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Nationwide Study of Short-Term Exposure to Fine Particulate Matter and Cardiovascular Hospitalizations among Medicaid Enrollees

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Abstract

Background: Fine particulate matter (PM_{2.5}) has been consistently linked to cardiovascular disease (CVD). Although studies have reported modification by income, to our knowledge no study to date has examined this relationship among adults in Medicaid, which provides health coverage to low-income and/or disabled Americans.

Methods: We estimated the association between short-term PM_{2.5} exposure (average of PM_{2.5} on the day of hospitalization and the preceding day) and CVD admissions rates among adult Medicaid enrollees in the continental US (2000–2012) using a time-stratified case–crossover design. We repeated this analysis at $PM_{2.5}$ concentrations below the World Health Organization daily guideline of 25 μ g/m³. We compared the PM_{2.5} – CVD association in the Medicaid 65 years old vs. non-Medicaid-eligible Medicare enrollees (65 years old).

Results: Using information on 3,666,657 CVD hospitalizations among Medicaid adults we observed a 0.9% (95%CI: 0.6, 1.1%) increase in CVD admission rates per 10 μ g/m³ PM_{2.5} increase. The association was stronger at low $PM_{2.5}$ levels (1.3%; 95%CI: 0.9, 1.6%). Among Medicaid enrollees 65 years old, the association was 0.9% (95%CI: 0.6, 1.3%) vs. 0.8% (95%CI: 0.6, 0.9%) among non-Medicaid-eligible Medicare enrollees 65 years old.

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Description of the process by which someone else could obtain the data and computing code required to replicate the results reported in your submission (or explanation why data or code are not available): Investigators can obtain the Medicaid claims used in this study from the Centers for Medicaid Services. The code used in this study is available on request.

Conclusion: We found robust evidence of an association between short-term $PM_{2.5}$ and CVD hospitalizations among the vulnerable subpopulation of adult Medicaid enrollees. Importantly, this association persisted even at $PM_{2.5}$ levels below the current national standards.

Keywords

Case–crossover; Cardiovascular; PM2.5; Short-term exposure; Medicaid; Medicare; Fine particles; Air pollution

Introduction

Ambient fine particulate matter pollution ($PM_{2.5}$; particulate matter with aerodynamic diameter 2.5 μm) has been consistently shown to be associated with cardiovascular morbidity and mortality. $1-7$ Several possible mechanisms have been proposed by which short-term exposure to PM_{2.5} may lead to cardiovascular disease (CVD): PM_{2.5}, with its high alveolar penetration capacity, can trigger systemic inflammation and oxidative stress, can alter sympathetic/parasympathetic balance, and can increase clotting factors leading to CVD $1-3$, one of the leading causes of mortality and morbidity globally.^{8,9}

The Clean Air Act requires that the National Ambient Air Quality Standards (NAAQS) in the United States protect "sensitive subgroups," including—but not limited to socioeconomically disadvantaged individuals. Socio-economic status (SES) and access to social support are fundamental drivers of health disparity; disadvantaged individuals and communities systematically lack access to resources that protect and improve health.¹⁰ Furthermore, disadvantaged communities experience higher exposures to environmental hazards, $11-14$ and may be more vulnerable to the effects of such hazards.¹⁵ In the United States, environmental risk varies spatially, with documented stark racial or ethnic and socioeconomic disparities in exposure to air pollution.^{11–13} Socio-economically disadvantaged Americans, thus, are a particularly sensitive subgroup that the NAAQS are designed to protect.

The paucity of studies characterizing the $PM_{2.5}$ – CVD association among socioeconomically disadvantaged Americans motivates the focus of our study on Medicaid enrollees. Medicaid is a joint federal–state program that provides health or nursing home coverage to certain categories of low-income Americans, including children, pregnant women, parents of eligible children, people with disabilities, and elderly needing nursing home care. Although Medicaid eligibility criteria vary by state and population groups (e.g., by children, pregnant women, families of different sizes), they are based on: (a) income level in comparison to the federal poverty line; and/or (b) disability; and/or (c) substantial medical needs. Previous studies have found that those enrolled in Medicaid are at higher risk of respiratory hospitalizations from increased air pollution exposures relative to individuals with private insurance.^{16,17} In addition, low-income Americans have the highest prevalence of CVD.18 These reasons, in combination with the increased detrimental environmental exposures among low-SES populations, $11-14$ further motivate our focus on the Medicaid cohort.

To our knowledge, this is the first study to estimate the association between short-term exposure to $PM_{2.5}$ and total and cause-specific CVD hospitalizations, among adult Medicaid enrollees, for the entire continental United States (2000–2012). We focused our analyses on PM_{2.5}—a mixture of solid particles and liquid droplets that can be primarily emitted by numerous sources, including but not limited to traffic, industrial processes, wildfires, etc, and secondarily formed in the atmosphere¹⁹—as it is an indicator of the air pollution mixture at each location. Previous studies of other populations have reported how factors such as race or ethnicity, sex, and age modify the relationship between $PM_{2.5}$ and CVD hospitalization rate.^{20,21} We have, therefore, assessed if these factors are also important effect modifiers in the adult Medicaid population. We also compared the association between short-term $PM_{2.5}$ exposure and total CVD in Medicaid enrollees aged 65 years and older with that of corresponding enrollees in Medicare (a national health insurance program that provides health insurance for Americans aged 65 years and older) who are not eligible for Medicaid. Eligibility for Medicaid is based on income and/or disability status, whereas eligibility for Medicare is primarily based on age. Therefore, a side-by-side comparison of the $PM_{2.5}$ –CVD association in these two populations provides information about how income may modify vulnerability to air pollution exposure among the elderly. Finally, we estimated the association between $PM_{2.5}$ and CVD hospitalizations in the adult Medicaid cohort at low PM_{2.5} concentrations ($25 \mu g/m^3$), the World Health Organization (WHO) guideline for the daily average $PM_{2.5}$.²²

Methods

Study Population

From the Center for Medicare and Medicaid (CMS)—the two largest health insurance providers in the US—we obtained access to two nationally representative open cohorts for the period 2000–2012: all fee-for-service (FFS) full-benefit Medicaid enrollees of all ages (low-income and disabled Americans) and all FFS Medicare enrollees (aged 65 years and older). Information on Medicaid enrollees was not available for Maine from 2005–2010 and for Kansas for 2010. We have, thus, also removed this information from the Medicare dataset from our analysis to facilitate comparison.

Both Medicaid and Medicare datasets provide demographic information, including age, sex, race/ethnicity, and residential ZIP Code. We focused our analyses on adult Medicaid enrollees (aged 18 years and older). For Medicaid enrollees this information is recorded at each hospitalization visit; if an enrollee suffered multiple hospitalizations, we extracted the demographic information from a random hospitalization record for that enrollee for our analyses.

Medicaid enrollees, unlike in Medicare, have to re-enroll themselves in the program on an annual basis. Therefore, individuals may leave and re-enter the program over the years. This can lead to intermittent enrollment if eligibility criteria are not satisfied every year, resulting in periods during which the health status of some individuals is not recorded in Medicaid claims.

All individuals aged 65 year and older are eligible for Medicare. However, only some are also eligible for Medicaid (Medicaid-eligible Medicare enrollees), depending on income and/or disability. Medicare is the primary payer for individuals aged 65 years and older, who are eligible for Medicaid, up to a payment limit, and Medicaid is the secondary payer.

This study was approved by the Institutional Review Board at the Harvard T.H. Chan School of Public Health.

Outcome Assessment

We defined CVD-related hospitalizations as events with a primary diagnosis (the condition chiefly responsible for the individual's hospitalization) corresponding to an International Classification of Diseases, 9th Revision (ICD-9) codes from 390 to 495. If any individual experienced multiple hospitalizations during the study period (2000–2012), we included the first hospitalization only. We also excluded any individual who had been hospitalized for CVD in 1999. We examined associations with the following cause-specific CVD hospitalizations: ischemic heart disease (IHD; ICD-9 codes: 410–414), congestive heart failure (CHF; ICD-9 code: 428), acute myocardial infarction (AMI; ICD-9 code: 410.9) and ischemic stroke (ICD-9 code: 434.91). CVD events during which individuals were not enrolled in Medicaid are not captured in our analyses.

Exposure Assessment

We obtained daily ambient $PM_{2.5}$ concentration estimates from a well-validated air pollution prediction model (2000–2012), described in detail elsewhere.²³ Briefly, these estimates were derived for 1 km² grid cells in the continental United States by integrating remote sensing, outputs from a chemical transport model, and other variables such as meteorological and land-use variables. Subsequently, $PM_{2.5}$ estimates were obtained from an ensemble model that integrated multiple machine learning algorithms. Cross-validation indicated excellent overall predictive accuracy (cross-validated R^2 =0.86). We used the gridded predictions to estimate daily ZIP Code-level averages and subsequently linked those to the residential ZIP Codes of Medicaid and Medicare enrollees.

Covariate Information

We retrieved air and dew-point temperatures from North American Regional Reanalysis data, 24 providing daily mean values for each 32 km² grid cell in the continental United States. ZIP Code-level daily temperature values were computed by using area-weighted averages for each ZIP Code.

Ozone (O_3) concentrations were derived from fitting a neural network model which integrated remote sensing, outputs from a chemical transport model, and meteorologic and land-use variables.²⁵ Daily ambient O₃ concentrations were predicted at 1 km² grid cells for the continental United States. The cross-validated \mathbb{R}^2 for the predicted values was 0.80 for the entire study period. For O_3 , ZIP Code-level daily values were obtained by taking the inverse-distance mean of the four nearest grid cells to each ZIP Code's centroid.

Statistical Analysis

We used a time-stratified case–crossover design to estimate the association between daily PM_{2.5} and total and cause-specific CVD hospitalizations. The case–crossover design, a variant of the case–control design, was developed to study the effects of transient exposures on acute events.26 In this design, the case days are identified as the days when the first hospitalization for CVD for a given individual occurred. For each case day—and for the same individual that experienced the event—control days are subsequently bidirectionally selected, defined as days when no hospitalization occurred, and matched on the same year, month, and day of the week as the case day. This design eliminates any confounding by factors that do not vary within an individual and month on average in the population, effectively eliminating any potential confounding bias by individual-level factors such as smoking and body mass index. This design also adjusts for measured and unmeasured confounding by seasonality and long-term trends by design.^{27,28} Further, by comparing the PM_{2.5} exposure distributions on case days with control days matched on the same day of the week within a month, we also accounted for the short-term serial correlation observed in $PM_{2.5}$ variations and potential confounding by day of week. For all analyses, we used the average $PM_{2.5}$ exposure on the day of and the preceding day of an individual's CVD hospitalization (which we denote as Lag01).

We used conditional logistic regression models to estimate the associations between shortterm exposure to $PM_{2.5}$ and CVD hospitalization rates. We also included the mean of the dew-point temperature and air temperature for the day of hospitalization and the day prior (Lag01)—since these factors vary within a month and could act as confounders—using natural splines with 3 degrees of freedom.

We performed analyses for all adult Medicaid enrollees and non-Medicaid-eligible Medicare enrollees. To examine whether the $PM_{2.5} - CVD$ association among adult Medicaid enrollees persists at PM_{2.5} concentrations below the WHO guidelines, we restricted case and control days to those with $PM_{2.5}$ concentrations below 25 $\mu\text{g/m}^3$ and repeated the analysis. In a separate analysis, we restricted case and control days to those with $PM_{2.5}$ concentrations above 25 μ g/m³. Finally, we estimated the association between Lag01 PM_{2.5} and causespecific CVD hospitalizations among all adult Medicaid enrollees.

We report all results as percent change in CVD admission rates (95% confidence interval [CI]) per 10 μ g/m³ increase in PM_{2.5}. We have chosen this increment for comparability with other studies examining the same association in other populations.29,30 We conducted all statistical analyses using the R Statistical Software, version 3.3.2 (Foundation for Statistical Computing, Vienna, Austria).³¹

Effect Modification

We assessed whether there is evidence of effect modification of the association between $PM_{2.5}$ and CVD hospitalization rates among adult Medicaid enrollees by the following factors: age group (18 to 44 years, 45 to 64 years, 65 years and older), sex and race/ethnicity (White non-Hispanic, Black non-Hispanic, Hispanic, and other, as well as White vs. non-White). To test for effect modification, we ran separate conditional logistic models that

included an interaction term between $PM_{2.5}$ and each of the above potential effect modifiers. We used likelihood ratio tests (LRT) to compare models with and without the interaction terms.

Sensitivity Analyses

We assessed the robustness of our results to several modelling choices, such as the degrees of freedom used for confounding adjustment for air and dew-point temperature. We compared results using 3, 6 and 9 degrees of freedom. Finally, we also assessed the robustness of our results to Lag01 $O₃$ adjustment.

Results

There were 3,779,051 first CVD hospitalizations (i.e., case days) among adult Medicaid enrollees between 2000 and 2012 in the continental United States. Of these, 3,666,657 (97%) had available information on date of birth and were aged 18 years and older. Table 1 provides summary statistics of the adult Medicaid enrollees that were hospitalized due to a CVD event. Of this population, 59.0% were female and 50.3% were White non-Hispanic.

The Figure provides a summary of CVD hospitalizations and $PM_{2.5}$ levels for each case day for adult Medicaid enrollees by state. IHD and CHF were the dominant causes for CVD hospitalizations, accounting for 24.9% and 14.8 % of all CVD hospitalizations, respectively. For the 3,666,657 case days, we selected 12,452,125 control days (3.4 controls per case on average). The average daily $PM_{2.5}$ concentration over all case days for the study period was 11.5 μ g/m³ (standard deviation 7.3 μ g/m³). The daily PM_{2.5} for each state during the study period is shown in eFigure 1.

Table 2 presents all estimated effects. Overall, we found that a 10 μ g/m³ increase in PM_{2.5} exposure was associated with a 0.9% (95%CI: 0.6, 1.1%) increase in the rate of CVD hospitalizations in the adult Medicaid population. When restricting case and control PM_{2.5} levels to $25 \mu g/m^3$, the association between PM_{2.5} and total CVD hospitalization rates in the adult Medicaid population remained elevated (1.3%; 95%CI: 0.9%, 1.6%). The association was highest for ischemic stroke hospitalizations, though the confidence intervals across all cause-specific CVD hospitalizations widely overlapped.

There were 11,252,963 CVD hospitalizations among Medicare enrollees (aged 65 years and older), 84.0% of which were among non-Medicaid-eligible Medicare enrollees (Table 1). We observed a 0.8% (95%CI: 0.6, 0.9%) among non-Medicaid-eligible Medicare enrollees.

Effect Modification

All estimated associations by subgroup are presented in Table 2. Although the estimated effects were slightly lower among younger Medicaid adults (18 to 44 years old), the confidence intervals across all age groups overlapped. We observed no effect modification by sex. We detected no evidence of effect modification by race/ethnicity when we used detailed race/ethnicity categories. However, we observed an effect modification when considering adult White vs. non-White enrollees, with highest estimates among White

Medicaid enrollees. Likelihood ratio tests confirmed the evidence of effect modification by the broader race or ethnicity classification.

Sensitivity Analyses

Our results were robust to confounding adjustment for air and dew-point temperature. Further adjusting for O_3 also only slightly changed the association between PM_{2.5} and CVD hospitalizations. The results from the sensitivity analyses are presented in eTable 1.

Discussion

We conducted a nationwide analysis among adult Medicaid enrollees to estimate the association between short-term $PM_{2.5}$ exposure and CVD hospitalization rates among lowincome and disabled Americans. We observed harmful associations that were robust to sensitivity analyses. We did not detect evidence of effect modification by sex or age. We also did not observe meaningful differences in effect estimates among Medicaid elderly vs. non-Medicaid-eligible Medicare enrollees. However, we found evidence for higher effect estimates among adult White Medicaid enrollees. Although we observed some variability in effect estimates across cause-specific CVD hospitalizations, the confidence intervals widely overlapped. Further research is warranted to draw more conclusive evidence on potential differences in associations with $PM_{2.5}$ across CVD outcomes in the Medicaid population.

Previous studies have reported effect modification by race or ethnicity, with higher estimates observed among Hispanic and Black Americans.^{32–34} For example, a previous study examined the association between daily $PM_{2.5}$ and CVD mortality in California and reported that Hispanic residents experienced higher effect estimates.34 In our study, however, we found that the association between $PM_{2.5}$ and CVD hospitalizations was highest among adult White Medicaid enrollees. Higher CVD mortality among non-White racial groups, with Black Americans experiencing the highest CVD mortality at all ages,^{18,35} and worse quality of and unequal access to care for racial or ethnic minorities, 36 could explain the results from our multiplicative models. More frequent fatal events among non-White Americans would reduce CVD-related admissions in these racial or ethnic groups.

With access to both Medicaid and Medicare cohorts, we had the opportunity to evaluate whether enrollment in Medicaid (low-income) aggravated estimated PM_{2.5} effects on CVD among elderly Americans. Specifically, we compared effect estimates among Medicaid enrollees aged 65 years and older to those obtained in analyses among non-Medicaideligible Medicare enrollees. Although the effect estimates among elderly Medicaid enrollees were slightly higher, the confidence intervals widely overlapped. The highest association was seen in Medicaid-eligible-Medicare enrollees. As discussed previously, there is no exact overlap between the Medicaid-eligible Medicare population and the elderly Medicaid population, which would explain the differences in the estimates for the elderly Medicaid enrollees and the Medicaid-eligible Medicare enrollees. A previous study of short-term PM_{2.5} exposure and mortality among Medicare enrollees reported elevated effects among Medicaid-eligible enrollees. 37 Although in our study we found no evidence of effect estimate heterogeneity in the Medicaid population aged 65 years and older and the non-Medicaid-eligible Medicaid cohort, further research is warranted to characterize the distinct

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effects of $PM_{2.5}$ on CVD among low-income and elderly Americans, two particularly vulnerable subpopulations.

One of our study goals was to examine whether Medicaid enrollees exposed consistently to low PM_{2.5} concentrations still experience adverse PM_{2.5}-related CVD impacts. To this end, we evaluated the association between short-term $PM_{2.5}$ exposure and CVD hospitalizations among adult Medicaid enrollees defining low daily $PM₂$ concentrations according to WHO guidelines $(25 \mu g/m^3)$. This guideline is different from the current United States Environmental Protection Agency (EPA) NAAQS for daily $PM_{2.5}$ concentrations (the 98th percentile, averaged over 3 years, should not exceed $35 \mu g/m^3$).³⁸ Which of the two standards is stricter depends on the distribution of the daily $PM_{2.5}$ concentrations at each location. We chose to use the WHO guidelines, however, because using as a cut-off a guideline for daily concentrations to define low-level exposures facilitates analyses and interpretation. In our study, the average $PM_{2.5}$ exposure was well below 25 $\mu\text{g/m}^3$ and the majority of our data were included in the low level-restricted analysis. Conversely, only a very small fraction of our observations occurred at $PM_{2.5} > 25 \mu g/m^3$ and the estimated association in this subpopulation was lower with wide confidence intervals. These two subpopulations, however, may not be directly comparable. $PM_{2.5}$ levels have been steadily decreasing over the US; the events, thus, included in the analyses restricted to PM_2 , \leq 25 μ g/m³ likely occurred earlier in our study period. The distribution of many other CVD risk factors that can modify the $PM_{2.5}$ –CVD association has also changed over the same time. $39-42$ Our findings of a stronger association at lower PM_{2.5} levels are in agreement with previous studies of both short- and long-term $PM_{2.5}$ exposures and adverse health.^{43–45}

Our study has several strengths. First, to our knowledge, this is the first nationwide study to estimate the association between short-term $PM_{2.5}$ exposure and CVD among adult Medicaid enrollees. Second, we assigned daily exposures using highly accurate air pollution prediction models providing highly resolved daily $PM_{2.5}$ estimates, including at areas with sparse or no monitoring. This increases the generalizability of our findings to Medicaideligible low-income Americans in both rural and urban areas. Third, we conducted the same statistical analysis with a side-by-side comparison of results among non-Medicaid-eligible Medicare enrollees and elderly Medicaid enrollees aged 65 years and older, which allowed us to evaluate the degree to which being enrolled in Medicaid may increase vulnerability to short-term $PM_{2.5}$ exposure. Finally, we conducted sensitivity analyses for confounding adjustment and found our effect estimates to be robust.

Our findings, nonetheless, should be interpreted in light of our limitations. First, because residential information was only available at the ZIP Code level, some exposure measurement error is to be expected. Nonetheless, any error is not likely to covary with date of CVD admission within month and ZIP code, that is, we do not expect any differential exposure measurement error, given our study design that benefits from within-person contrasts. Our estimates, thus, are likely attenuated.46,47As the Medicaid eligibility criteria are different across states, the Medicaid population also differs by state. There are, for example, more Medicaid beneficiaries in states with less stringent eligibility criteria than in other states. This hinders generalizability of our results to all low-income Americans. Medicaid eligibility criteria also change over time. The largest Medicaid expansion in recent

history was a result of the Affordable Care Act (ACA). The Affordable Care Act (ACA) was signed into law in 2010 and coverage under the Medicaid expansion became effective in most states as early as January 2014 (and later in other states). Our study period (2000– 2012) does not cover the Medicaid population under this expansion; therefore, ACA has not influenced Medicaid eligibility in our study.

Finally, we did not adjust our main models for other pollutants. Given that $PM_{2.5}$, a mixture itself partially primarily emitted from numerous sources and partially secondarily formed, is an indicator of the overall air pollution mixture at each location, adjustment for pollutants emitted from the same sources would change the interpretation of the $PM₂$ effect estimates. For instance, adjustment for a traffic emissions tracer, such as nitrogen dioxide, would change the interpretation of the $PM_{2.5}$ estimate—i.e., that of an overall air pollution mixture estimate—to a non-traffic air pollution estimate. Nonetheless, we adjusted for O_3 in a sensitivity analysis. O_3 is a secondarily formed gas through similar photochemical processes as secondary particles. Adjusting for O_3 could remove some of the outcome variability that is due to secondary particles. In our data, nonetheless, O_3 and $PM_{2.5}$ were weakly correlated (r=0.19). The PM_{2.5} effect estimate, thus, did not change in the O₃-adjusted model.

In conclusion, our study provides robust evidence of a harmful association between shortterm PM2.5 exposure and rate of CVD hospitalizations in the United States Medicaid population. During our study period, the average $PM_{2.5}$ concentration was much lower than the current daily WHO guidelines for daily $PM_{2.5}$ concentrations, revealing elevated adverse PM_{2.5} estimated effects on CVD even at low exposures. Furthermore, the observed association remained elevated, and became even larger, when we restricted analyses to PM_{2.5} levels below the WHO guidelines.

Our findings are consistent with the hypothesis of adverse $PM_{2.5}$ health effects in vulnerable subpopulations, such as low-income and disabled Americans, at $PM_{2.5}$ concentrations well below the current standards,⁴⁸ such as low-income and disabled Americans.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure:

Daily average PM_{2.5} concentrations (μ g/m³) corresponding to case days in each state from 1 Jan 2000 to 31 Dec 2012, and the number of first hospitalizations for adult Medicaid enrollees, i.e., case days, in each state.

Table 1:

Characteristics of adult Medicaid enrollees (aged 18 years and older) who experienced a CVD hospitalization during 2000 – 2012.

AMI: Acute Myocardial Infarction; CHF: Congestive Heart Failure; IHD: Ischemic Heart Disease

Table 2:

Percent change in CVD hospitalization rates per 10 μ g/m³ increase in PM_{2.5}.

 $b_{\text{Ncases}} = 3,666,490$

 $c_{\text{Ncases}} = 3,339,790$

 $d_{\text{Ncases}} = 3,514,773$

 $e_{\text{Ncases}} = 151,884$

AMI: Acute Myocardial Infarction; CHF: Congestive Heart Failure; IHD: Ischemic Heart Disease