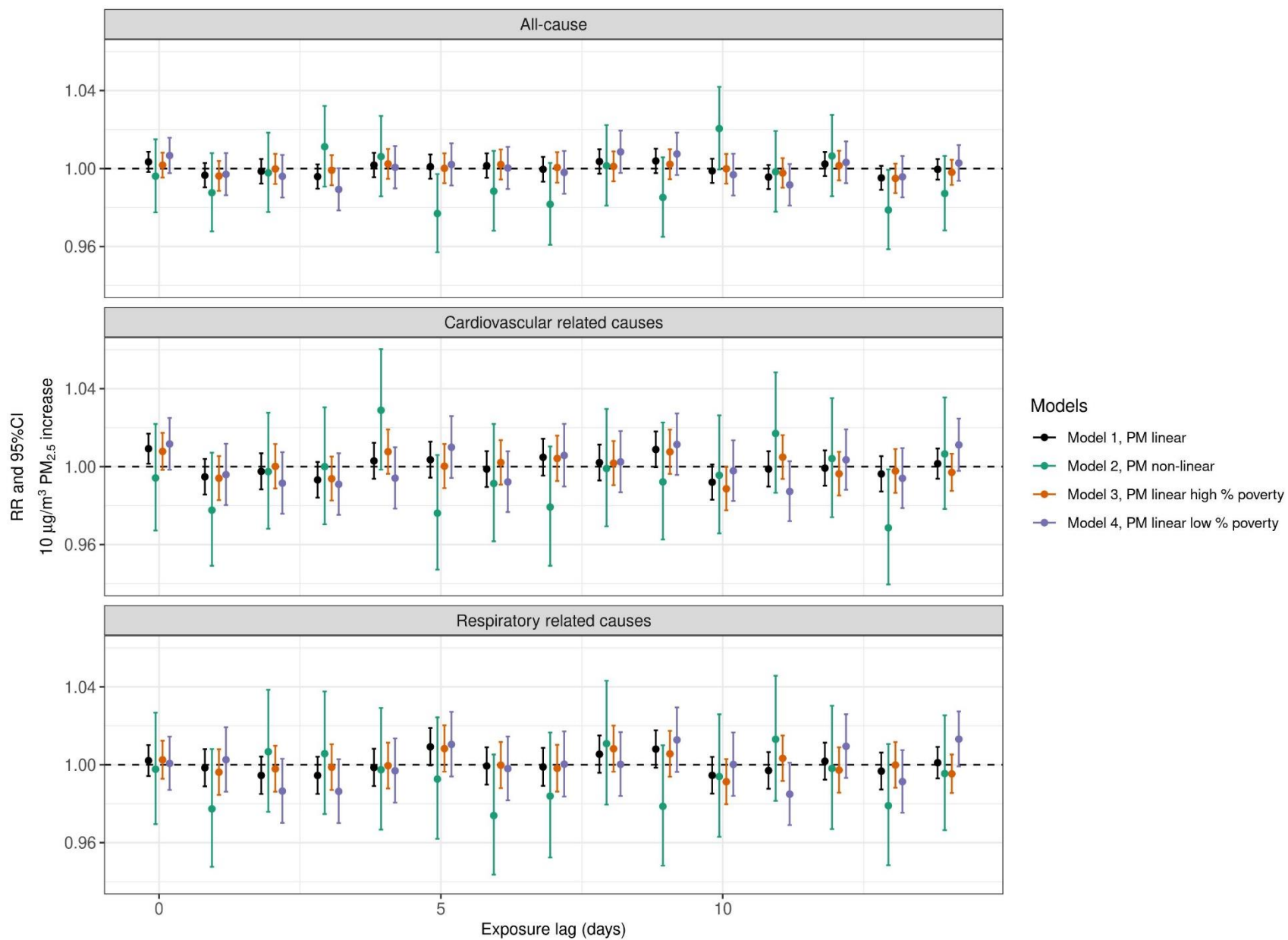
B) 20% of county days are above PM<sub>2.5</sub> (80th percentile)



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3 17 **Figure S1.** County PM<sub>2.5</sub> levels for the 530 counties included in the study. PM<sub>2.5</sub> levels shown  
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5 18 include the A) long-term average and B) 80th percentile (indicating that 20% of county days are  
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7 19 at or above this PM<sub>2.5</sub> level) for the years 2008-2014.  
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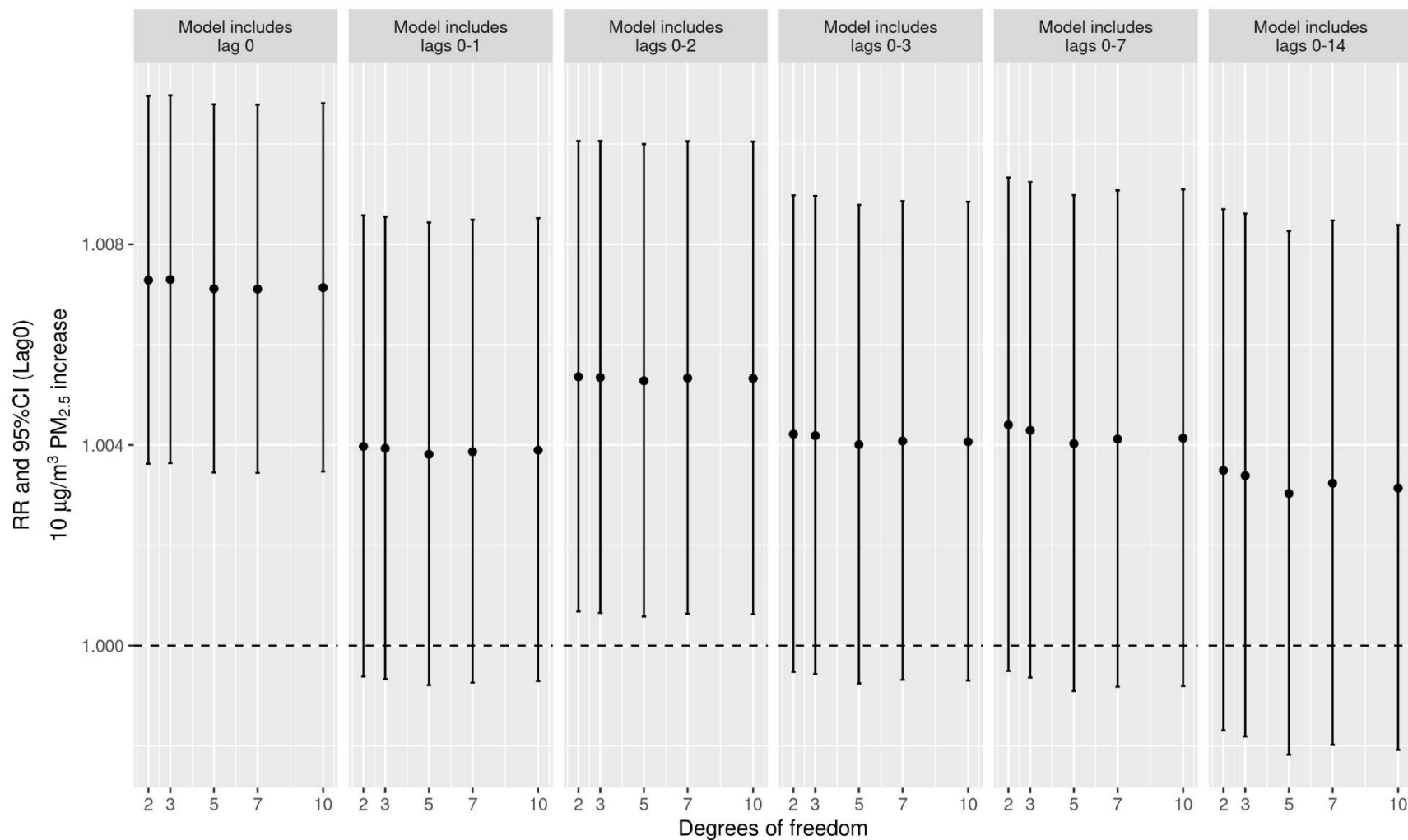
For peer review only



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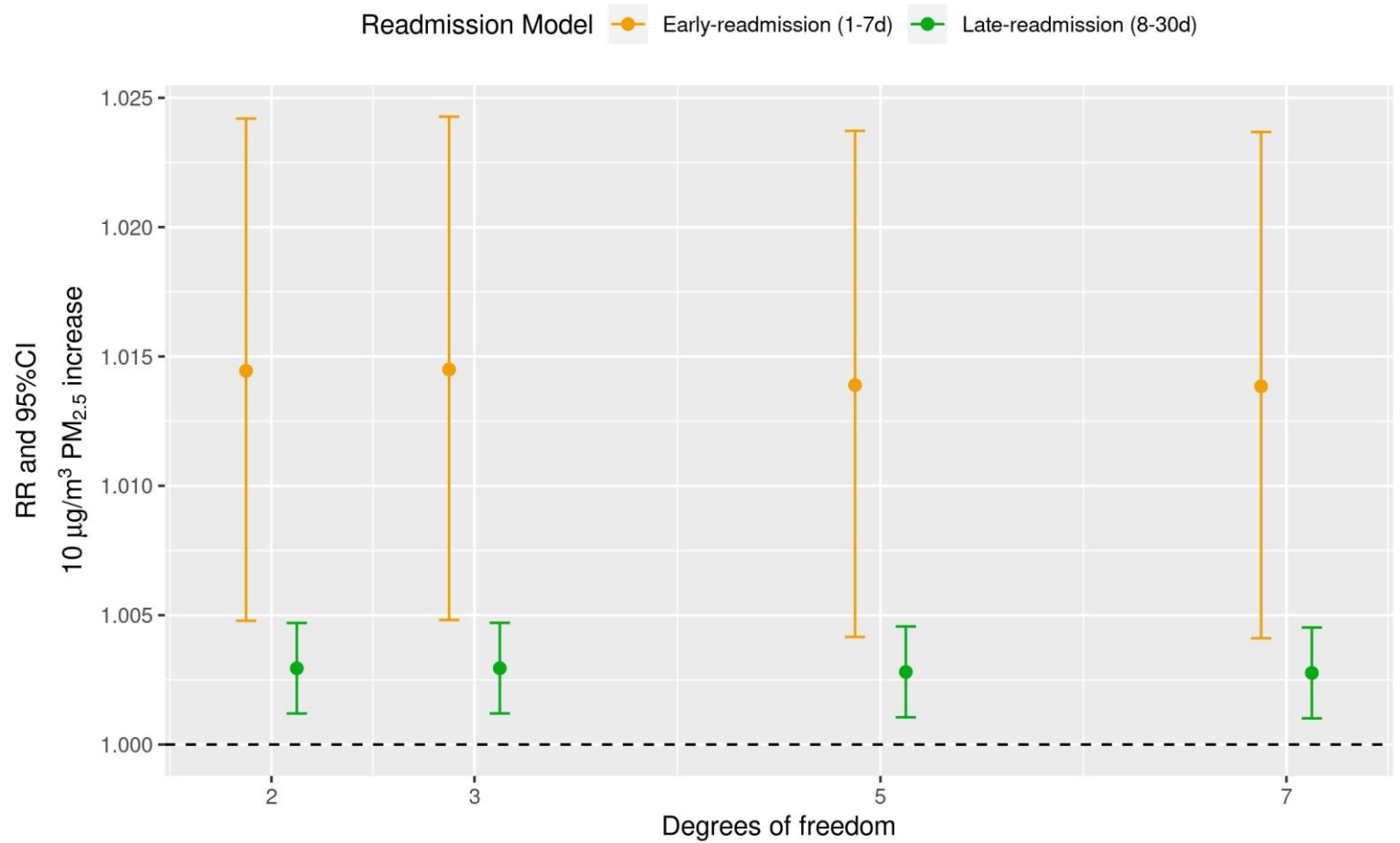
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3 21 **Figure S2.** Relative risk (RR  $\pm$  95%CI) for daily county admission rates for all-cause hospitalization associated with a 10  $\mu\text{g}/\text{m}^3$   
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5 22 increase in  $\text{PM}_{2.5}$  for exposure lags 0-14 days using an unconstrained distributed lag model. Models presented include the main  
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7 23 model presented in the paper (model 1) where  $\text{PM}_{2.5}$  is considered as a linear variable in black and a model that considers  $\text{PM}_{2.5}$  as a  
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9 24 non-linear variable (model 2) in green. Additionally, the main model was stratified on the median of percent of individuals below  
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11 25 poverty with respect to county (12.5% below poverty), with model 3 representing the model with counties with high % below poverty  
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13 26 in orange and model 4 representing counties with low % below poverty in purple (Table S2).  
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30 **Figure S3.** Sensitivity analysis for all-cause admissions models showing the impact on the lag 0 estimate from changing the number  
31 of lags considered (grouped figures), and the number of degrees of freedom (x-axis) for the temperature and relative humidity  
32 variables. Relative risk (RR ± 95%CI) of all-cause daily county admission rates associated with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> on lag 0.

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35 **Figure S4.** Sensitivity analysis for all-cause readmission models showing the impact on the lag 0 estimate from changing the number  
 36 of degrees of freedom (x-axis) for the temperature and relative humidity variables. Relative risk (RR ± 95%CI) of all-cause daily  
 37 county admission rates associated with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> on lag 0.

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7-9
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	8-9
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9-10
Outcome data	15*	Report numbers of outcome events or summary measures over time	10

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-12
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
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11	<b>Discussion</b>			
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13	Key results	18	Summarise key results with reference to study objectives	12-13
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15	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
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17	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-16
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20	Generalisability	21	Discuss the generalisability (external validity) of the study results	16
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22	<b>Other information</b>			
23	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17
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\*Give information separately for exposed and unexposed groups.

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