HHS Public Access

Author manuscript

Sci Total Environ. Author manuscript; available in PMC 2023 May 25.

Published in final edited form as:

Sci Total Environ. 2022 November 25; 849: 157934. doi:10.1016/j.scitotenv.2022.157934.

Fine particle components and risk of psychiatric hospitalization in the U.S.

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Abstract

Background—There is a lack of evidence for the associations between atmospheric particle components exposure and psychiatric health. We aimed to identify the most toxic particle component(s) and source(s) related with psychiatric illness.

Methods—Using Health Cost and Utilization Project (HCUP) State Inpatient Databases (SIDs), we analyzed the relative risk (RR) of psychiatric hospitalization associated with increased residential exposure to 14 particle components (Zn, V, Si, Pb, Ni, K, Fe, Cu, Ca, Br, sulfate (SO_4^{2-}), nitrate (NO_3^-), organic carbon (OC), and elemental carbon (EC)). We covered the residents of eight U.S. states, who contributed to 5,012,041 psychiatric admissions over 2002–2018. Single component models were conducted via fitting zero-inflated negative binomial regression for each component with aggregated counts of total psychiatric hospitalizations per ZIP code per year as dependent variable. We used Nonnegative Matrix Factorization (NMF) to identify particle source factors and obtained the source-specific estimates. Generalized Weighted Quantile Sum (gWQS) Regression was applied to obtain an overall mixture effect. Separate but similar models were fitted for different age groups (<30 yrs. vs. ≥ 30 yrs) and psychiatric illness sub-categories to assess effect heterogeneity.

Results—Sulfate, Fe, Pb and Zn were associated with the largest risk increases in single-component models. The biggest harmful associations were observed for metal industry source (high loadings of Pb and sulfate). For one quartile increase in components mixture score, we observed an adjusted RR of 1.24 (95 % CI, 1.21–1.26). Older population were more affected. We

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CRediT authorship contribution statement

Xinye Qiu: Conceptualization, Methodology, Software, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Yaguang Wei:** Methodology, Data curation, Resources, Validation, Writing – review & editing. **Heresh Amini:** Data curation, Resources, Writing – review & editing. **Cuicui Wang:** Methodology, Conceptualization, Resources, Writing – review & editing. **Marc Weisskopf:** Conceptualization, Supervision, Writing – review & editing. **Petros Koutrakis:** Funding acquisition, Supervision, Writing – review & editing. **Joel Schwartz:** Conceptualization, Methodology, Funding acquisition, Supervision, Writing – review & editing.

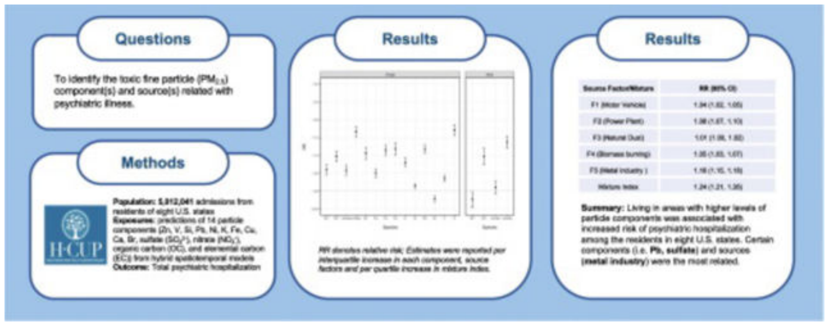
Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

also observed higher increase in bipolar and psychotic admission risk for increased components source and mixture level.

Conclusion—Living in areas with higher levels of particle components was associated with increased risk of psychiatric hospitalization among the residents in eight U.S. states. Certain components (i.e. Pb, sulfate) and sources (metal industry) were the most related.

Graphical Abstract



Keywords

Population mental health; Lead; Sulfate; Metal industry

1. Introduction

Genetics and environmental exposures are two major risk factors for psychiatric health. Literature review has shown there is emerging evidence indicating an adverse link between air pollutants and various mental health outcomes including anxiety, mood symptoms and psychotic experiences (Ventriglio et al., 2021). More recently, a case-crossover study conducted in Cincinnati Ohio found that each 10 μg/m^3 increase in daily fine particulate matter ($PM_{2.5}$) levels was associated with a significant increase in all psychiatric emergency department (ED) visits in children (OR: 1.07 [95 % CI: 1.02–1.12]) (Brokamp et al., 2019). Consistently, lag 1 day exposure to $PM_{2.5}$ was associated with an increased risk of mental health-related ED visits among youth aged 8–24 yrs. in Toronto of Canada (RR = 1.02 (1.01–1.03)) (Szyszkowicz et al., 2020). In fact, studies on the associations between air pollution exposure and adverse mental health have been increasing in recent years across the globe, including North America (Pun et al., 2017), East Asia (Wang et al., 2019; Xue et al., 2021) and Europe (Altuğ et al., 2020; Bakolis et al., 2020; Vert et al., 2017). While the evidence supporting harmful effects of particles (such as $PM_{2.5}$) is growing clearer, it remains unknown which particle components are most involved. Air pollution is usually a diverse mixture of substances including particles, gas, organic compounds and toxic metals. Different particle components have different neuro-toxicological profiles (Genc et al., 2012; Kelly and Fussell, 2012; Potter et al., 2021), and thus may have heterogeneous impacts on mental health. In addition, identifying the relative toxicity of different particle components can help us understand more of the involved pathways of actions and inform targeted policy making.

In this study, we aimed to estimate the associations between residential exposure to fine particle components ($PM_{2.5}$ compositions) and psychiatric hospitalization risk in a U.S. general population over the study period of 2002–2018, using the Health Cost and Utilization Project State Inpatient Databases. Fine resolution ambient predictions of annual average $PM_{2.5}$ components were matched based on residential ZIP codes in eight states of U.S. We undertook a detailed research approach from single-component modeling to source factorization analysis and mixture analysis. The present study is the first study looking at the associations between residential long-term average exposure to particle components and risk of psychiatric hospitalization. The unique contributions of this analysis include: a) wide population and area coverage; b) exploring not only single component associations but also particle components as a mixture; and c) estimating source-specific associations to identify the biggest source effect contributor(s) and further inform policy making.

2. Material and methods

2.1. Study population

Health Cost and Utilization Project (HCUP) State Inpatient Databases (SIDs) were used (HCUP April 2021). In this study, we covered residents of eight states of U.S. (source population) including Arizona (AZ), Maryland (MD), Michigan (MI), New York (NY), New Jersey (NJ), North Carolina (NC), Rhode Island (RI) and Washington (WA). Because of the high coverage of the HCUP SIDs data regardless of the expected payer (Medicare, Medicaid, private insurance, self-pay or no charge), the study population is representative of all-age individuals in the included states. Due to the availability of components exposure and hospital admission data, the study sample was further restricted to admissions over the years of 2002–2018, and with both hospital and residential addresses located in the same state. To reduce the noise from low population areas and increase the analytical power, we restricted to ZIP code areas (5 digits) with over 100 residents. Further details about the inpatient databases, data availability and regulation could be found in the Supplement. This study was approved by the Human Subjects Committee of the Harvard T. H. Chan School of Public Health.

2.2. Particle components assessment

Annual average ambient $PM_{2.5}$ components levels were predicted based on a combination of machine learning algorithms in a geographically weighted regression at the 50 m × 50 m spatial resolution for urban areas and 1 km × 1 km for non-urban areas (Amini et al., 2022a). Data is publically available at U.S. National Aeronautics and Space Administration (NASA) Socioeconomic Data and Applications Center (Amini et al., 2022b). The algorithms fused ground monitoring data collected from 987 monitoring sites across the contiguous U.S. (majority from US Environmental Protection Agency (EPA) regulatory monitors but also included study-specific sites due to monitoring data scarcity) over 2000–2018, satellite-derived measurements (including but not limited to enhanced vegetation index, aerosol optical depths (AOD), Normalized Difference Vegetation Index (NDVI), emissivity, day/night land surface temperature, land use cover, UV Absorbing Aerosol Index (AAI) and Nighttime Lights, etc.) available through the Google Earth Engine, chemical transport model simulations, meteorological conditions, and land-use data such as traffic counts, distance to OpenStreetMap features and many others. The predicted components we studied include Zinc (Zn), Vanadium (V), Silicon (Si), Lead (Pb), Nickel (Ni), Potassium (K), Iron (Fe), Copper (Cu), Calcium (Ca), Bromine (Br), sulfate (SO_4^{2-}), nitrate (NO_3^-), organic carbon (OC), and elemental carbon (EC) (We did not include ammonia in this study due to its strong attachment to SO_4^{2-} and NO_3^-). Excellent model performance was achieved with ten-fold out of sample cross-validation R^2 for individual components ranging from 0.821 (Br) to 0.975 (SO_4^{2-}). The entire locations were held out to assess performance when predicting an unmonitored location. The monitoring data was split into 70 % for training and 30 % for testing. Hyper parameter tuning was done on the training data, and model evaluation on the testing data. We further matched the annual average components data with each residential address based on ZIP code of residence and year at the time of admission in the study population.

2.3. Outcome assessment

The outcome of interest is total psychiatric hospitalization identified using SIDs clinically verified Major Diagnostic Category (MDC) identifier for all psychiatric disorders and illnesses (MDC = 19), which is assigned by the Medicare Diagnosis Related Group (DRG) grouper during HCUP processing (Agency for Healthcare Research and Quality August 2008; CMS, 2022).

2.4. Covariates

Information on individual age, sex, race/ethnicity, hospital discharge state, length of stay, admission cost and primary diagnosis codes, etc. was obtained for each psychiatric admission within the SIDs. We controlled for a key set of covariates, including admission state (same as residential state after study restriction), admission year, area-level long-term socioeconomic status (SES) factors (poverty, education and ambulatory visit level), population density (proxy for urbanity) as well as climate factors (temperature, relative humidity (RH), precipitation and solar radiation) in our single/multi-component, multi-sources and mixture analysis. The adjustment of state and year variables is to additionally control for the spatial and temporal variation in components exposure as well as psychiatric inpatient healthcare access. More details about the data sources of the covariates can be found in the Supplement.

2.5. Statistical analysis

For each state, we aggregated the psychiatric admissions to counts of admission for each ZIP code (the smallest spatial unit of analysis) and per calendar year. Annual linear interpolated area-level population counts from the U.S. Census 2000–2010 and American Community Survey (ACS) after 2010 (BureauUC, 2000, BureauUC, 2010; NationalResearchCouncil, 2007) were linked with psychiatric admission counts by ZIP code and calendar year, and treated as an offset during modeling. We examined the associations with an exposure window of moving average of current and previous two years (lag02) for the main models. Currently, many of the air pollution long-term epidemiological analysis utilized the current and past 1 year exposure window to create an average long-term exposure window. However, this window may not be enough to capture the longer-term exposure history. The use of lag02 window is to have a longer-term average exposure measure that utilized more of the years we can match our exposure predictions (2000–2018) to the available hospital admission files from HCUP SIDs (2002–2018). Additional sensitivity analyses exploring lag0, lag1, lag2, lag01 specific window estimates were also conducted (Supplement Table S1). Correlations among particle components were computed (Supplement Fig. S1). State-level annual average $PM_{2.5}$ temporal trends over the study period were generated (Supplement Fig. S2).

Overall, we went through four steps of modeling. First, single component models were conducted using zero-inflated negative binomial regression (Moghimbeigi et al., 2008). For each particle component, we ran separate model adjusting for key covariates set to obtain the component-specific effect estimates (Supplement Table S2).

Second, focusing on the four main mass components (OC, EC, nitrate and sulfate), we ran zero-inflated negative binomial regression and included all four components concurrently in the same model. This gave us the effect estimates for each of the major components controlling for the other components. The application of a multi-component model including the four main mass components in the same model is to control for residual confounding from the other main mass components, and also to allow for better comparison with the current literature evidence reported based on mutually adjusted models. Sensitivity analyses were also conducted among the four main mass components to check the robustness and change of their effect estimates based on three- or two-components settings (Supplement Table S3).

Then, we conducted Nonnegative Matrix Factorization (NMF) analysis to obtain components clusters (Gaujoux and Seoighe, 2010). NMF is similar to Principal Components Analysis (PCA) but instead constrains the loading of each component to the factor to be no less than zero. We tested for possible factor numbers of 4, 5 and 6. For each possible factor number (or factorization rank r), 100 multiple runs were conducted to obtain the best factorization fit over all runs that achieved the lowest approximation error. After examining the mixture coefficient heat maps for components clustering based on basis and consensus matrix (Brunet et al., 2004), we chose $r = 5$ as the best possible scenario in this study (Supplement Fig. S3). Additional parameters (cophenetic coefficient, residual sum of squares (RSS) trends) were also considered to determine the possible rank r (Supplement Fig. S4). It should be noted that the purpose of using NMF for this study is to obtain components clusters that inform the best and most realistic scenario of components sources. Therefore, existing knowledge on components clustering/loading characteristics for different sources should be sought as a priority as compared with replying on the performance of statistical parameters. Based on our trials, we found that factor number $r = 5$ produced the best scenario that fits the US emission source components clustering as suggested by current literature and best discriminates between different sources (Thurston et al., 2011). In summary, we identified a total of five independent source factors (Source 1: Motor vehicle, oil combustion; Source 2: Power plant, coal burning; Source 3: Soil, natural dust, terrestrial; Source 4: Biomass burning; Source 5: Metal Industry). With those five source factors, we ran a multi-factor zero-inflated negative binomial regression including all five factors concurrently adjusting for covariates to obtain the source-specific effect estimates.

Last, we applied the generalized Weighted Quantile Sum (gWQS) Regression to analyze the association between fine particles components mixture and the total psychiatric admission risk (Czarnota et al., 2015; Renzetti et al., 2019). The WQS is a measure that summarizes the multiple exposure species (fine particle components in this study) to a mixture while taking into account the outcome information. It generates a mixture index within the correlated particle components, and further estimates the associations between the mixture index and the outcome of interest. Additionally, the estimated component weights (together summed to 1) provide us information to make inference about the relative component importance. Specifically, the weights generated from WQS regression represent the relative strengths of the association with each component on psychiatric admission risk relative to the other components. In this study, the gWQS model is adapted to the zero-inflated negative binomial regression with positive constrains and generated a pooled effect using a bootstrap sample size of 100. Continuous particle components were transformed into quartiles, quintiles or deciles before running WQS. We treated quartile based WQS as the main analysis and the quintile, decile based WQS as sensitivity analysis (Supplement Table S4).

Sub-group analyses were conducted by different age groups (older vs. younger population via the cutoff of age 30 yrs.) as well as by psychiatric condition sub-categories (bipolar disorder, depressive disorder, psychotic disorder and all other disorders using primary diagnosis International Classification of Diseases (ICD) codes). Additional sensitivity analysis was conducted by extra adjustment of co-pollutants (NO_2, O_3) in all models (Supplement Table S5). Final estimates to report are relative risks (RRs) and 95 % confidence intervals (CIs) of psychiatric hospitalization within a given ZIP code across the study window (2002–2018) per interquartile (IQR) increase in components/sources concentration, and per quartile increase in WQS components mixture index. All analyses were conducted in R 4.0.1.

3. Results

3.1. Study population characteristics

Table 1 provides the summary characteristics of the study population and areas covered. In this study, we had a total of 5,012,041 psychiatric admissions in the included states and study years after restriction. We covered a total of 6818 unique zip codes (>100 residents). The majority of the psychiatric admissions come from young adults (20–29 yrs.) and adults (30–64 yrs.), and non-Hispanic whites. Additional information on neighborhood contextual factors and ambient environmental exposures is also provided in Table 1.

3.2. Distribution of particle components

The summary characteristics of particle components is presented in Table 2. Among the states and years we studied, we have an annual average ambient EC level of 0.48 μg/m^3 (SD: 0.28) and OC level of 1.61 μg/m^3 (SD: 0.54). The annual average ambient nitrate and sulfate level is 0.95 μg/m^3 (SD: 0.50) and 1.89 μg/m^3 (SD: 1.06) in the study areas. Detailed percentile levels (minimum, 5th, 25th, median, 75th, 95th and maximum) are also provided. Temporal distribution patterns of the annual average $PM_{2.5}$ level among each of the included states over the study period are included in the Supplement (Fig. S2). Overall, all the states saw decreasing trends of annual $PM_{2.5}$ level over the study period. Michigan and North Carolina had annual levels of fine particles exceeding the current long-term standards (12 $\mu g/m^3$) prior to 2005.

3.3. Single component

Fig. 1 (Single) presents the results for the RR estimates per IQR increase in each of the components without adjusting for co-components. Overall, we observed harmful associations between all the components and increased risk of psychiatric hospitalization, except for Si (slightly protective). Among them, sulfate, Fe, Pb and Zn were associated with the largest risk increase. Detailed estimates can be seen in Table S2 in the Supplement. Residual confounding from lack of adjustment of co-components is highly possible in the single-component setting.

3.4. Multi-components

Based on the multi-components model including OC, EC, nitrate and sulfate simultaneously, we observed that OC and sulfate remained harmfully associated with increased risk of psychiatric hospitalization (Fig. 1, Multi). In particular, for each IQR increase in OC, we observed an RR of 1.10 (95 % CI, 1.07–1.12). For each IQR increase in sulfate, we observed an RR of 1.14 (95 % CI, 1.12–1.16). Detailed estimates can be seen in Table S3 in the Supplement. Sensitivity analyses for three or two multi-components setting indicated that the results for OC and sulfate remained robust and significantly harmful under different settings (Supplement Table S3). However, the association between EC and total psychiatric hospitalization risk could be influenced by the adjustment of OC possibly due to high collinearity between the two (Supplement Fig. S1).

3.5. Source factors

The NMF source factor analysis showed that except for Source factor 3 (Soil, natural dust, terrestrial), we observed harmful associations between increased exposure to particle sources and increased psychiatric hospital admission risk. In particular, each IQR increase in particles with a source of metal industry was associated with a RR of 1.16 (95 % CI, 1.15–1.18) (Table 3). Fig. S3 in the Supplement shows the factorization heat map clustering of the particle sources from the components. In our age-group specific analyses, we found that older population (≥ 30 yrs.) had a higher risk of psychiatric hospital admission as compared with younger population (<30 yrs.) related with exposure to each components source (Table 3). Table 4. presents the psychiatric illness sub-category effect estimates. In summary, we found overall harmful associations with each of the sub-categories of psychiatric illness but also examined some effect heterogeneity across different sources and sub-outcomes risks. Consistently with the total psychiatric admission results, metal industry source remained the top associated source. In addition, consistent harmful and strongest associations were observed for bipolar and psychotic disorder –related hospitalization.

3.6. Components mixture

Fig. 2 presents the spatial distribution maps showing ZIP code average WQS score and total psychiatric admission rate among the 8 included states across the study period of 2002–2018. Overall, we saw spatial heterogeneity in the mixture index distribution within each state as well as across different states. In addition, we observed clusters of ZIP code areas with higher psychiatric admission rate which were also areas with higher mixture exposure level as indicated by the WQS score. This pattern is most apparent for the state of Rhode Island. Besides, many of the clustered ZIP code areas with higher WQS score belong to city or more populated areas as compared with their neighbor areas. In this study, areas with high WQS score indicate that they were exposed to types of fine particle mixtures more relevant to psychiatric admission risk. The WQS regression results indicated that Pb, sulfate, K and Si are the four most influential particle components driving the association (Fig. 3). Overall, for one quartile increase in the WQS score of particle components mixture, we observed an increased RR of psychiatric hospitalization of 1.24 (95 % CI, 1.21–1.26) adjusted for covariates (Table 3). Similar to the findings of the source analysis, we identified that components mixture was associated with higher psychiatric hospitalization risk in older age group (≥ 30 yrs.) vs. younger age group (<30 yrs.). Specifically, per quartile mixture WQS score increase was linked with a RR of 1.30 (95 % CI, 1.28–1.32) in older population as compared with a RR of 1.06 (95 % CI, 1.04–1.08) in younger population ($P < 0.0001$). The harmful associations for the overall mixture index remained robust when looking into per quintile or decile increase (Supplement Table S4) as well as by psychiatric illness sub-category (Table 4). Again, we observed the strongest harmful associations between the components mixture and increased risk of bipolar and psychotic hospitalization as compared with depressive or all other conditions. Each WQS score quartile increase was associated with a bipolar hospitalization RR of 1.30 (95 % CI, 1.28–1.33) and a psychotic hospitalization RR of 1.64 (95 % CI, 1.60–1.68), as compared with 1.16 (95 % CI, 1.14–1.18) and 1.07 (95 % CI, 1.05–1.10) for depressive and all other hospitalization risk, respectively. This finding indicated that the particle components mixture was positively associated with psychiatric admission risk with Pb, sulfate having the strongest individual weights in the mixture index.

4. Discussion

This study found that living in ZIP code areas with higher long-term average levels of multiple particle components is associated with increased risk of psychiatric hospitalization among the residents in eight states of U.S. We found evidence of heterogeneous associations between different particle components and risk of psychiatric hospital admission. Based on the source analysis, significant harmful associations were observed for multiple particle sources with metal industry source most associated, followed by power plant coal burning and biomass burning. The WQS mixture analysis revealed that the overall particle components mixture is strongly associated with increased risk of psychiatric hospitalization. Besides, after accounting for co-components exposure simultaneously, the component loading weights distribution from WQS regression indicated that Pb, sulfate are the top two components affecting psychiatric hospitalization risk in this study. Older population (>30 yrs.) were more affected. We also observed higher increase in bipolar and psychotic admission risk as compared with depressive and other conditions. To our knowledge, this is the first study which investigated the associations between particle components and risk of psychiatric hospitalization in a large U.S. general population. These findings suggest that residential exposure to particle components has a meaningful link with adverse population psychiatric health with certain components (such as Pb, sulfate) and source (metal industry) being the most influential. Future ambient environment policy implementation should take into consideration the above research findings to reduce the related healthcare burden and psychiatric disease risk.

One key particle component we identified with a potent of triggering adverse psychiatric impact is airborne heavy metals, especially lead. Existing human and animal model based studies demonstrated a harmful association between airborne metal absorption and brain health (Potter et al., 2021). Among all the metals, the adverse effects of lead on human neurological system is observed to be the strongest (Bowler and Lezak, 2015). Xenobiotic exposure to elevated Pb levels has been linked to increased risk of developing psychosis based on a review study polling evidence from 13 related research reported and 16 review articles (Attademo et al., 2017). In addition, childhood blood lead level was observed to be associated with increase in the general psychopathology symptoms in adulthood (Reuben et al., 2019). In a study by Opler, et al. looking at prenatal exposure to lead and schizophrenia risk in later life, the researchers reported that the odds ratio for developing schizophrenia was estimated to be 1.92 (95 % CI, 1.05–3.87) with blood lead level of 15 μg/dL vs. non-exposed (Opler et al., 2008). Adults who were exposed to higher levels of lead in occupational settings have reported feeling more tied, tense and depressed than their peers who were less exposed (Baker et al., 1984). Once reducing the lead level, the emotional symptoms can be improved (Baker et al., 1985). One most prevalent and best proved mechanism is that lead (Pb), can suppress the *N*-methyl-D-aspartate (NMDA) subtype of glutamate receptors (Guilarte et al., 2012; Marchetti, 2014). Other possible mechanisms include reduction of antioxidants and disruption of dopaminergic system.

Another important contributor we identified is the sulfate component. Sulfate emissions originate mostly from power plants operations. In a study looking into 95 US counties, researchers have found that different chemical components of $PM_{2.5}$ are linked with different levels of reduced life expectancy with sulfate being the most linked (Dominici et al., 2015). This is consistent with the strong association between sulfate and psychiatric hospitalization in this study. Current large population-based evidence for linking sulfate and mental outcomes is still lacking. However, Ghio et al. report that concentrations of soluble Fe from particles collected from the ambient air correlate with sulfate concentrations in those particle filters, and that the ability of soluble extracts from the particles to generate damaging oxidants was directly proportional to the sulfate concentrations (Ghio et al., 1999). In general, the existence of acids such as sulfuric acid or ammonium sulfate can substantially increase the solubility of particle metals, which as a consequence increased their bioavailability and toxicity. This may explain the observed strong associations on increased psychiatric hospitalization risk for both lead and sulfate in our study. Studies have also suggested that the bioactivity of ambient particles may depend on the relative proportion of soluble versus insoluble mass, in addition to particle size and surface area (Kelly and Fussell, 2012). In a multi-location study collecting samples from St. Louis, MO, Washington, DC, Dusseldorf, Germany, and Ottawa, researchers observed higher levels of cardiopulmonary injury in rats when they were exposed to ambient particles that contain higher levels of water soluble metals (Costa and Dreher, 1997).

In our age-group specific analysis, we found that older age residents were more sensitive to fine particle components exposure in terms of getting psychiatric hospital admission. This could either be due to their higher sensitivity or exposure to particle components, better access to psychiatric inpatient care or higher chance of developing violent or life-threatening behaviors that required hospitalization. We would like to note that the weaker associations with the younger age group (sometimes even protective) does not necessarily mean particle components exposure less affecting their psychiatric health. Many of the younger, less severe and initial psychiatric outbreaks were taken care of in outpatient setting, which cannot be captured in this analysis. Nevertheless, this additional analysis provided extra evidence on potential age difference in air pollution's effect heterogeneity on psychiatric health.

The psychiatric disorders sub-category analysis showed that there could be effect heterogeneity for the associations between particle components exposure and risk of psychiatric hospitalization depending on the specific sub-diagnoses. In this study, we observed the strongest harmful associations for the risk of bipolar and psychotic hospitalization. The slight protective associations between some source factors and risk of depressive and all other disorder hospitalization may indicate residual confounding for depressive and all other psychiatric illness since they belong to the group of psychiatric illness more related with social relationship and adverse personal events triggers as compared with external toxic factors. In addition, being hospitalized required others noticing risky and life-threatening behaviors in the patients. This is less occurred in depressed patients as compared with psychotic patients. Many of the depression or other mental condition cases showed up in outpatient settings rather than inpatient setting.

It is worth noting that the moderate association with Pb in single-component model setting is likely a result of residual confounding by other components since it did not adequately account for the effect of other components. However, the mixture analysis showed that after accounting for all the other correlated components as well as their relationship with the outcome risk in the WQS regression, Pb carried the largest influence. The adjustment and methodology difference of these two models explained the discrepancy of the results. In addition, the small protective association we examined with Si in single-component model may also be related to residual confounding from lack of adjustment of co-components. Si obtained top 4 loading weights in mixture analysis after accounting for the co-components.

This study has a couple of strengths. First, it is the largest study on particle components and risk of psychiatric hospitalization which covered the all-age residents in multiple states of U.S. from children to elderly. It included 6818 ZIP code areas (>100 residents size) and an annual average of 89,949,373 residents over 2002–2018. This covered about 29.1 % of the total US population of 308,745,538 persons in 2010 (used as a comparable year to our estimate) according to the US 2010 Census covering all 50 states (https://www.census.gov/programs-surveys/decennial-census/decade.2010.html). In addition, the included ZIP codes covered 5,012,041 total psychiatric hospitalizations over the study period, which equals to an annual average of ~300,000 admissions per year. This is about 11.6 % of the total psychiatric admission counts across the nation in 2007 (Blader, 2011). Second, the application of fine geographical resolution components data allows us to have less exposure measurement error and wider area coverage as compared to county or city level studies using monitoring exposures. We are able to estimate the epidemiological associations for not only the four main mass components (OC, EC, sulfate and nitrate) but also multiple atmospheric metal exposures. Third, this is the first study that reported on the associations between psychiatric admission risk and particle components. Associations for single component, source factors, and components mixture as a whole were reveled and found consistent and strongest signal for lead and sulfate. Lastly, the source components and mixture analysis evidence has policy implications.

This study is also limited in the following aspects. First, we were not able to capture the entire residential history of the residents which could result in exposure measurement error. Second, residual confounding from co-exposures such as co-pollutants (NO_2, O_3) and other key SES factors that correlate both exposure level and outcome risk is possible. However, in our sensitivity analyses with additional adjustment of NO_2 and O_3, the observed harmful association remained robust for the main WQS mixture analysis. In addition, we were able to control for several key contextual and socioeconomic factors (such as population density, neighborhood poverty level, and education) in our study. In the future, a composite score for SES could be used to more comprehensively capture and combine the different dimensions of social and neighborhood characteristics that can influence population mental health. Third, the findings of this study may only inform associations. This is a cross-sectional analysis due to lack of information on follow-up for the psychiatric admissions in HCUP SIDs. In the future, more causal evidence is needed via better study design (such as longitudinal designs) or causal inference methods. Fourth, this study may have limited generalizability in terms of the types of psychiatric patients covered and study regions. The included 8 states may not represent enough for the south and middle parts of the US due to particle emission source difference. The study analyzed on the risk of psychiatric hospitalization and thus only captured the more severe psychiatric cases that were admitted to hospitals. It may not be able to identify the milder cases. Further studies in outpatient settings should also be conducted. Last but not least, selection bias is likely if the selection of the study population is associated with different levels of components exposure and baseline psychiatric hospitalization risk from the general population. For example, the truncation of low population area (<100 population ZIP code areas excluded) may cause selection bias if components levels are lower in those less populated areas and psychiatric admission risk is also lower due to limited psychiatric healthcare access.

In the research area of exploring the roles of air pollution exposure on population mental health, the current knowledge gaps include establishing sensitive time windows of pollutant exposure, identifying susceptible and disadvantaged populations that are at a higher risk of either being exposed to higher pollution levels or risk of getting mental illness. In addition, most of the current evidence is still exploratory and aim to detect the associations. More solid evidence is needed via well designed experimental studies, large-population longitudinal settings as well as rigid causal inference methods. Environmental pollution exposure may not be the direct cause of mental illness, but can act as enhancer for physiological reactivity to social stressors (Miller et al., 2019).

Our source factors findings have substantial and more direct policy implications in that they provide evidence that particles originating from metal industry and power plants are associated with higher risk of psychiatric hospitalization as compared with other sources. Similar to what was reported before on mortality risk and other health outcomes, particles of terrestrial origin (as marked by higher loadings of Si and Ca) are not associated with psychiatric admission risk in this study. The strong associations we observed with both Pb and sulfate indicated that future air pollution regulation should consider control for acidic compounds as a whole and monitor both acids and soluble metal components to achieve the best outcome.

5. Conclusions

Residential exposure to $PM_{2.5}$-associated constituents was associated with increased psychiatric hospitalization risk among U.S. residents in eight states. Certain components (such as lead and sulfate, and K) are more influential. Future ambient environment policy implementation should take into consideration the above research findings to help protect vulnerable populations with psychiatric patients being one of them.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was made possible by U.S. Environmental Protection Agency (EPA) grant RD-835872. Its contents are solely the responsibility of the grantee and do not necessarily represent the official views of the U.S. EPA. Further, U.S. EPA does not endorse the purchase of any commercial products or services mentioned in the publication. It was also supported by National Institutes of Health (NIH) grant R01 ES032418-01 and National Institute of Environmental Health Sciences (NIEHS) grant (P30 ES000002). Dr. Heresh Amini is supported by Novo Nordisk Foundation Challenge Programme (NNF17OC0027812). We want to specially thank U.S. Agency for Healthcare Research and Quality Health Cost and Utilization Project (HCUP) for giving us access to the State Inpatient Databases (SIDs) to conduct this study.

Data availability

The authors do not have permission to share data.

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Highlights

- The associations between atmospheric particles components exposure and psychiatric illness are unclear.
- This study covered psychiatric hospital admissions from all-age residents of eight U.S. states over 2002–2018.
- The use of fine geographical resolution components predictions leads to less exposure error and wider area coverage.
- We explored effects of particle components individually, from sources and as a mixture.
- Consistent and strongest signals were found for lead, sulfate and particles with major source from metal industry.

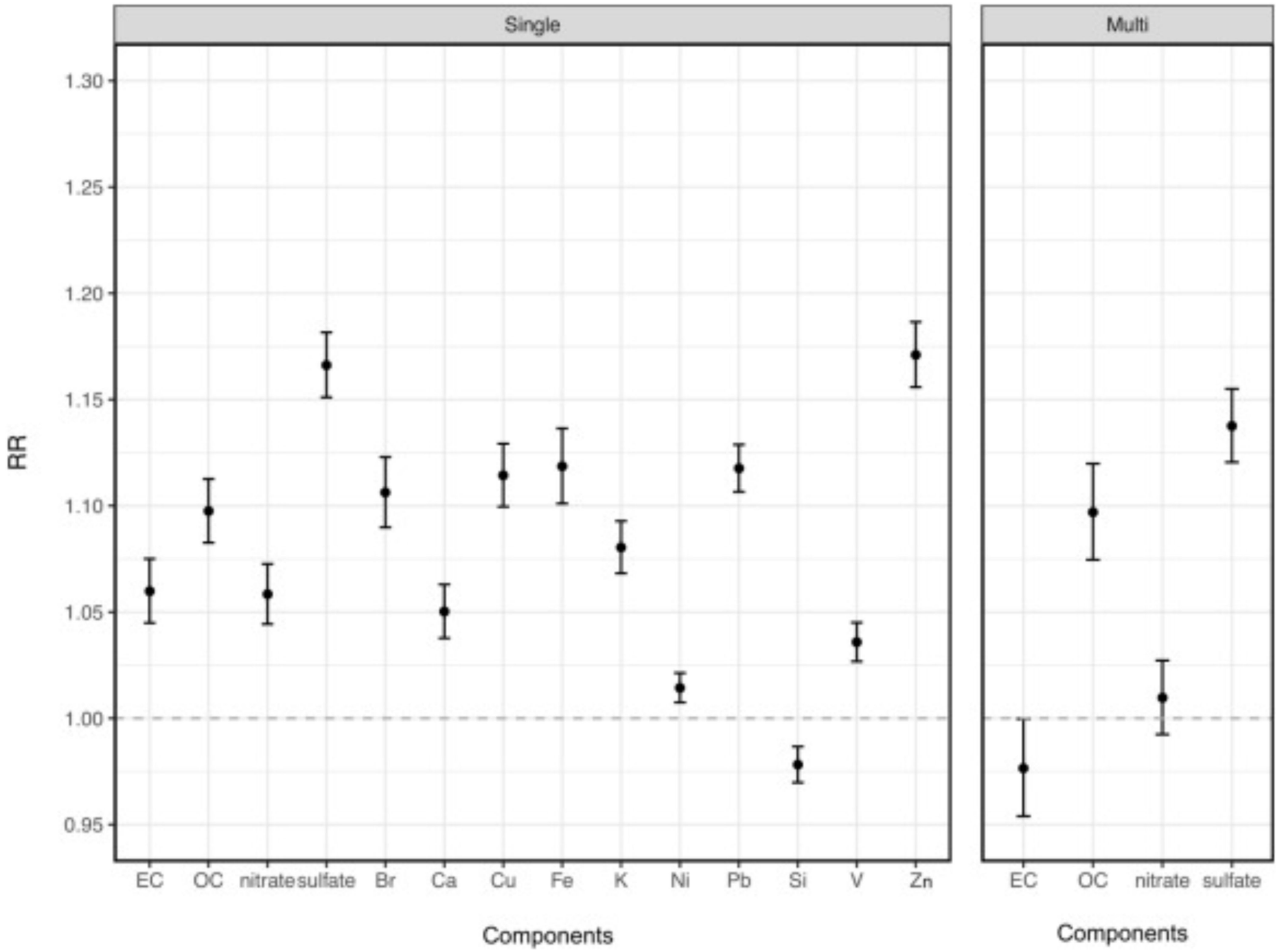

Fig. 1.

Relative risk (RR) of total psychiatric hospitalization per interquartile (IQR) increase in exposure to particle components (single component setting, multi main components setting). Adjusted for temperature, RH, precipitation and solar radiation, admission year, admission state, population density, area level poverty level, area level education level, area-level ambulatory visit level.

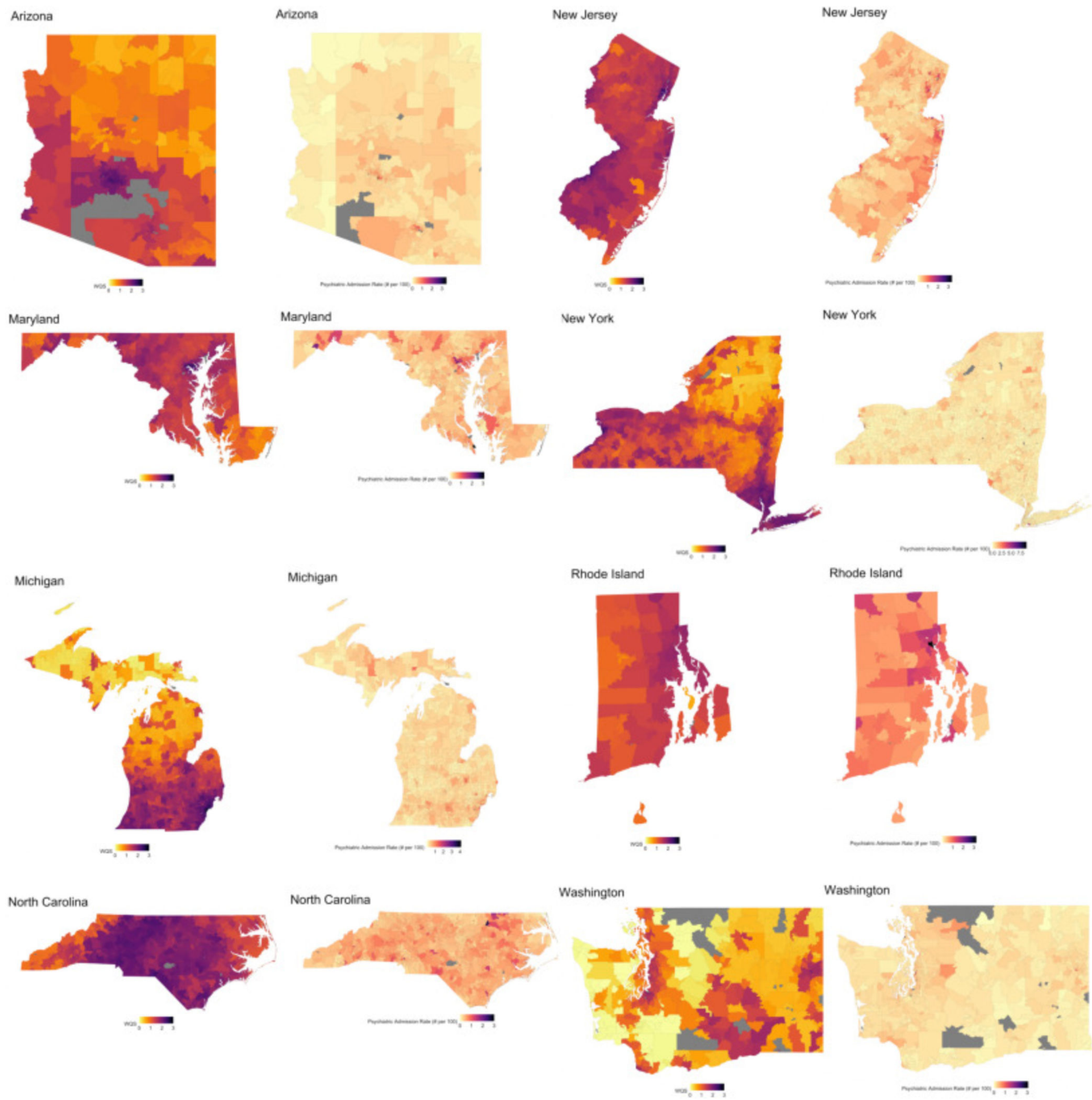

Fig. 2.

Spatial maps showing ZIP code average $PM_{2.5}$ components mixture index (as represented by weighted quantile sum score) and total psychiatric admission rate among the 8 included states across the study period (2002–2018). For each state, left-side color patterned maps represented the spatial distribution maps for weighted quantile sum (WQS) score; right-side color patterned maps represented the spatial distribution maps for total psychiatric admission rate (counts per 100 population per zip code per year). Grey shaded areas are areas with missing values or excluded from this study.

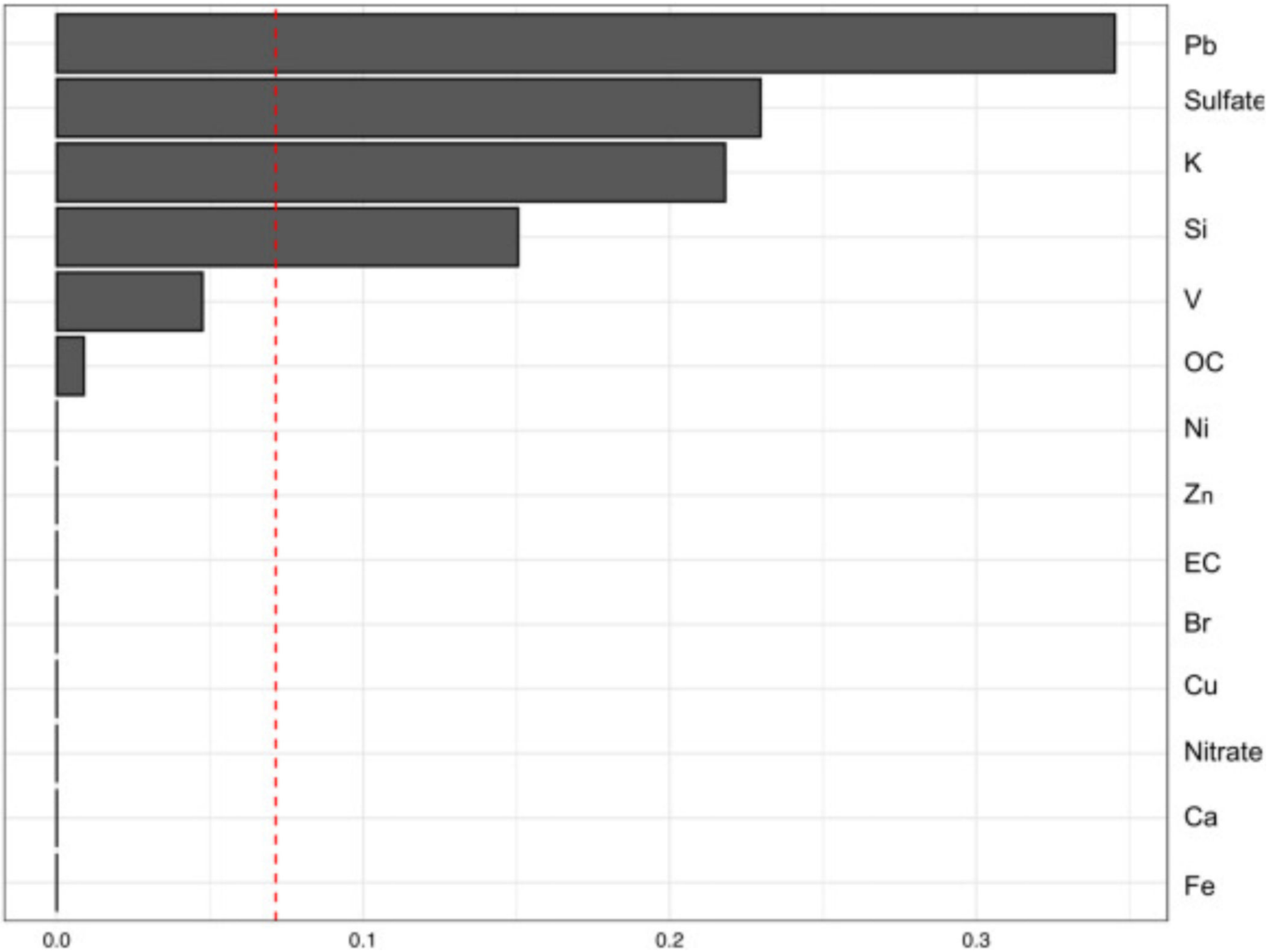

Fig. 3.

Weights of particle components in mixture index. Red dashed line indicated the suggested threshold of most influential components (weights above the threshold) which equals to 1 over the number of components (14) in this study.

Table 1.

Summary of study population characteristics.

Characteristics	Overall
No. of psychiatric admissions [a]	5,012,041
Zip code covered (>100 residents)	6818
Population covered [b]	89,949,373
Age, No. (%)	
Children (age ≤9 yrs.)	54,354 (1.1)
Adolescents (10–19 yrs.)	629,733 (12.6)
Young Adults (20–29 yrs.)	933,435 (18.6)
Adults (30–64 yrs.)	2,843,364 (56.7)
Elderly (≥ 65 yrs.)	550,983 (11.0)
Other unidentified	172 (0.0)
Sex, No. (%)	
Male	2,440,394 (48.7)
Female	2,571,097 (51.3)
Other unidentified	550 (0.0)
Race/Ethnicity, No. (%)	
Non-Hispanic black	974,127 (19.4)
Non-Hispanic white	2,772,848 (55.3)
Other combined races [c]	646,314 (12.9)
Other unidentified [d]	618,752 (12.3)
Neighborhood contextual factors, median (25th, 75th)	
Poverty rate, %	7.4 (4.3, 12.2)
High school or less education, %	20.9 (12.5, 31.9)
Ambulatory visits per year per 100 population	80.0 (76.3, 83.0)
Population density, people per mile2	283.2 (63.3, 2034.5)
Ambient exposures, mean (standard deviation)	
Temperature, °C	11.8 (4.0)
Relative Humidity, %	73.6 (13.2)
Cumulative Precipitation, m	1.1 (0.4)
Solar shortwave radiation, W/m^2	310.5 (31.1)

[a] Total number of psychiatric admissions we used for this study after restriction criteria (described in Methods, Study Population).

[b] Population covered is the number of all-age persons covered in the included zip code areas of the eight states with residents' size >100 and is reported as an annual average over the study period due to changing population size over the years.

[c] Other combined races include Hispanic/Latino, Asians/Pacific Islanders, Native Americans and other races.

[d] Missing race/ethnicity information, majority of the admissions in this category come from WA state which does not provide information on race in the HCUP.

Table 2.

Distribution of particle components.

Component	Mean	SD [a]	Min	5th	25th	Median	75th	95th	Max
EC	0.48	0.28	0.04	0.16	0.29	0.43	0.61	1.00	2.39
OC	1.61	0.54	0.31	0.86	1.23	1.53	1.92	2.64	5.09
NO_3^-	0.95	0.50	0.05	0.31	0.59	0.84	1.20	1.99	2.93
SO_4^{2-}	1.89	1.06	0.17	0.53	1.00	1.73	2.59	3.92	5.10
Br	2.52	0.66	0.41	1.45	2.03	2.52	3.01	3.58	5.72
Ca	32.90	24.98	6.61	14.87	20.91	25.87	32.81	100.61	283.28
Cu	2.20	1.72	0.02	0.43	0.87	1.65	3.04	5.76	11.80
Fe	51.60	32.85	5.05	17.38	28.54	42.73	64.85	116.70	252.59
K	52.07	17.30	9.70	30.42	43.79	49.93	57.06	76.54	187.17
Ni	0.61	0.72	0.01	0.03	0.20	0.44	0.77	1.69	6.23
Pb	2.20	1.31	0.23	0.81	1.24	1.77	2.79	5.13	8.57
Si	77.54	62.87	12.35	35.77	48.50	59.80	77.38	253.38	593.06
V	0.77	0.78	0.00	0.08	0.29	0.47	1.01	2.27	8.05
Zn	7.49	4.19	0.61	2.45	4.59	6.75	9.30	15.36	43.22

[a]Standard deviation, SD. The unit for EC, OC, NO_3^- and SO_4^{2-} are μg/m^3. The unit for the other components are ng/m^3.

Table 3.

Relative risk (RR) of psychiatric hospitalization associated with increased exposure to particle components sources and mixture index (total and by age group).

Sources [a]/Mixture [b]	**Total**	**By age group**		
		<30 yrs.	**≥ 30 yrs.**	***P* [c]**
Motor, oil combustion	1.04 (1.02, 1.05)	0.98 (0.97, 1.00)	1.07 (1.06, 1.08)	<0.0001
Power plant, coal burning	1.08 (1.07, 1.10)	1.05 (1.04, 1.07)	1.08 (1.06, 1.09)	0.0431
Soil, natural dust	1.01 (1.00, 1.02)	0.97 (0.96, 0.98)	1.03 (1.02, 1.04)	<0.0001
Biomass burning	1.05 (1.03, 1.07)	0.94 (0.91, 0.96)	1.14 (1.12, 1.17)	<0.0001
Metal industry	1.16 (1.15, 1.18)	1.05 (1.03, 1.08)	1.24 (1.22, 1.25)	<0.0001
WQS [d]	1.24 (1.21, 1.26)	1.06 (1.04, 1.08)	1.30 (1.28, 1.32)	<0.0001

[a] Relative risk (RR) and 95 % confidence interval (CI) per interquartile increase in components sources level adjusted for temperature, RH, precipitation and solar radiation, admission year, admission state, population density, area level poverty level, area level education level, area-level ambulatory visit level from a mutually adjusted multi-source model.

[b] Relative risk (RR) and 95 % confidence interval (CI) per quartile increase in the weighted quantile sum score adjusted for same list of covariates in source analysis.

[c] Heterogeneity test p.

[d] Weighted quantile sum (WQS) score.

Table 4.

Relative risk (RR) of psychiatric hospitalization associated with increased exposure to particle components sources and mixture index (by sub-category).

	By Sub-category			
Sources [a]/Mixture [b]	**Bipolar**	**Depressive**	**Psychotic**	**All other**
Motor, oil combustion	1.05 (1.04, 1.06)	0.99 (0.97, 1.00)	1.20 (1.19, 1.22)	0.97 (0.95, 0.98)
Power plant, coal burning	1.03 (1.02, 1.05)	1.06 (1.04, 1.07)	1.13 (1.11, 1.15)	0.99 (0.97, 1.00)
Soil, natural dust	1.00 (0.99, 1.01)	0.98 (0.97, 0.99)	1.08 (1.06, 1.09)	0.99 (0.98, 1.00)
Biomass burning	1.16 (1.14, 1.18)	0.97 (0.96, 0.99)	1.19 (1.17, 1.22)	0.95 (0.93, 0.97)
Metal industry	1.13 (1.11, 1.14)	1.14 (1.13, 1.16)	1.33 (1.30, 1.35)	1.02 (1.00, 1.03)
WQS [c]	1.30 (1.28, 1.33)	1.16 (1.14, 1.18)	1.64 (1.60, 1.68)	1.07 (1.05, 1.10)

[a]Relative risk (RR) and 95 % confidence interval (CI) per interquartile increase in components sources level adjusted for temperature, RH, precipitation and solar radiation, admission year, admission state, population density, area level poverty level, area level education level, area-level ambulatory visit level from a mutually adjusted multi-source model.

[b]Relative risk (RR) and 95 % confidence interval (CI) per quartile increase in the weighted quantile sum score adjusted for same list of covariates in source analysis.

[c]Weighted quantile sum (WQS) score.