Short term exposure to low level ambient fine particulate matter and natural cause, cardiovascular, and respiratory morbidity among US adults with health insurance: case time series study

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ABSTRACT

OBJECTIVE

To estimate the excess relative and absolute risks of hospital admissions and emergency department visits for natural causes, cardiovascular disease, and respiratory disease associated with daily exposure to fine particulate matter ($PM_{2.5}$) at concentrations below the new World Health Organization air quality guideline limit among adults with health insurance in the contiguous US.

DESIGN

Case time series study.

SETTING

US national administrative healthcare claims database.

PARTICIPANTS

50.1 million commercial and Medicare Advantage beneficiaries aged ≥18 years between 1 January 2010 and 31 December 2016.

MAIN OUTCOME MEASURES

Daily counts of hospital admissions and emergency department visits for natural causes, cardiovascular disease, and respiratory disease based on the primary diagnosis code.

RESULTS

During the study period, 10.3 million hospital admissions and 24.1 million emergency department visits occurred for natural causes among 50.1 million adult enrollees across 2939 US counties. The daily $PM_{2.5}$ levels were below the new WHO guideline limit of 15 µg/m^3 for 92.6% of county days (7 360 725 out of 7 949 713). On days when daily $PM_{2.5}$ levels were below the new WHO air quality guideline limit of 15 µg/m^3, an increase of 10 µg/m^3 in $PM_{2.5}$ during the current and previous day was associated with higher risk of hospital admissions for natural causes, with an excess relative risk of 0.91% (95% confidence interval 0.55% to 1.26%), or 1.87 (95% confidence interval 1.14 to 2.59) excess hospital admissions per million enrollees per day. The increased risk of hospital admissions for natural causes was observed exclusively among adults aged ≥65 years and was not evident in younger adults. $PM_{2.5}$ levels were also statistically significantly associated with relative risk of hospital admissions for cardiovascular and respiratory diseases. For emergency department visits, a 10 µg/m^3 increase in $PM_{2.5}$ during the current and previous day was associated with respiratory disease, with an excess relative risk of 1.34% (0.73% to 1.94%), or 0.93 (0.52 to 1.35) excess emergency department visits per million enrollees per day. This association was not found for natural causes or cardiovascular disease. The higher risk of emergency department visits for respiratory disease was strongest among middle aged and young adults.

CONCLUSIONS

Among US adults with health insurance, exposure to ambient $PM_{2.5}$ at concentrations below the new WHO air quality guideline limit is statistically significantly associated with higher rates of hospital admissions for natural causes, cardiovascular disease, and respiratory disease, and with emergency department visits for respiratory diseases. These findings constitute an important contribution to the debate about the revision of air quality limits, guidelines, and standards.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Short term exposure to fine particulate matter ($PM_{2.5}$) has been associated with increased risk of morbidity and mortality

Previous studies have primarily focused on older adults or used data on hospital admissions

Evidence for the association between short term exposure to $PM_{2.5}$ and morbidity at levels below the new World Health Organization air quality guideline limit remains unclear

WHAT THIS STUDY ADDS

In this nationwide study in the US, exposure to ambient $PM_{2.5}$ at levels below the new WHO air quality guideline limit of 15 µg/m^3 was statistically significantly associated with hospital admissions for natural causes, cardiovascular disease, and respiratory disease, and emergency department visits for respiratory disease

These findings provide evidence of health harms associated with short term exposure to $PM_{2.5}$ even at levels below the new WHO air quality guideline limit

Introduction

A large number of epidemiological studies have consistently reported that exposure to ambient fine particulate matter ($PM_{2.5}$) is associated with increased risk of morbidity and mortality.[1-6] According to the Global Burden of Disease study,[7] exposure to $PM_{2.5}$ accounts for an estimated 7.6% of total global mortality and 4.2% of global disability adjusted life years. In light of this extensive body of evidence, the World Health Organization recently introduced an ambitious new air quality guideline limit in 2021, recommending that the 24 hour average $PM_{2.5}$ levels should not exceed 15 µg/m^3 on more than 3-4 days each year.[8] In the US, the current national ambient air quality standards for the 24 hour average $PM_{2.5}$ (calculated as 98th centile concentrations averaged over a three year period) were set at 35 µg/m^3 in 2012, and a revision of these standards is currently being considered.[9]

Although the literature on the adverse health effects of short term exposure to PM$_{2.5}$ is vast,[1-6] several key knowledge gaps remain. Specifically, owing to the accessibility of national vital statistics data and Medicare data, most large scale studies in the US have focused on the health effects of PM$_{2.5}$ among adults aged ≥65 years,[1 5] with relatively few studies including young or middle aged adults; most studies have focused on mortality and hospital admissions as the outcomes,[1 2 3 5 6 10] with relatively less information available on the impact of PM$_{2.5}$ on emergency department visits (ie, where individuals are treated in the emergency department room but not admitted to hospital for inpatient care)[11]; and no study has specifically examined whether the observed associations persist at daily PM$_{2.5}$ levels below the 2021 WHO air quality guideline limit.

To tackle these knowledge gaps, we estimated the association between short term exposure to PM$_{2.5}$ at concentrations below the 2021 WHO air quality guideline limit and the risks of hospital admissions and emergency department visits for natural causes, cardiovascular disease, and respiratory disease among adults with health insurance in the contiguous US from 2010 to 2016 using the healthcare utilization deidentified claims data from the Optum Laboratories Data Warehouse (OLDW). We also examined whether the observed associations of PM$_{2.5}$ level and morbidity differed across strata defined by age, sex, insurance type, and geographic region.

Methods
Study population
This study used deidentified medical claims data between 1 January 2010 and 31 December 2016 from OLDW.[12] This database includes facility and physician claims and enrollment records for enrollees with either commercial or Medicare Advantage health insurance. The database contains longitudinal health information on more than 200 million enrollees, representing a diversity of ages and geographic regions across the US.

Medical claims in OLDW are classified using ICD-9 and ICD-10 (international classification of diseases, ninth revision and 10th revision, respectively) codes, revenue codes, current procedure terminology codes, and place of service codes (see supplementary table S1). We used claims to identify clinical encounters classified as either hospital admissions or emergency department visits. For each patient encounter, we extracted information on age, sex, county of residence, date of service, insurance type, and principal diagnoses. Analyses were limited to adults aged ≥18 years who had hospital admissions or emergency department visits for natural causes (ICD-9: 0-799 or ICD-10: A0-R99), cardiovascular disease (ICD-9: 390-459 or ICD-10: I00-I99), or respiratory disease (ICD-9: 460-519 or ICD-10: J00-J99).

For each health outcome, we aggregated medical claims into daily counts of hospital admissions or emergency department visits by age (18-29, 30-39, 40-49, 50-64, 65-74, or ≥75 years), sex (male *v* female),

insurance type (commercial insurance *v* Medicare Advantage), and geographic regions of the country, as defined by the US Global Change Research Program's Fourth National Climate Assessment (NCA4) for each county (see supplementary figure S1).

Environmental data
To estimate daily concentrations of 24 hour average PM$_{2.5}$ at 1 km × 1 km grid cells in the contiguous US, we used a previously developed spatiotemporal ensemble model.[13] The model incorporates three machine learning algorithms: neural network, random forest, and gradient boosting. These algorithms relied on multiple predictor variables, including satellite data at 1 km × 1 km resolution, meteorological conditions, such as ambient temperature, land use variables, such as elevation and road density, and predictions from chemical transport models.[13] The predictions of daily PM$_{2.5}$ level from each algorithm were then combined with a geographically weighted generalized additive model.[13 14] Additionally, we obtained monitoring data for PM$_{2.5}$ from 2156 surveillance sites operated by the US Environmental Protection Agency. To account for spatial and temporal autocorrelation, we calculated lagged PM$_{2.5}$ levels from monitoring sites and incorporated these as supplementary inputs into the ensemble models, along with the aforementioned predictor variables.[13 14] The final ensemble model showed good performance when predicted values were compared with monitored data, achieving a 10-fold cross validation R^2 of 0.86.[13 14]

We also derived meteorological variables, including daily outdoor ambient air temperature and relative humidity, from the Parameter-elevation Relationships on Independent Slopes model (PRISM) dataset, which is a publicly available gridded climate dataset.[15 16] The dataset we used provides daily estimates of several meteorological variables at a horizontal grid spacing of about 4 km across the contiguous US.[15 16]

Daily PM$_{2.5}$ concentrations and meteorological variables were calculated at the county level by extracting the grid values at the population centroids for each census tract (based on the 2000 US Census) within a given county. We then calculated the population weighted average values based on the proportion of the county's population residing in each census tract.[15 17] The concentration of PM$_{2.5}$ and meteorological variables were assigned to each county and the exposure data linked with time series data of hospital admissions and emergency department visits in each respective county.

Statistical analysis
To estimate the association between short term exposure to PM$_{2.5}$ and risks of hospital admissions and emergency department visits for natural causes, cardiovascular disease, and respiratory disease, we used a case time series design—a novel approach suitable for analyzing small area data.[18 19] This design incorporates the self-matched structure in case only models into a traditional time series form, providing

a flexible and computationally efficient tool for complex longitudinal data.[18 19] In the case time series design, observations defined as cases are collected longitudinally over a period of time at equally spaced time intervals, forming a set of case level time series data.[18] The time series of cases can be either individual level outcomes or aggregated measurements over small geographic areas.[18 19] In our study, we aggregated medical claims into county specific daily time series of hospital admission and emergency department visit counts and linked these case time series with county level $PM_{2.5}$ concentrations and meteorological conditions. We chose a case time series design because of its suitability to accommodate the longitudinal time series structure of health outcomes at small area level, strict control for time invariant confounding, and flexibility to adjust time varying confounding in the modeling framework.[18 19]

We used a conditional quasi-Poisson log-link regression model stratified by year, month, day of week, and county of residence, therefore adjusting for the differential baseline morbidity risk and trends across the different spatiotemporal strata. Meanwhile, we controlled the residual temporal variations with time varying covariates, such as ambient temperature and relative humidity. Consistent with previous studies,[1 2 6] our primary analyses considered the moving average of the current and previous day (lag 0-1) $PM_{2.5}$ as the exposure of interest and assumed a linear exposure-response association between exposure to $PM_{2.5}$ and risk of morbidity. In the models, we adjusted for the two day moving average of daily mean ambient temperature using a natural cubic spline function with three degrees of freedom, and the two day moving average of daily mean relative humidity using a natural cubic spline function with three degrees of freedom.[1] To account for spatial heterogeneity of ambient temperature, we interacted the temperature splines with NCA4 regions. We additionally adjusted for federal holiday (dummy variable). Low level $PM_{2.5}$ was defined as daily $PM_{2.5}$ concentrations below the 2021 WHO air quality guideline limit of 15 µg/m³. To estimate the association between short term exposure to low level $PM_{2.5}$ and risk of morbidity, we restricted our analyses to days with daily $PM_{2.5}$ concentrations <15 µg/m³. To examine the lag structure of the association, we also fitted the models with separate terms for $PM_{2.5}$ on the same day of admission (lag 0) and 1 day previously (lag 1).

We presented results as both the excess relative risk and the excess absolute risk of hospital admissions or emergency department visits associated with a 10 µg/m³ increase in $PM_{2.5}$ concentrations.[1 4 20] Excess relative risk was defined as (relative risk−1)×100%, and excess absolute risk was calculated as α×(relative risk−1)/relative risk, where α is the incidence rate of cause specific hospital admissions or emergency department visits (see supplementary eAppendix).

Several sensitivity analyses were performed to examine the robustness of our findings. First, to examine the exposure-response association between exposure to $PM_{2.5}$ and risk of morbidity, we used a natural cubic spline with three degrees of freedom for lag 0-1 $PM_{2.5}$. Second, to assess whether our findings were robust to the choice of temperature metric, we replaced the daily mean ambient temperature in the models with daily maximum ambient temperature or daily minimum ambient temperature. Third, to account for spatial heterogeneity in relative humidity, we additionally included an interaction term between relative humidity splines and NCA4 regions in the models. Fourth, to examine the association between exposure to $PM_{2.5}$ and morbidity across the range of $PM_{2.5}$ levels, we repeated the main analysis without restricting our analyses to days with daily $PM_{2.5}$ concentrations <15 µg/m³.

To evaluate potential differences in susceptibility, we examined whether the association between exposure to $PM_{2.5}$ and risk of morbidity differed across subgroups of the population defined by age, sex, insurance type, and geographic region. We fit separate models for each stratum and conducted Wald tests to evaluate the heterogeneity across these strata.[21]

All statistical analyses were conducted in R software (version 4.0.2). We used the "gnm" (version 1.1.1) package[22] to fit the conditional Poisson regression models and the "dlnm" (version 2.4.2) package[23] to model the non-linear exposure-response functions.

Patient and public involvement
As the study used deidentified medical claims data, no patients or members of the public were involved in implementing the study design.

Results
Descriptive statistics
Of the 3144 counties in the contiguous US, we excluded those with no recorded hospital admissions or emergency department visits during the study period, resulting in a total of 2935 to 2939 counties included in the analysis, depending on the specific outcome (see supplementary table S2). Between 1 January 2010 and 31 December 2016, a total of 10.3 million hospital admissions and 24.1 million emergency department visits for natural causes were recorded among 50.1 million adults aged ≥18 years with commercial or Medicare Advantage health insurance (see supplementary table S3). The incidence rates of hospital admissions and emergency department visits for natural causes were 207.9 and 485.7 per million enrollees per day during the study period, respectively (see supplementary table S4).

Of these healthcare encounters, more than 50% of hospital admissions and 28% of emergency department visits were for cardiovascular and respiratory diseases, and the distribution varied considerably across different age groups (fig 1 and fig 2). For example, among adults aged <30 years, only 11.3% of all hospital admissions were attributed to cardiovascular or respiratory diseases, but this percentage increased to 92.7% among those aged ≥75 years. In terms of absolute numbers, the incidence rates
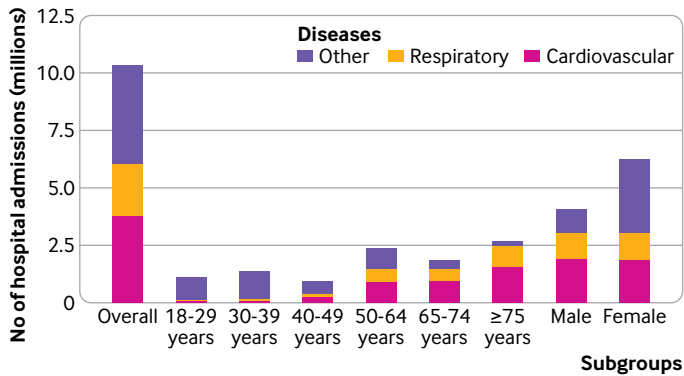
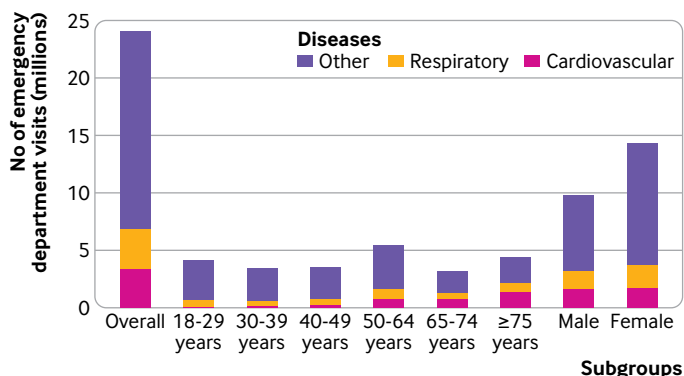**Fig 1 | Number of hospital admissions for cardiovascular, respiratory, and other diseases categorized by age and sex among adults with commercial or Medicare Advantage health insurance in the contiguous US, 2010-16. The width of age groupings is not uniform. The higher number of hospital admissions observed among adults aged 50-64 years partly results from the expansion of age ranges**

for hospital admissions and emergency department visits increased with age and tended to be higher in women compared with men, except for cardiovascular disease (see supplementary table S4).

Incidence rates of hospital admissions and emergency department visits also varied across geographic regions. The highest incidence rates for hospital admissions related to natural causes were observed in the northern Great Plains and the northeast, whereas the highest incidence rates for emergency department visits for natural causes were documented in the southeast and midwest (fig 3). Supplementary tables S3 and S4 show the total number and incidence rates of hospital admissions and emergency department visits for natural causes and for cardiovascular and respiratory diseases across different geographic areas, respectively.

During the study period, only 0.1% of county days (8344 out of 7 949 713) recorded daily PM$_{2.5}$ concentrations that exceeded the current national ambient air quality standards of 35 µg/m^3; these

counties were primarily located in central California, northwestern Utah, southwestern Montana, and east Idaho. Daily PM$_{2.5}$ levels were below the new WHO air quality guideline limit of 15 µg/m^3 in 92.6% of county days (7 360 725 out of 7 949 713) (see supplementary figure S2). Restricting our sample of events to days below this level resulted in the exclusion of 9.4% of hospital admissions and 9.1% of emergency department visits.

Regression results

Exposure to PM$_{2.5}$ at concentrations below the new WHO air quality guideline limit was associated with an increased risk of hospital admissions for natural causes, cardiovascular disease, and respiratory disease. Specifically, each 10 µg/m^3 increase in lag 0-1 PM$_{2.5}$ was associated with a 0.91% (95% confidence interval 0.55% to 1.26%) higher relative risk of hospital admissions for natural causes, 1.39% (0.81% to 1.98%) higher relative risk of hospital admissions for cardiovascular disease, and 1.90% (1.15% to 2.66%) higher relative risk of hospital admissions for respiratory disease (fig 4, also see supplementary table S5). The corresponding excess absolute risk was 1.87 (95% confidence interval 1.14 to 2.59), 1.04 (0.61 to 1.48), and 0.85 (0.52 to 1.18) per million enrollees per day for hospital admissions related to natural causes, cardiovascular disease, and respiratory disease, respectively (fig 4, also see supplementary table S6).

The association between exposure to PM$_{2.5}$ and risk of hospital admissions was most pronounced at lag 0, but with little evidence of continued higher risk at lag 1, except for respiratory diseases. For example, a 10 µg/m^3 increase in PM$_{2.5}$ was associated with a 0.86% (95% confidence interval 0.52% to 1.19%) higher relative risk at lag 0 and a 0.04% (−0.31% to 0.38%) higher relative risk at lag 1 for hospital admissions related to natural causes. The corresponding excess relative risk for respiratory disease was 0.86% (95% confidence interval 0.16% to 1.57%) at lag 0 and 1.03% (0.31% to 1.76%) at lag 1 (see supplementary table S7).

For emergency department visits, a 10 µg/m^3 increase in lag 0-1 PM$_{2.5}$ was associated with a 1.34% (95% confidence interval 0.73% to 1.94%) excess relative risk of emergency department visits for respiratory disease (fig 4, also see supplementary table S5), corresponding to 0.93 (95% confidence interval 0.52 to 1.35) additional emergency department visits per million enrollees per day (fig 4, also see supplementary table S6). The estimated association between exposure to PM$_{2.5}$ and emergency department visits for natural causes or for cardiovascular disease was weaker and not statistically significant.

We performed a series of sensitivity analyses to evaluate the robustness of our findings. In analyses that allowed for a flexible exposure-response relation for the association between exposure to PM$_{2.5}$ and morbidity, we found a monotonic association between exposure to PM$_{2.5}$ and the relative risk of hospital admissions for natural causes, cardiovascular disease, and respiratory

Fig 2 | Number of emergency department visits for cardiovascular, respiratory, and other diseases categorized by age and sex among adults with commercial or Medicare Advantage health insurance in the contiguous US, 2010-16. The width of age groupings is not uniform. The higher number of hospital admissions and emergency department visits observed among adults aged 50-64 years partly results from the expansion of age ranges
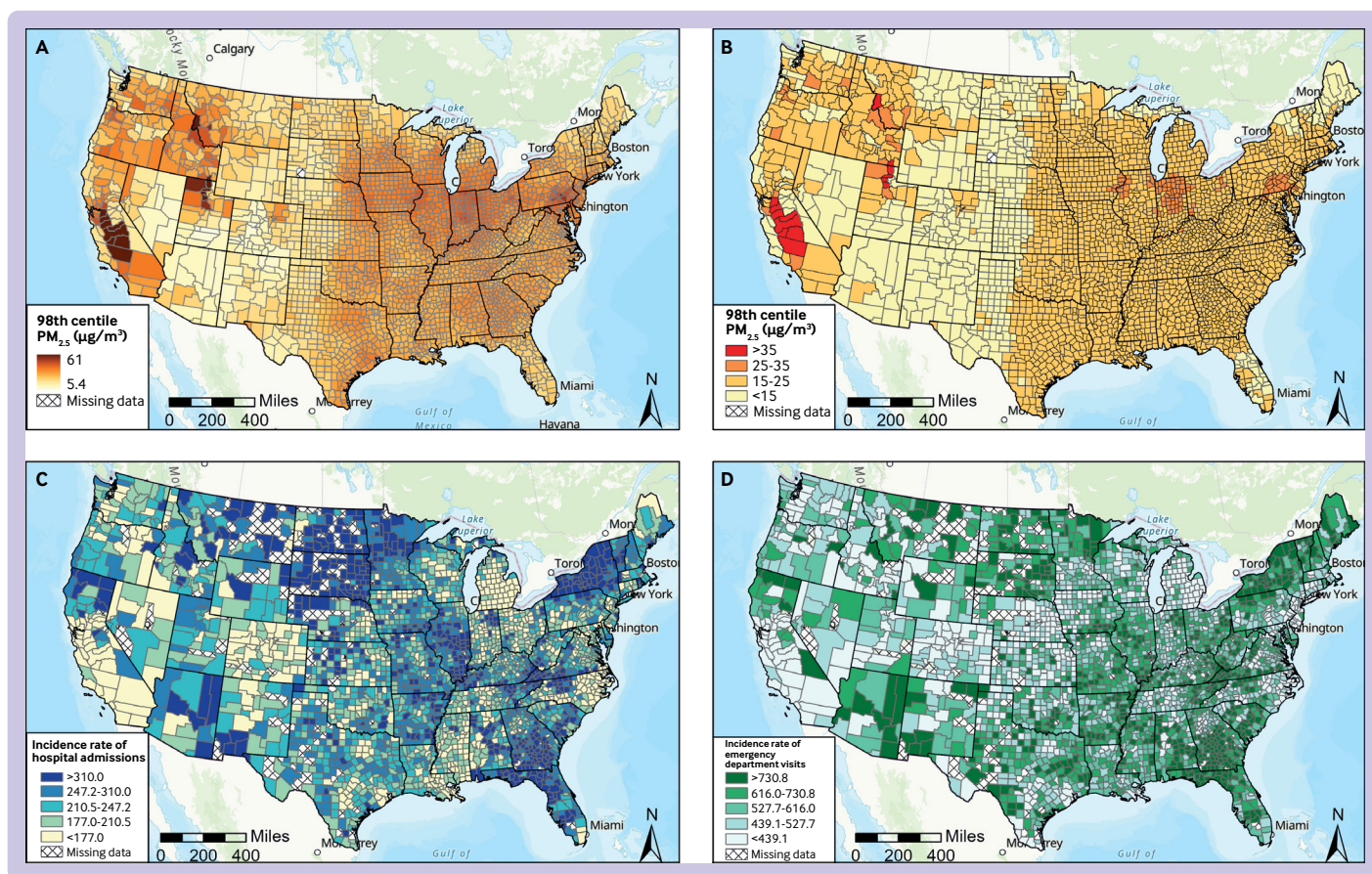
Fig 3 | Maps of the 98th centile distribution of PM$_{2.5}$ (fine particulate matter) concentrations and incidence rates per million enrollees per day of hospital admissions and emergency department visits for natural causes across US counties, 2010-16: (A) 98th centile distributions of PM$_{2.5}$ concentrations; (B) 98th centile distributions of PM$_{2.5}$ concentrations categorized by World Health Organization and national ambient air quality standards; (C) incidence rate per million enrollees per day of hospital admissions for natural causes in US counties; (D) incidence rate per million enrollees per day of emergency department visits for any cause in US counties. Crosshatching represents counties with missing air pollution data—the total number of hospital admissions or emergency department visits in these counties fell below the small cell suppression limit of 11

disease, with no indication of a threshold at lower concentrations (fig 5). We found a monotonic association between exposure to PM$_{2.5}$ and relative risk of emergency department visits for respiratory disease, with the association appearing more pronounced at lower PM$_{2.5}$ levels (fig 5). When we adjusted for daily maximum ambient temperature or daily minimum ambient temperature instead of daily mean temperature, the results remain consistent with our main findings, except for the association between PM$_{2.5}$ level and emergency department visits for natural causes and cardiovascular disease, which became statistically significant when we adjusted for daily minimum temperature (see supplementary table S8). Our results were not materially different when we additionally included an interaction term between relative humidity splines and NCA4 regions in the models (see supplementary table S9). Additionally, when we expanded our analysis beyond days with daily PM$_{2.5}$ concentrations <15 µg/m^3, we generally found an attenuation in the association for PM$_{2.5}$ compared with low level exposure to PM$_{2.5}$, suggesting that PM$_{2.5}$ concentrations are even more

strongly associated with adverse outcomes <15 µg/m^3 versus >15 µg/m^3 (see supplementary table S10).

We found that the association between exposure to PM$_{2.5}$ and hospital admissions for natural causes was statistically significant only among adults aged ≥65 years (fig 6). For example, a 10 µg/m^3 increase in PM$_{2.5}$ was associated with an excess relative risk of 0.36% (95% confidence interval −0.72% to 1.45%) among adults aged 18-29 years compared with 1.43% (0.60% to 2.26%) and 2.21% (1.52% to 2.91%) among those aged 65-74 years and ≥75 years, respectively. The corresponding excess absolute risks were 0.41 (95% confidence interval −0.84 to 1.67), 4.76 (2.04 to 7.48), and 14.57 (10.09 to 19.06) per million enrollee per day for adults aged 18-29 years, 65-74 years, and ≥75 years, respectively. The association between exposure to PM$_{2.5}$ and hospital admissions for natural causes was more pronounced among men, those residing in the northeast US, and those with Medicare Advantage health insurance.

For emergency department visits, we found a statistically significant association between exposure to PM$_{2.5}$ and respiratory disease (see supplementary
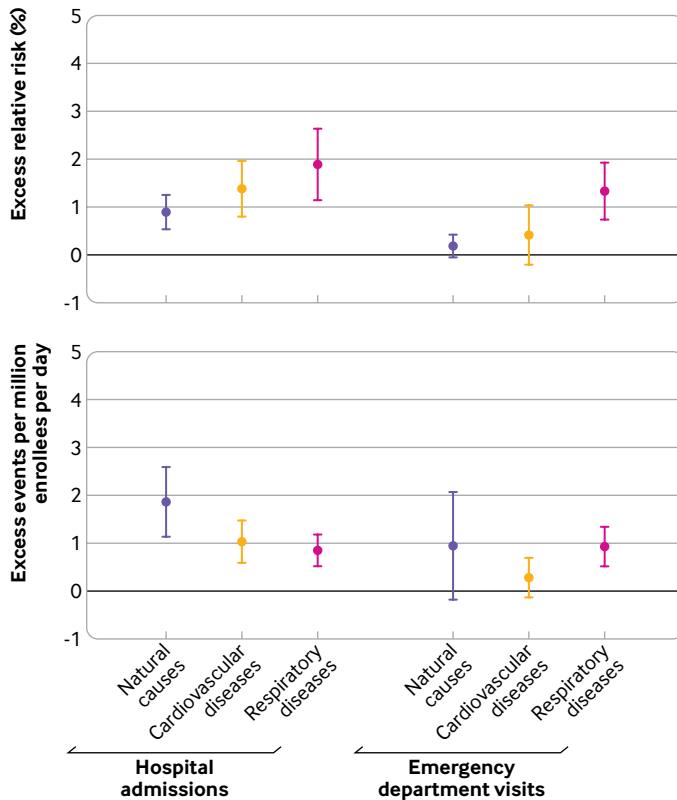
Fig 4 | Excess relative risk (percentage) and excess events of hospital admissions and emergency department visits for natural causes, cardiovascular disease, and respiratory disease associated with each 10 μg/m³ increase in fine particulate matter (PM₂.₅) during the current and previous day

figure S3). This association was most pronounced in young and middle aged adults and in the southern Great Plains. For example, we found that adults aged 40-49 years had the highest excess relative risk of 2.57% (95% confidence interval 0.87% to 4.30%) compared with the older population among whom the association was attenuated and not statistically significant. A 10 μg/m³ increase in PM₂.₅ was associated with an excess relative risk of 5.64% (3.77% to 7.54%) in the southern Great Plains versus 1.07% (−0.43% to 2.59%) in the US northeast.

Discussion

Using data encompassing more than 10 million hospital admissions and 24 million emergency department visits across the contiguous US from 2010 to 2016, we found that short term exposure to PM₂.₅, even at concentrations below the new WHO air quality guideline limit of 15 μg/m³, was statistically significantly associated with a higher risk of hospital admissions for natural causes, cardiovascular disease, and respiratory disease, as well as emergency department visits for respiratory disease.

Comparison with other studies

Studies of the potential health effects of PM₂.₅ at low levels (by today's standards) provide valuable insights and critically inform national health policies. However,

relatively few such studies have been conducted.[1 24 25] For example, in a pooled analysis of multiple European cohorts, one study evaluated the association between long term exposure to PM₂.₅ and mortality, with a focus on the health effects of such exposure below the current standards and guidelines of the European Union (25 μg/m³) and US (12 μg/m³) and previous guidelines from WHO (10 μg/m³).[24] Another study used mortality data from the US Medicare fee-for-service population to estimate the association between short term exposure to PM₂.₅ below the current daily national ambient air quality standard (35 μg/m³) and mortality in the US.[1] In a recent study, researchers found that the adverse health effects of PM₂.₅ on all cause mortality persisted at lower levels of PM₂.₅ below the previous WHO air quality guideline limit of 25 μg/m³.[3 26] Our study investigated whether the risk of morbidity occurs at levels of PM₂.₅ below the newly revised WHO air quality guideline limit of 15 μg/m³, using data on both hospital admissions and emergency department visits among younger and older adults in the US.

The new WHO air quality guideline calls for a limit on 24 hour mean PM₂.₅ concentrations to 15 μg/m³, a reduction from the previous limit of 25 μg/m³ set in 2005, in response to compelling evidence of substantial health effects of PM₂.₅ even at concentrations below the earlier limit. Our study identified a consistent monotonic exposure-response association between exposure to PM₂.₅ at levels below the new WHO air quality guideline limit and hospital admissions for natural causes, cardiovascular disease, and respiratory disease, and emergency department visits for respiratory diseases. Notably, when examining emergency department visits, we noted that the association between PM₂.₅ level and respiratory disease appears to be more pronounced at lower PM₂.₅ levels. These findings provided evidence that PM₂.₅ continues to pose adverse health risks even when concentrations are below the newly revised WHO air quality guidelines, which corroborates the conclusion that probably no safe level of exposure to PM₂.₅ exists—that is, the level below which no adverse health effects are observed.[1 24-26]

Our findings that PM₂.₅ level was associated with hospital admissions among adults ≥aged 65 years but not among adults aged <65 years were consistent with previous studies.[10 27] For example, a nationwide study in Italy, examining the link between air pollution and hospital admissions for respiratory disease, found that PM₂.₅ level was associated with higher risk of hospital admissions among adults aged ≥75 years but not among adults aged <75 years.[10]

We found statistically significant associations between exposure to PM₂.₅ and increased risk of emergency department visits for respiratory disease exclusively among adults aged <50 years. These findings indicate that previous studies that focused on older populations may not have fully captured the adverse health effects of PM₂.₅ on respiratory related emergency department visits. Relying on such studies could potentially lead to an underestimation of the
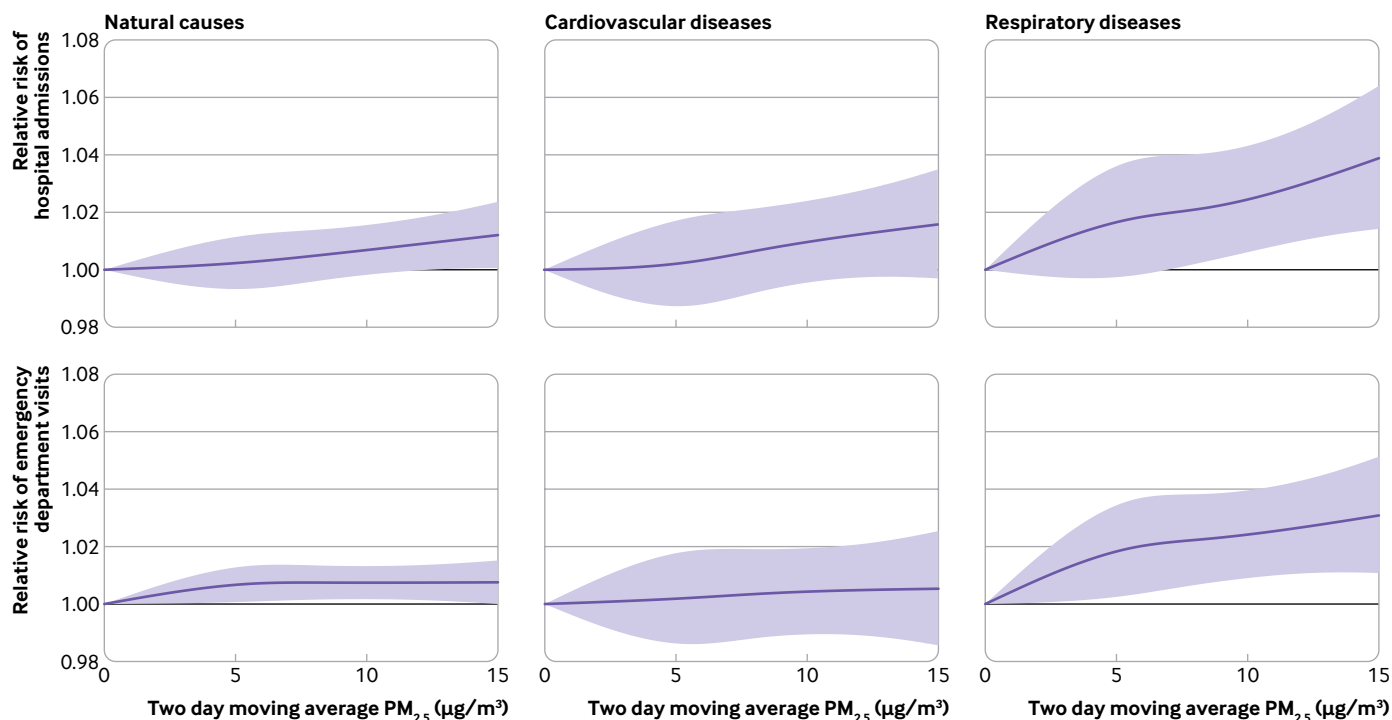
Fig 5 | Exposure-response curve for association between two day moving average of $PM_{2.5}$ (fine particulate matter) concentrations and hospital admissions and emergency department visits for natural causes, cardiovascular disease, and respiratory disease. The reference point on the curve is the counterfactual concentration at 0 µg/m^3 of the two day moving average $PM_{2.5}$ during the study period

health effects of $PM_{2.5}$, particularly among younger age groups. Our findings were consistent with a US nationwide study among 40 million respiratory related emergency department visits collected through the Centers for Disease Control and Prevention's national environmental public health tracking network.[11] This study found a strong association between $PM_{2.5}$ level and emergency department visits for respiratory disease among children and young people aged 0-18 years, a moderate association among adults aged 19-64 years, and no significant association among older adults aged ≥65 years.[11]

We found that most of the adverse health effects of $PM_{2.5}$ were more pronounced among adults with Medicare Advantage health insurance than among adults with commercial health insurance. Enrollees in the Medicare Advantage programme are largely adults aged >65 years. Thus, the health effect of $PM_{2.5}$ among Medicare enrollees is similar to that among people aged ≥65 years. For example, no association was found between short term exposure to $PM_{2.5}$ and emergency department visits for respiratory disease among both Medicare enrollees and older adults. We observed geographic differences in the health effects of $PM_{2.5}$, with beneficiaries residing at higher latitudes tending to show higher risk of hospital admissions and emergency department visits for cardiovascular disease associated with exposure to $PM_{2.5}$. We speculate that geographic locations may modify the association between exposure to $PM_{2.5}$ and morbidity, possibly through factors such as differences

in local temperature,[28 29] and particle composition contributing to varying levels of oxidative potential.[30]

Limitations and strengths of this study
Our study has several limitations. First, we used county level $PM_{2.5}$ level as a proxy for personal exposure to $PM_{2.5}$, which could potentially lead to misclassification of exposure. Additionally, the absence of information on patients' time-activity patterns might introduce additional misclassification of exposure. Nevertheless, we expect that any potential misclassification would likely be non-differential and would tend to bias our results toward the null hypothesis of no association.[31] Second, our study population was limited to US adults with health insurance, which may limit the generalizability of our findings to individuals without medical insurance, children and adolescents, and individuals living outside the contiguous US. Third, our analysis was conducted using data available up to 2016. Future studies with more recent data on exposure to air pollution and morbidity are warranted to provide further evaluation of the evidence on the association between exposure to $PM_{2.5}$ and morbidity, particularly at daily $PM_{2.5}$ levels below the 2021 WHO air quality guideline limit.

Our study has three main strengths. First, our study population included more than 10 million hospital admissions and 24 million emergency department visits among beneficiaries with commercial and Medicare Advantage insurance. The enrollees span a broad spectrum of age groups older than 18 years, and
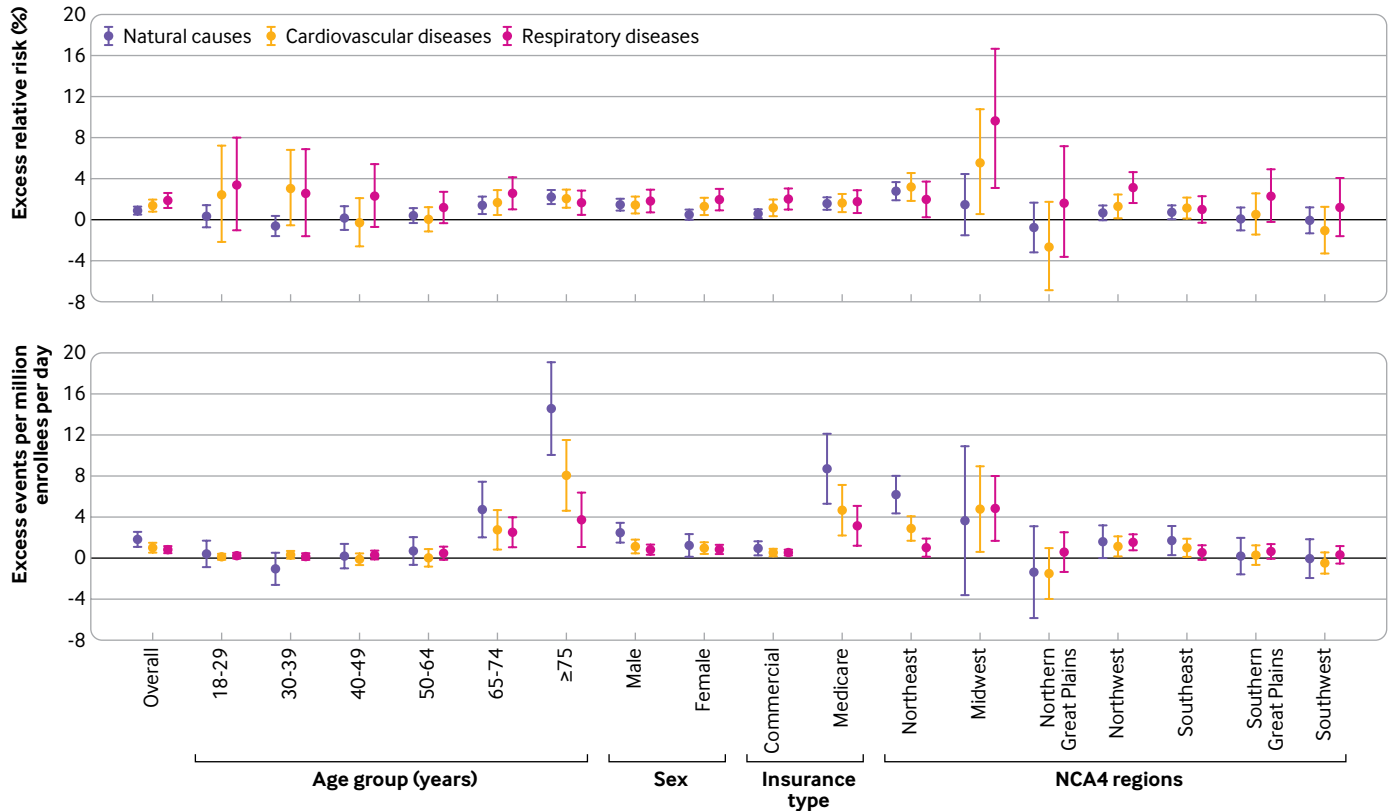
Fig 6 | Excess relative risk (percentage) and excess events of hospital admissions for natural causes, cardiovascular disease, and respiratory disease associated with each 10 μg/m³ increase in PM₂.₅ (fine particulate matter) during the current and previous day, stratified by age, sex, insurance type, and NCA4 (US Global Change Research Program's Fourth National Climate Assessment) regions

they are distributed across different climate regions in the contiguous US. Second, we not only assessed the excess relative risk of morbidity for natural causes, cardiovascular disease, and respiratory disease but also quantified the absolute risk associated with short term exposure to PM₂.₅. Therefore, our study provides a comprehensive evaluation of the health effects of daily PM₂.₅ at levels below the new WHO air quality guideline limit of 15 μg/m³. Third, we included both hospital admissions and emergency department visits as our primary health outcomes, allowing us to compare the health impacts of PM₂.₅ levels on different morbidity metrics.

Conclusions and policy implications

Short term exposures to PM₂.₅ below the new WHO air quality guideline limit of 15 μg/m³ are associated with higher risks of hospital admission for natural causes, cardiovascular disease, and respiratory disease as well as for emergency department visits for respiratory disease among adults with health insurance in the contiguous US. Our study contributes to the evidence that ambient air pollution is associated with morbidity even at PM₂.₅ levels below the current WHO air quality guideline limit. Our study provides an initial assessment of the newly revised WHO guidelines for PM₂.₅ and provides valuable reference for future national air pollution standards.

results of the research to the general public through media outreach, including press releases by the media departments of the authors' research institutes and plain language messaging in social media.

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Supplementary information: eAppendix, tables S1-S10, and figures S1-S3