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Association of short-term exposure to ambient $PM_{2.5}$ with hospital admissions and 30-day readmissions in end-stage renal disease patients: population-based retrospective cohort study

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ABSTRACT

Objectives To examine the effect of short-term exposure to ambient fine particulate matter ($PM_{2.5}$) on all-cause, cardiovascular and respiratory-related hospital admissions and readmissions among patients receiving outpatient haemodialysis.

Design Retrospective cohort study.

Setting Inpatient hospitalisation claims identified from the US Renal Data System in 530 US counties.

Participants All patients receiving in-centre haemodialysis between 2008 and 2014.

Primary and secondary outcome measures Risk of all-cause, cardiovascular and respiratory-related hospital admissions and 30-day all-cause and cause-specific readmission following an all-cause, cardiovascular, and respiratory-related discharges. Readmission risk was evaluated for early (1–7 days postdischarge) and late (8–30 days postdischarge) readmission time periods. Relative risk is expressed per 10 µg/m^3 of $PM_{2.5}$.

Results Same-day ambient $PM_{2.5}$ was associated with increased hospital admission risk for cardiovascular causes (0.9%, 95% CI 0.2 to 1.7). Greater $PM_{2.5}$-related associations were observed with 30-day readmission risk. Early-readmission risk was increased by 1.6%–1.8% following all-cause (1.6%, 95% CI 0.6% to 2.6%), cardiovascular (1.8%, 95% CI 0.4% to 3.2%) and respiratory (1.8%, 95% CI 0.4% to 3.2%) discharges; while late-readmission risk increased by 1.2%–1.3% following all-cause and cardiovascular discharges. $PM_{2.5}$-related associations with readmission risk were greatest for certain cause-specific readmissions ranging 4.0%–6.5% for dysrhythmia and conduction disorder, heart failure, chronic obstructive pulmonary disease, other non-cardiac chest pain or respiratory syndrome and pneumonia. Following all-cause discharges, the cause-specific early-readmission risk was increased by 6.5% (95% CI 3.5% to 9.6%) for pneumonia, 4.8% (95% CI 2.3% to 7.4%) for dysrhythmia and conduction disorder, 3.7% (95% CI 1.4% to 6.0%) for heart failure and 2.7% (95% CI 1.2% to 4.2%) for other non-cardiac chest pain or respiratory syndrome-related causes.

Conclusions Daily ambient $PM_{2.5}$ was associated with an increased risk of cardiovascular admissions and 30-day readmissions following cardiopulmonary-related discharges in a vulnerable end-stage renal disease population. In the first week following discharge, greater $PM_{2.5}$-related risk of rehospitalisation was identified for some diagnoses.

Strengths and limitations of this study

- Nearly complete representation of hospitalisation records (>1.8 million inpatient admissions), identified using the US Renal Data System, of patients undergoing in-centre haemodialysis between 2008 and 2014.
- Location of last dialysis visit was linked with daily population-weighted air pollution.
- Admission risk estimated using time and county stratified design to control for county-level time trends.
- Cox proportional hazard model with time-varying exposure was used to estimate readmission risk associated with daily fluctuations in ambient particulate matter ($PM_{2.5}$) controlled for time-varying confounders.
- Potential diagnosis misclassification from using diagnosis codes to classify cause-specific hospitalisations and exposure misclassification related to $PM_{2.5}$ exposure not captured by ambient air quality near dialysis centres.

INTRODUCTION

Ambient fine particulate matter ($PM_{2.5}$) is a leading risk factor for all-cause mortality,[1–4] accounting for millions of premature deaths each year.[5] Daily variation in ambient $PM_{2.5}$ is also associated with increased rates of unplanned hospital admissions, urgent care visits and medication usage.[6 7] Greater health impacts have been observed consistently in sensitive populations, including the elderly and individuals with chronic health conditions such as chronic kidney disease (CKD).[3 8–11]

Additionally, $PM_{2.5}$ exposure during wildfire periods has been shown to increase the risk of mortality among patients managing their end-stage renal disease (ESRD) with haemodialysis.[12] However, the role of short-term $PM_{2.5}$ exposure at ambient levels on progression of disease and cause-specific morbidities has not been characterised.

CKD is a progressive condition that affects 8%–16% of the population worldwide,[13–15] and in the final stage, ESRD, many patients are transitioned to haemodialysis to prolong life. Patients receiving dialysis represent a particularly vulnerable population because of high rates of comorbidities, including diabetes and cardiovascular disease, which may contribute to the greater likelihood of hospital admission and readmission following PM exposure. In the USA, patients on haemodialysis average 1.7 inpatient admissions annually with a 30-day readmission rate twice that of other Medicare beneficiaries,[16] contributing to a substantial economic impact.[17] In 2016, US$35.4 billion in Medicare fee-for-service costs were attributed to ESRD,[16] motivating health promotion and cost-containment efforts to slow the progression of CKD and reduce hospitalisations and readmissions.[18] While many current strategies to reduce hospitalisations focus on care processes and patient-level factors,[19–22] there is a knowledge gap on the role of modifiable environmental risk factors—specifically ambient $PM_{2.5}$.[2 23–25]

In this study, we examined the risk of daily hospitalisation and subsequent 30-day readmission in relation to daily ambient $PM_{2.5}$ using data from the US Renal Data System (USRDS) over a 7-year period. We focused on all-cause, cardiovascular and respiratory hospitalisations and estimated changes in risk for early (1–7 days postdischarge) and late (8–30 days postdischarge) readmission accounting for the influence of different causal factors (ie, acute and chronic illness burden) that may influence early versus late readmissions.[26 27]

METHODS

Setting and study population

Using patient-level data from the USRDS, we constructed an open cohort of individuals receiving in-centre haemodialysis between 2008 and 2014. USRDS is a national data registry for dialysis services and includes records of patient demographic characteristics, hospitalisations and provider information on all patients receiving haemodialysis. Baseline demographic characteristics (sex, birth date, race and smoking status) recorded at the initiation of dialysis were extracted from the Medical Evidence Form CMS-2728 for each patient. For every inpatient hospital visit, we extracted the admission date, discharge date, discharge diagnoses codes and discharge status.

For the analysis of 30-day readmission risk, we considered only admissions where patients were discharged alive. Each readmission was counted once as a readmission relative to the prior index admission and was then considered as a new index admission. Thus, each admission could serve as both an index admission and readmission, consistent with previous studies.[28] An admission that occurred on the same day as a discharge was combined with the previous admission. These readmissions are likely to represent facility transfers for which we were not able to obtain information. Discharges occurring within 30 days of the end of the study period were excluded, as 30 days of follow-up data were not available. For both admissions and readmissions, patients could be represented more than once if they were admitted multiple times during the study period.

Health outcomes

The primary outcomes included daily counts of all-cause, respiratory and cardiovascular-related admissions and the time to readmission following the cause-specific discharges. All-cause and cause-specific readmissions were examined separately. Readmissions were classified further as early readmissions, occurring within 1–7 days of an index hospitalisation discharge and late readmissions, occurring 8–30 days postdischarge.

International Classification of Diseases, 9th Revision (ICD-9) codes were used to identify cause-specific hospitalisations. Cardiovascular-related diagnoses included hypertension (ICD-9 codes 401–405), myocardial infarction (410), ischaemic heart disease (410–411, 413), pulmonary embolism (415), dysrhythmia and conduction

Table 1 Baseline demographic characteristics of the study population between 2008 and 2014 by hospital admission category

	No (%)		
	All cause	Cardiovascular	Respiratory
Characteristic	n=351 294	n=262 385	n=247 829
Age (year), 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)

Table 2 Hospital admission characteristics among the study population between 2008 and 2014

	No of events (no of unique patients)		
Outcome	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 eadmission (1–7days)	176 822 (91 508)	83 193 (52 374)	78 392 (49 343)
Late readmission (8–30 days)	317 948 (130 454)	150 080 (80 851)	141 656 (76 444)
Length of stay, days			
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)

disorder (426–427), heart failure (428) and peripheral arterial disease (444). Respiratory-related diagnoses included asthma (493), chronic obstructive pulmonary disease (COPD) (491–492, 496), pneumonia (480–486) and other non-cardiac chest pain or respiratory syndrome (786).

Environmental data

Daily concentrations of fine $PM_{2.5}$ were estimated using a previously described exposure prediction model.[29 30] Briefly, this model estimates daily $PM_{2.5}$ on a 1 km grid for the entire continental USA by incorporating satellite aerosol optical depth measurements, chemical transport model simulations, meteorology, land use and other variables. Gridded $PM_{2.5}$ estimates were subsequently converted to population-weighted county-level estimates using 2010 Census tract population values. To enable adjustment for potential confounding by weather conditions, temperature and relative humidity data were obtained from the National Centers for Environmental Information's Global Historical Climatology Network (Global Surface Summary of the Day)[31] and using the Community Multiscale Air Quality model, respectively. The study area was restricted to all counties containing at least one land surface station from the Global Historical Climatology Network (n=530).

Daily $PM_{2.5}$ was linked to patient hospitalisations based on the county of their last dialysis visit. Previous work has shown that patients in the USRDS cohort that receive in-centre dialysis three times a week have a median travel distance of 5.7 miles to their initial dialysis centre.[32 33]

Study design and statistical analysis

Daily county hospital admissions

The relative risks of hospital admissions associated with daily $PM_{2.5}$ were estimated using a case-crossover design with conditional Poisson models for each of the three health outcomes separately (all-cause, cardiovascular, respiratory). Aggregated counts of daily admissions were time stratified by county-day, where each county served as its own control. For each county-day strata, $PM_{2.5}$ on the day of admission was compared with $PM_{2.5}$ concentrations on control days. Control days were defined as occurring on the same day of the week in the same month and year. This, by design, enabled us to control for differences in county characteristics, such as population size and risk characteristics, and the influence of day of the week, seasonal and long-term time trends.[34]

The relative risk of hospital admissions related to daily $PM_{2.5}$ for each health outcome was estimated using daily counts with respect to county-time strata, adjusted for meteorological conditions (temperature and humidity). Temperature and humidity effects were averaged over lag days 0, 1 and 2 and modelled using natural splines (df=3) to allow for non-linear effects.[35]

We evaluated immediate (same day) and delayed $PM_{2.5}$ effects on all-cause and cause-specific hospital admissions. Unconstrained distributed lag models were used to assess the delayed effects of short-term exposures to $PM_{2.5}$. Delayed exposure up to 14 days and models stratified on county socioeconomic status were considered. To assess the impact of county socioeconomic level, we used the percent of individuals below poverty from the 2010 US Census. Associations were assessed for counties both above and below the median poverty level (12.5%).

Early and late readmissions occurring within 30 days of discharge

Cox proportional hazards models were used to assess the relative risk of early (1–7 days postdischarge) and late (8–30 days postdischarge) readmission associated with daily $PM_{2.5}$ following all-cause and cause-specific index hospitalisations. Early-readmission models were censored at 7 days and late-readmission models at 30 days.

Models for readmissions incorporated both time-dependent and time-independent risk factors. Time-dependent variables included daily $PM_{2.5}$, daily temperature, daily relative humidity and day-of-the-week.

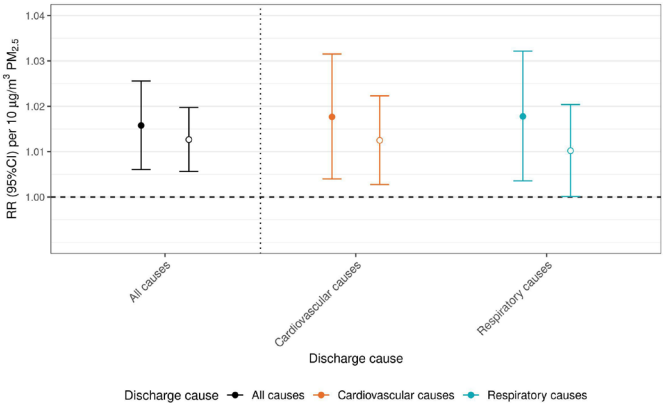

Figure 1 The relative risk (RR, 95% CI) for an all-cause early and late-readmission following all-cause and cause-specific discharges. Discharges are colour coded: all-cause discharges are indicated in black, cardiovascular causes in orange and respiratory causes in blue. Early readmissions are indicated with filled in circles, late readmissions with open circles. RR is expressed per 10 µg/m^3 increase in particulate matter ($PM_{2.5}$).

Time-independent factors included patient-specific, hospitalisation event-specific and county socioeconomic variables. Patient-specific variables included indicator of sex, race, baseline smoking status, whether the patient had three or more previous hospital visits in the year prior and age at discharge. Event-specific variables included whether the discharge occurred on a holiday and length of stay. To adjust for county socioeconomic level, the per cent of individuals below poverty was included as a covariate. Models were also adjusted for patient-specific clusters to account for repeated measures by individual. Lastly, models were adjusted for the competing cause of death by including death as an additional censoring criteria. The presented models represent the cause-specific readmission hazard. Non-linear $PM_{2.5}$ associations were also explored.

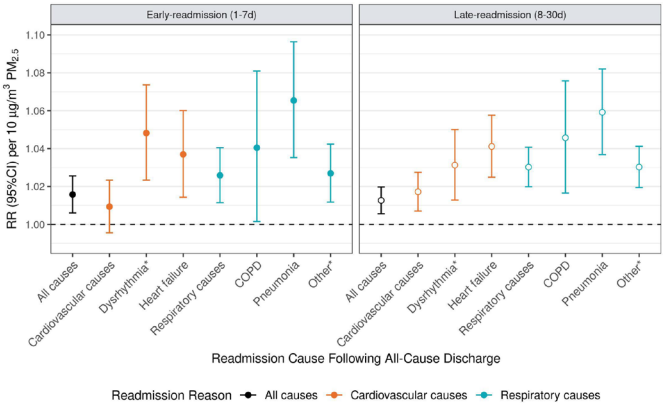

Figure 2 The relative risk (RR, 95% CI) of cause-specific early and late-readmission following all-cause discharge. Readmission causes are colour coded: all-cause readmissions are indicated in black, cardiovascular causes in orange and respiratory causes in blue. RR is expressed per 10 µg/m3 increase in particulate matter ($PM_{2.5}$). COPD, chronic obstructive pulmonary disease; RR, rate ratio.

Daily county admission and readmission risks were expressed as the rate ratio (RR) per 10-µg/m^3 increase in $PM_{2.5}$. The proportion hospital admissions and readmissions associated with $PM_{2.5}$ is reported as the attributable fraction (AF), where AF = (RR-1) / RR.[36] All statistical analyses were performed with R software (V.3.6.0).[37]

RESULTS

Characterisation of clinical cohort and daily $PM_{2.5}$

Among 361 568 patients who were hospitalised during the study period, 10 274 were excluded due to missing baseline demographic values, with 351 294 patients remaining. Demographic descriptions are in table 1. Patients had on average 2.97 hospital visits in the year prior to an admission and more than 70% of patients had at least one hospital admission related to cardiovascular and respiratory causes (table 2). The average daily county-level $PM_{2.5}$ concentration was 9.3 µg/m^3 (range: 0.05–155.16 µg/m^3) (online supplemental table S1). The highest daily county-level $PM_{2.5}$ was observed in California (online supplemental figure S1).

Description of clinical events, hospital admissions and readmissions

In total, there were 1 801 966 hospital admissions, of which 1 493 795 recorded the patient as alive at discharge. Of admissions that were discharged alive, 11.8% were readmitted within 7 days and 21.3% were readmitted 8 to 30 days postdischarge. The mean length of stay for all-cause, cardiovascular and respiratory admissions was 7.0, 7.0 and 7.1 days, respectively (table 2).

Associations between $PM_{2.5}$ and readmission

Early readmission

Daily $PM_{2.5}$ was positively associated with increased risk for early readmission following all-cause, cardiovascular and respiratory-related discharges. Same day (lag 0) $PM_{2.5}$ was associated with a 1.6% (95% CI 0.6% to 2.6%), 1.8% (95% CI 0.4% to 3.2%) and 1.8% (95% CI 0.4% to 3.2%) increased risk of an early readmission for any cause following all-cause, cardiovascular and respiratory-related discharges, respectively (figure 1 and online supplemental table S2).

$PM_{2.5}$ associated early-readmission risk was greater for certain cause-specific outcomes. Following all-cause discharges, same day (lag 0) $PM_{2.5}$ was associated with increased early-readmission risk for dysrhythmia and conduction disorder (4.8%, 95% CI 2.3% to 7.4%), heart failure (3.7%, 95% CI 1.4% to 6.0%]), pneumonia 6.5%, (95% CI 3.5% to 9.6%) and other non-cardiac chest pain or respiratory syndrome (2.7%, 95% CI 1.2% to 4.2%) causes. $PM_{2.5}$ associated early-readmission risk was greatest for pneumonia-related readmissions following cardiovascular-related discharges (7.5%, 95% CI 3.5% to 11.7%). Other cause-specific early-readmission risks following cardiovascular and respiratory-related discharges were similar to estimates observed following discharge for any cause (figure 2 and online supplemental table S2).

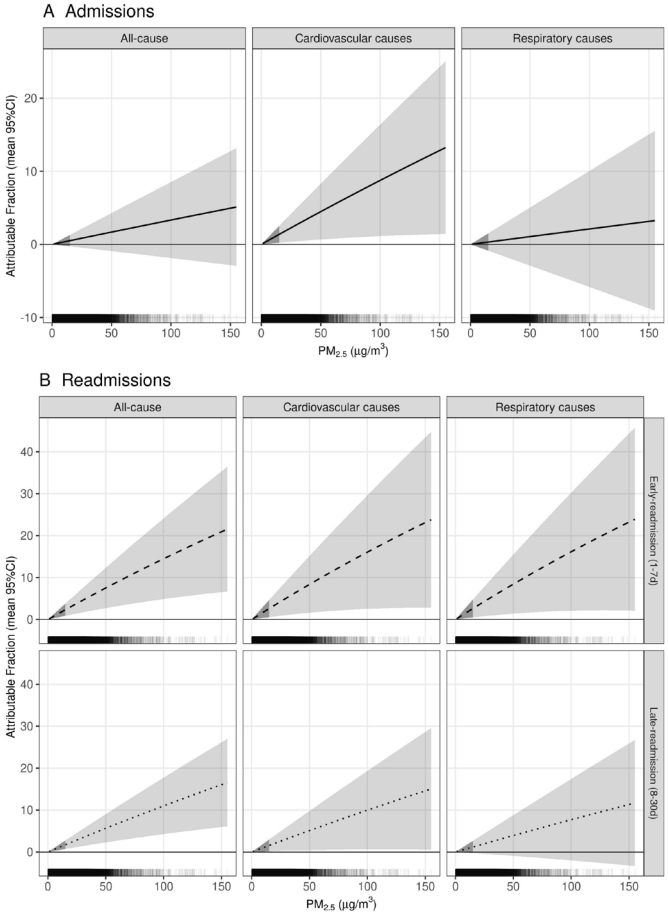

Figure 3 Mean proportion (95% CI) of all-cause and cause-specific hospital admissions, early readmissions (1–7 days) and late readmissions (8–30 days) with respect to particulate matter ($PM_{2.5}$) (µg/m^3). Hash marks above the x-axis represent the density of daily county $PM_{2.5}$. The 95% CI under 15.9 µg/m^3 is shaded darker to indicate where 90% of the data falls.

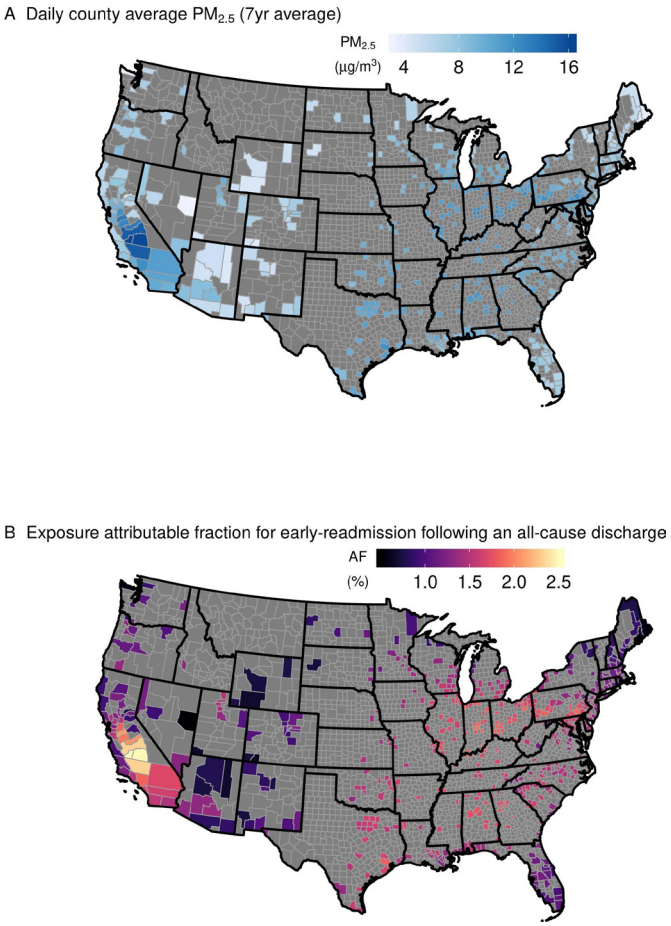

Figure 4 Average daily county particulate matter ($PM_{2.5}$) (µg/m^3) between 2008 and 2014 (A) and the attributable fraction (AF) for early-readmission following an all-cause discharge based on the average $PM_{2.5}$ (B) for the 530 counties included in the study.

An average AF at 10 µg/m^3 of $PM_{2.5}$ at lag 0 was 1.5% (95% CI 0.6% to 2.5%), 1.7% (95% CI 0.4% to 3.1%) and 1.7% (95% CI 0.3% to 3.2%) for an early-readmission for any cause following all-cause, cardiovascular and respiratory discharges, respectively (figure 3). County AF ranged 0.5%–2.5%, 0.6%–2.8% and 0.6%–2.8% for an early-readmission following all-cause, cardiovascular and respiratory-related discharges, respectively (figure 4).

Late readmission

Daily $PM_{2.5}$ was also associated with increased risk of late-readmission following all-cause, cardiovascular and respiratory-related discharges and the magnitude of risk related to all-cause readmissions was similar to that observed with early-readmission. Same day $PM_{2.5}$ was associated with a 1.3% (95% CI 0.6% to 2.0%), 1.2% (95% CI 0.3% to 0.2.2%) and 1.0% (95% CI 0.01% to 2.0%) increased risk of a late all-cause readmission following all-cause, cardiovascular and respiratory-related discharges, respectively (figure 1 and online supplemental table S2).

Similar to observations made for early-readmissions, $PM_{2.5}$ associated late-readmission risk was greater for certain cause-specific outcomes. Following all-cause discharges, a 10 µg/m^3 increase in same day (lag 0) $PM_{2.5}$ was associated with increased late-readmission risk for dysrhythmia and conduction disorder (3.1%, 95% CI 1.3% to 5.0%), heart failure (4.1%, 95% CI 2.5% to 5.8%), COPD (4.6%, 95% CI 1.7% to 7.6%), pneumonia (5.9%, 95% CI 3.7% to 8.2%) and other non-cardiac chest pain or respiratory syndrome (3.0%, 95% CI 1.9% to 4.1%) (figure 2 and online supplemental table S2).

The average AF at 10 µg/m^3 was 0.1% (95% CI 0.5% to 1.8%) and 1.0% (95% CI 0.1% to 2.0%) for a late readmission following all-cause and cardiovascular discharges, respectively (figure 3). County AF ranged 0.3%–1.9% for a late readmission following any cause (data not shown).

Associations between $PM_{2.5}$ and daily admissions

Same day $PM_{2.5}$ was associated with an increase in RR of 0.3% (95% CI −0.2% to 0.9%) for all-cause admissions and 0.9% (95% CI 0.2% to 1.7%) for cardiovascular admissions (online supplemental figure S2 and table S3). We estimated 0.9% (95% CI 0.1% to 1.7%) of cardiovascular admissions could be attributed to 10 µg/m^3 ambient $PM_{2.5}$ (figure 3). Across counties, exposures accounted

for 0.3%–1.5% of cardiovascular admissions when evaluated at the average daily $PM_{2.5}$ for each county (data not shown).

No change in risk of all-cause and cardiovascular admissions was observed related to prior exposure (lags 1–14). Similarly, no change in risk for respiratory admissions was observed with same day exposure (lag 0) or prior exposure (lags 1–14) (online supplemental figure S2 and table S3). The model with a dose-specific association for $PM_{2.5}$ (non-linear dose-response function) did not improve model fit. Models stratified on median percent below poverty were similar (online supplemental figure S2 and table S3). In a sensitivity analysis, changing the number of df considered for temperature and relative humidity had a negligible effect (online supplemental figures S3 and S4).

DISCUSSION

In a nationwide cohort study of 351 294 patients with ESRD managed with haemodialysis, we evaluated the association between 1.8 million inpatient admissions and nearly 0.5 million corresponding 30-day readmissions and the variation in daily ambient $PM_{2.5}$ in the USA over 7 years, 2008–2014. Daily variation in $PM_{2.5}$ was associated with increased risk of hospital admission and even greater risk of rehospitalisation. Following all-cause, cardiovascular and respiratory-related discharges, the early-readmission risk for any cause was increased by 1.6, 1.8, 1.8%, respectively per 10 µg/m^3 increase in daily $PM_{2.5}$. Importantly, readmissions related to some cardiorespiratory diagnoses had the greatest $PM_{2.5}$ attributed readmission risk that was observed to be elevated for both early and late readmissions. The early-readmission risk following all-cause discharges was increased by 6.5, 4.8, 3.7 and 2.7% for pneumonia, dysrhythmia and conduction disorder, heart failure, and other non-cardiac chest pain or respiratory syndrome-related readmissions, respectively. Overall, these results suggest that at 10 µg/m^3, 1.5%–1.7% of early-readmissions for any cause were attributable to short-term exposure. In the context of the daily $PM_{2.5}$ National Ambient Air Quality Standard (35 µg/m^3), this AF would be 5.3%–6.0%.

Our findings are consistent with previous studies that observed increased admission risks in elderly populations[6 9 38–42] and patients with cardiovascular health complications,[7 43] and increased readmission risk following cardiovascular-related admissions.[7 43 44] Studies in the Medicare population similarly observed a 1%–2% increase in cardiovascular hospital admissions associated with same-day $PM_{2.5}$ concentrations.[6 9 38 40] Risk appears to vary by diagnosis, as the increased risk was slightly less (0.13%) for ST-elevation myocardial infarction related admissions in a Chinese population[7] and greater (29%) for incident heart failure admissions in an Australian population.[43] Increases in respiratory admissions (1%–2%) have been noted in the Medicare population,[6 9 38–40] but were not observed in this study. Prior studies provide evidence that air pollution exposure is associated with adverse health outcomes including increased infection rates, acute lung edema and elevated concentrations of systematic inflammation markers.[45–47] Despite known associations between PM exposure and adverse cardiovascular and respiratory health outcomes, previous studies have not evaluated the impacts on hospital readmissions among individuals with ESRD.

Few studies have examined $PM_{2.5}$-related effects on readmissions, and those that have report on the long-term (>1 year) risk following cardiovascular-related admissions. Following cardiovascular hospitalisation, greater $PM_{2.5}$-related rehospitalisation risk was observed for some cardiac and respiratory readmissions (dysrhythmia, pneumonia) compared with our observations of all-cause readmissions (4.3%–7.5% vs 1.6%).

Studies in other populations have noted similar same-day cardiovascular-related readmission risks of 5.5%–7.7% and 2.6% associated with $PM_{2.5}$[7] and PM_{10},[44] respectively. Additionally, one study in an Australian population with very low ambient air pollution concentrations (mean $PM_{2.5}$=2.9 µg/m^3) found no relationship between $PM_{2.5}$ and all-cause readmissions after an incident heart failure hospitalisation.[43] In some instances, short-term readmission risks were greater in comparison to the long-term readmission risks, suggesting the week following a discharge to be a window of heightened vulnerability. Prior work indicates that factors related to index hospitalisations and acute illness burden are predictive of an early readmission.[26 27] This may indicate that hospital readmissions related to certain acute illness burdens may be more susceptible to $PM_{2.5}$ exposure.

Our study contributes to the currently limited literature on the association between air pollution and health impacts among haemodialysis patients and shines a light on the vulnerability in this clinical population related to ambient airborne PM2.5. The 30-day rehospitalisation rate is 33% in this population, which is twice that of older Medicare beneficiaries without a kidney disease diagnosis.[16] As many as 70% of readmissions are thought to be unnecessary,[48] prompting efforts to improve outcomes. Economic healthcare costs associated with short-term increases in $PM_{2.5}$ are considerable; annual inpatient and postacute care costs related to a 10 µg/m^3 in daily $PM_{2.5}$ ranges US$30–US$70 million for cardiovascular and respiratory-related diseases.[49] $PM_{2.5}$ is a modifiable risk factor and reductions in short-term exposures could contribute to reduced healthcare costs. Our findings suggest that short-term increases in $PM_{2.5}$ contribute to healthcare usage through unplanned admissions and readmissions.

Additionally, the findings of the study may have a broader public health implication. In the conceptual framework for public health action, ambient airborne PM2.5 fits well into the base of a 5-tiered pyramid as a socioeconomic or social determinant of health.[50] Interventions that address the base of the pyramid may provide the greatest potential impact given the widespread population exposure

of such a determinant of health like ambient airborne PM2.5. Mitigation strategies would need to include policy initiatives to curb the expulsion of airborne pollutants, as well as education of persons, patients, hospital staff and others. Areas with the higher concentrations of ambient airborne PM2.5 may see the greatest benefit from mitigation strategies.

Strengths and limitations

This study included a nearly complete cohort of US patients undergoing in-centre haemodialysis. To our knowledge, this is the largest analysis of short-term exposure to air pollution in the USA in this highly vulnerable population. The USRDS registry provides a complete registry of all hospitalisations and contains detailed information regarding demographics, dialysis, hospitalisation, rehospitalisation and comorbid conditions. Second, ambient $PM_{2.5}$ was estimated using a prediction model with highly resolved spatial and temporal resolution with proven accuracy.[29 30] Third, the time-stratified design allowed for county matching that reduced the potential confounding by factors that very slowly with time and those that are time-invariant. Fourth, the use of time-dependent risk factors in the Cox proportional hazard model allowed for readmission risk estimates to reflect the risk associated with daily fluctuations in ambient $PM_{2.5}$ and time-varying confounders.

This study also had some limitations. First, there was the potential for exposure misclassification as the location of the last dialysis visit was used to estimate individual level exposures. $PM_{2.5}$ around dialysis centres could differ from concentrations around hospitals and patient residences. However, given that patients generally reside less than six miles from their initial dialysis centre, differences in temporal variation of exposure should be small and not likely to contribute a systematic bias favouring an association between ambient $PM_{2.5}$ and clinical events.[32 33] Second, diagnosis misclassification was possible but was not likely to confound the relationship because it is not likely to vary on the same temporal scale as $PM_{2.5}$. Third, there is the possibility that some unmeasured time variant factors may have confounded our estimates (smoking status, medication usage, behaviours, lipid levels, C reactive protein levels, etc). Data availability restricted the consideration of some patient-level confounders, such as smoking status, to values recorded at baseline. We used a time stratified design to control for time-varying confounding for time scales larger than a month, such as the number of patients enrolled in the USRDS. At scales smaller than a month, the control of person time was not possible. Lastly, generalisation of the results is limited to the Medicare population with ESRD managed with haemodialysis treatment. Future studies are needed to understand $PM_{2.5}$-related impacts on specific health conditions, and if health impacts vary based on race, socioeconomic indicators or other individual and population factors.

CONCLUSION

In conclusion, this US-wide cohort study identified increased risk in patients receiving in-centre haemodialysis associated with short-term increases in ambient air particle pollution. Elevated $PM_{2.5}$ concentrations were found to be associated with increased inpatient hospital admissions related to cardiovascular causes, and an increased likelihood of hospital readmission following cardiovascular and respiratory-related hospitalisations. Medicare spending for beneficiaries with ESRD is high. Traditional efforts to reduce the burden of disease focus on patient factors; however, these data suggest that air particle pollution is a factor that contributes to increased risks for hospital admission and subsequent readmission. To reduce $PM_{2.5}$-related morbidities, we echo the recommendations made in the Million Hearts initiative, that healthcare systems, insurers, physicians, and healthcare professionals should incorporate health risks related to ambient PM into patient care.

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Contributors LW and AGR conceived and designed the study. TW, WEC and AK provided subject expert input into the study design and interpretation of evidence. AK, QD and CW-C provided access to the data for the study; LW managed and analysed the data and AGR oversaw the analysis. LW and AGR wrote the first draft of the manuscript. LW, YX, AK, CW-C, TW, WEC and AGR critically contributed to the manuscript and approved the final draft. LW and AGR are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Data availability statement The USRDS data may be obtained from a third party and are not publicly available to researchers. Data access to USRDS data sets is through an internal data use agreement with the University of North Carolina at Chapel Hill's Cecil G. Sheps Center. PM2.5 data were obtained through collaboration with Drs Joel Schwartz (Harvard TH Chan School of Public Health) and QD (Tsinghua University). For general data sharing inquiries contact rappold.ana@epa.gov or wyatt.lauren@epa.gov.

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Supplemental Materials

Table S1. Summary statistics of $PM_{2.5}$ and meteorological variables across 530 counties.

Variable	Mean ± SD	Minimum	Maximum
$PM_{2.5}$ ($\mu g/m^3$)	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

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 μg/m^3 increase in $PM_{2.5}$. Models presented include the main model presented in the paper (model 1) where $PM_{2.5}$ is considered as a linear variable and a model that considers $PM_{2.5}$ as a non-linear variable (model 2).

			Model 1 PM linear	Model 2 PM non-linear
Readmission model	Discharge cause	Readmission cause	RR (95%CI)	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)

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

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Table S3. Relative risk (RR ± 95% CI) of all-cause and cause-specific daily county admission rates associated with a 10 μg/m^3 increase in $PM_{2.5}$ for exposure lags 0-14 days. Models presented include the main model presented in the paper (model 1) where $PM_{2.5}$ is considered as a linear variable and a model that considers $PM_{2.5}$ 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)

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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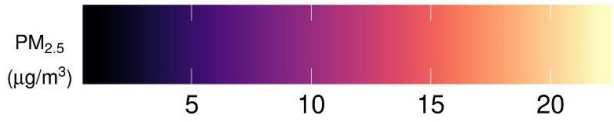
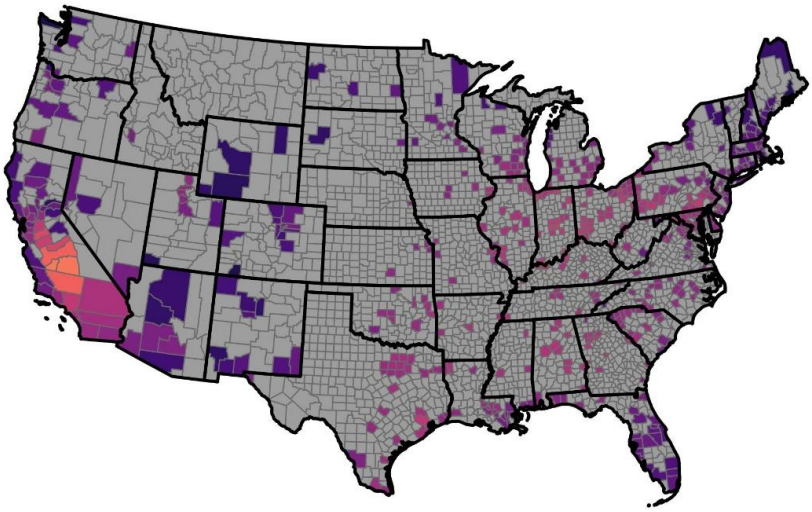


A) Long-term county $PM_{2.5}$ (7yr average)



B) 20% of county days are above $PM_{2.5}$ (80th percentile)

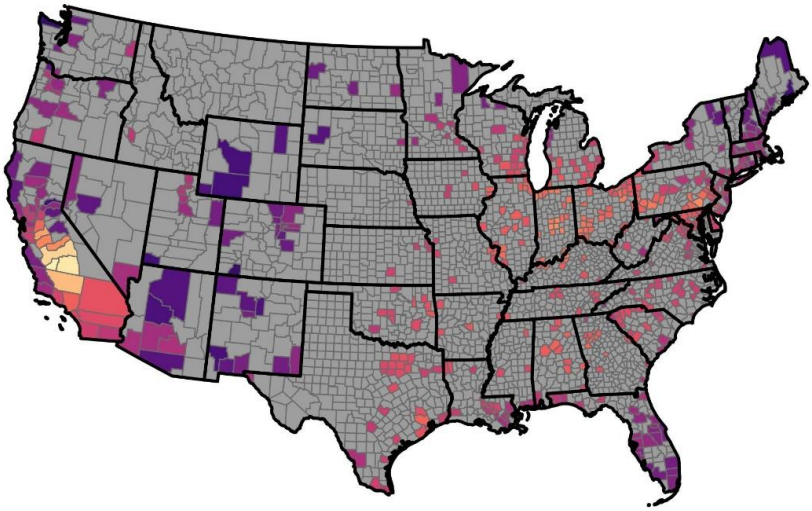


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Figure S1. County $PM_{2.5}$ levels for the 530 counties included in the study. $PM_{2.5}$ levels shown include the A) long-term average and B) 80th percentile (indicating that 20% of county days are at or above this $PM_{2.5}$ level) for the years 2008-2014.

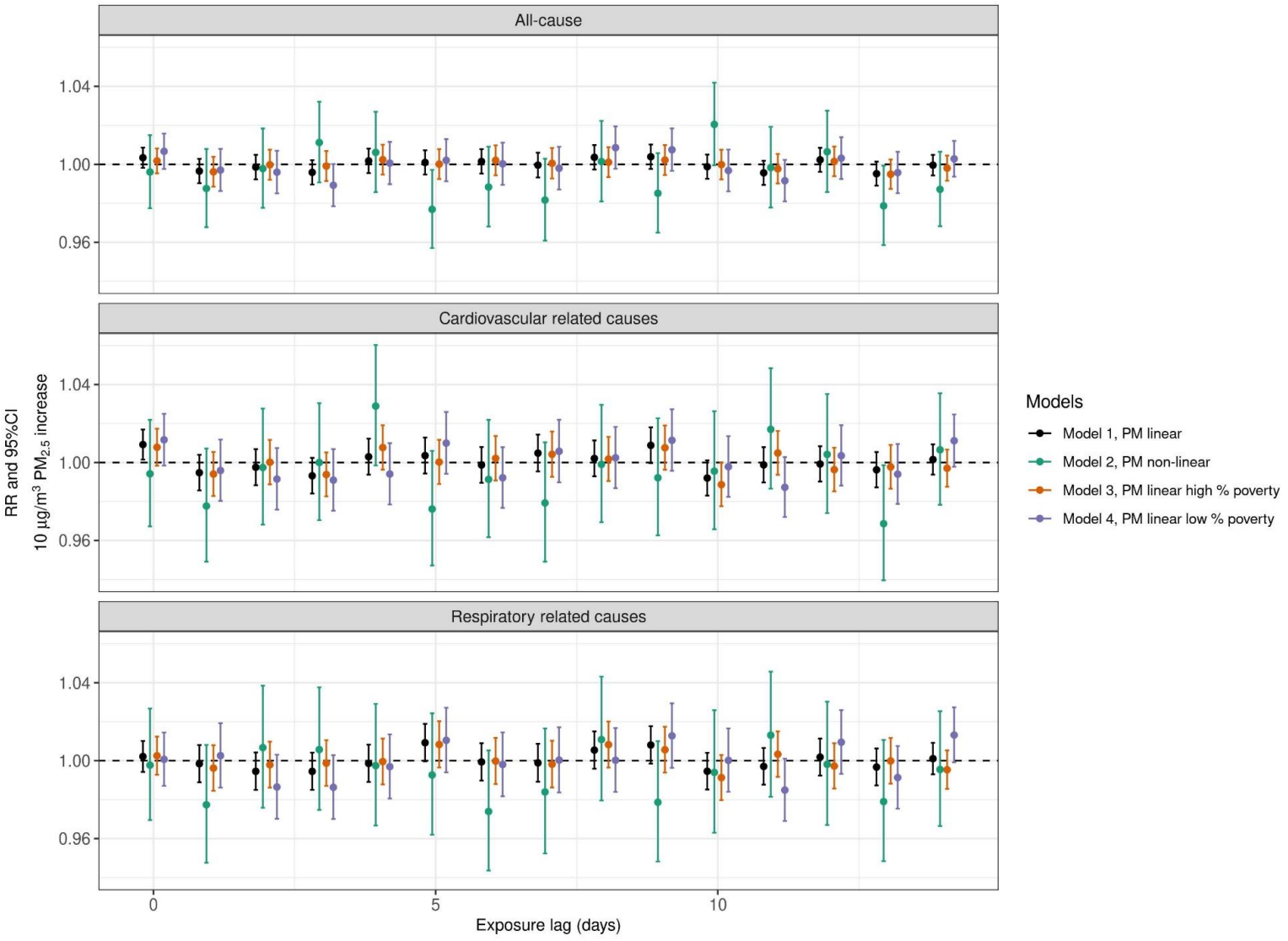
All-cause
Cardiovascular related causes
Respiratory related causes
1.04
1.00
0.96
RR and 95%CI
10 µg/m³ PM2.5 increase
0
5
10
Exposure lag (days)
Models
Model 1, PM linear
Model 2, PM non-linear
Model 3, PM linear high % poverty
Model 4, PM linear low % poverty

Figure S2. Relative risk (RR ± 95%CI) for daily county admission rates for all-cause hospitalization associated with a 10 μg/m^3 increase in $PM_{2.5}$ for exposure lags 0-14 days using an unconstrained distributed lag model. Models presented include the main model presented in the paper (model 1) where $PM_{2.5}$ is considered as a linear variable in black and a model that considers $PM_{2.5}$ as a non-linear variable (model 2) in green. 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 in orange and model 4 representing counties with low % below poverty in purple (Table S2).

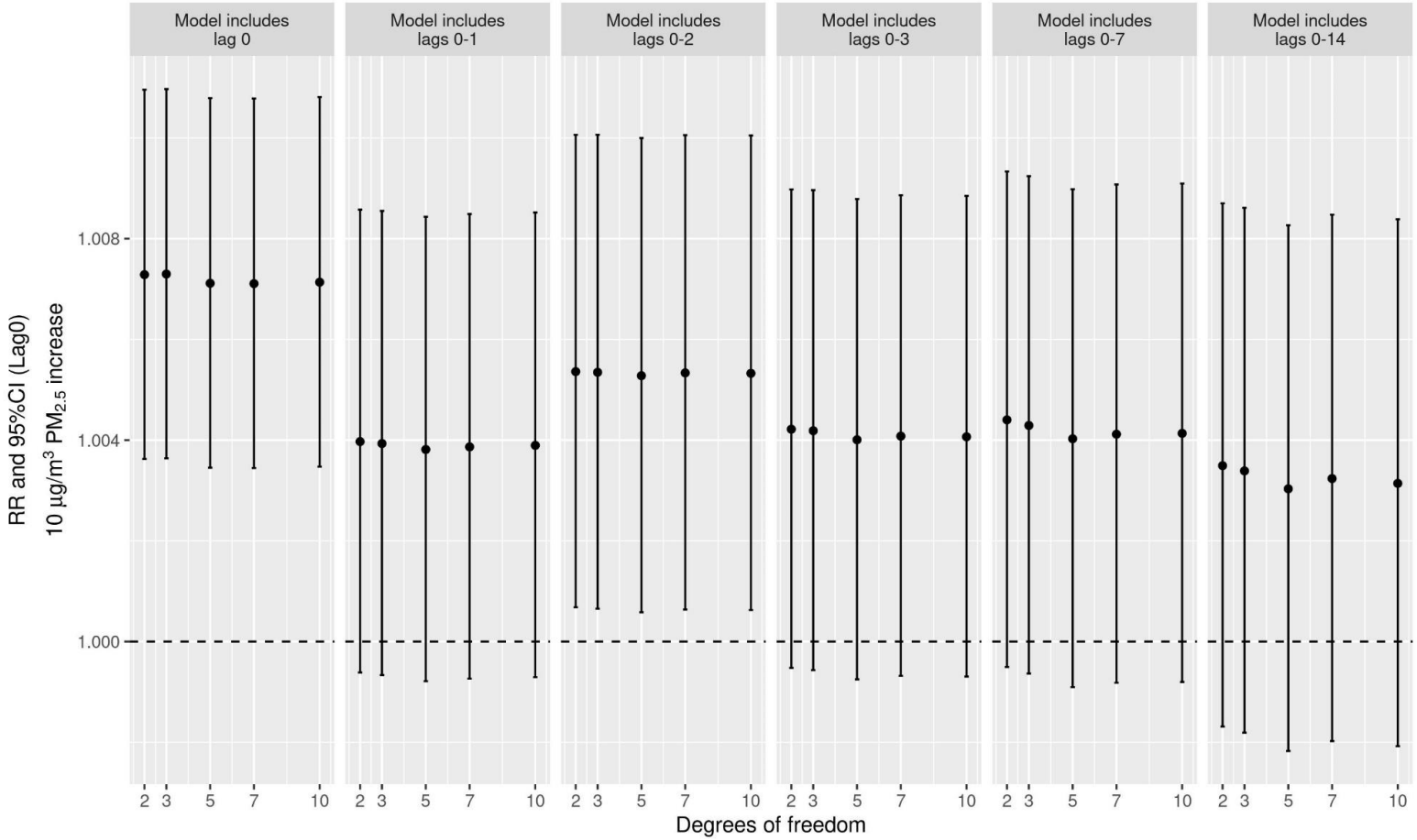

Figure S3. Sensitivity analysis for all-cause admissions models showing the impact on the lag 0 estimate from changing the number of lags considered (grouped figures), and the number of degrees of freedom (x-axis) for the temperature and relative humidity variables. Relative risk (RR ± 95%CI) of all-cause daily county admission rates associated with a 10 µg/m^3 increase in $PM_{2.5}$ on lag 0.

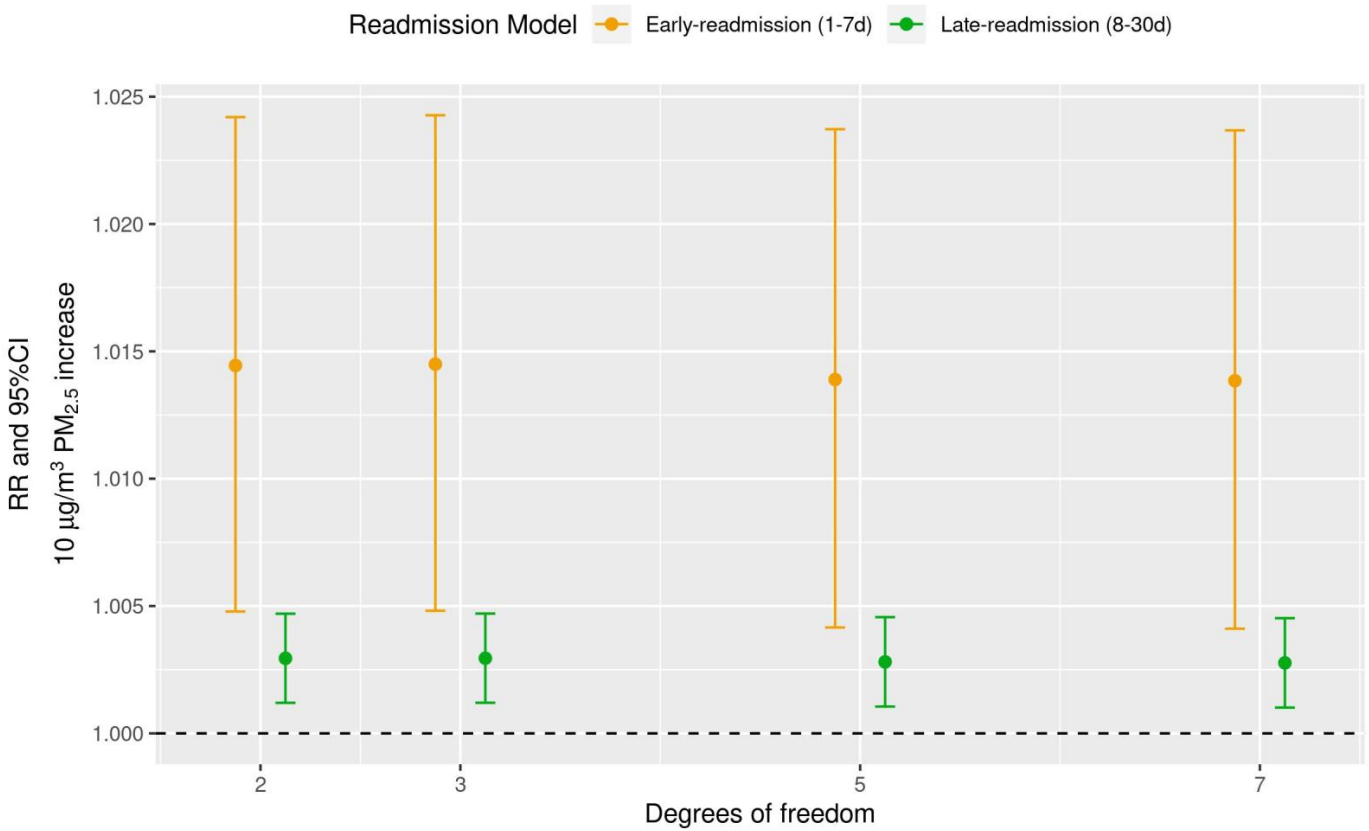

Figure S4. Sensitivity analysis for all-cause readmission models showing the impact on the lag 0 estimate from changing the number of degrees of freedom (x-axis) for the temperature and relative humidity variables. Relative risk (RR ± 95%CI) of all-cause daily county admission rates associated with a 10 µg/m^3 increase in $PM_{2.5}$ on lag 0.