A fingerprint of source-specific health risk of $PM_{2.5}$-bound components over a coastal industrial city

Jéssica Caroline dos Santos Silva[1], Sanja Potgieter-Vermaak[2,3], Sandra Helena Westrupp Medeiros[4], Luiz Vitor da Silva[4], Danielli Ventura Ferreira[4], Ana Flávia Locateli Godoi[5], Carlos Itsuo Yamamoto[6], Ricardo Henrique Moreton Godoi[1,5,6*]

1- Postgraduate Program in Water Resources and Environmental Engineering, Federal University of Paraná, Curitiba, Paraná, Brazil;

2- Ecology & Environment Research Centre, Department of Natural Science, Manchester Metropolitan University, Manchester M1 5GD, United Kingdom;

3- Molecular Science Institute, University of the Witwatersrand, Johannesburg, South Africa;

4- Department of Environmental and Sanitary Engineering, University of the Region of Joinville, Joinville, Santa Catarina, Brazil;

5- Department of Environmental Engineering, Federal University of Paraná, Curitiba, Paraná, Brazil;

6- Department of Chemical Engineering, Federal University of Paraná, Curitiba, Paraná, Brazil.

* Corresponding author. E -mail: rhmgodoi@ufpr.br. Postal address: Rua Francisco H. dos Santos, 210, Jardim das Américas, Curitiba, Paraná, Brazil.

Abstract

The influence of specific local land-use activities (continuously redistributing elements across environments) and environmental conditions (altering the chemical composition of airborne particulate matter) on the intrinsic health risk of $PM_{2.5}$ exposure is sparsely reported. To fill this gap, we employed a novel integrated approach to address the influence of short-term changes in source-specific $PM_{2.5}$ composition on the exposure-response risk, while controlling for weather conditions. We combine receptor-based source apportionment with conditional logistic regression in a space-time-stratified case-crossover design. This approach is different from previous studies as it: i) controls the impact of spatiotemporal variations in air pollution and human mobility using multilocation-specific fixed and disjointed space-time strata ii) addresses

the spatial heterogeneity of personal exposure separating its variable effect from other predictors by allowing different baseline hazards for each space-time stratum; iii) aligns case/control periods with strong/regular episodes of source-specific PM-multipollutant fingerprint contributions rather than health outcomes. This enabled comprehensive examination of the association between source-specific $PM_{2.5}$-bound species and cardiorespiratory disease hospitalizations. The epidemiological findings were that primary anthropogenic emissions [industrial (ORs 2.5 – 4.8)] were associated with higher 1-day moving average PM-induced risks. Natural-related sources [fresh / aged sea salt aerosol, dust, soil resuspension] and secondary sulfate formation were consistently associated with higher health risks (ORs 1.0 – 1.54) after 1 to 5-days since exposure. The results emphasize the importance of source-specific air quality management in complex areas and our research provides an adaptable universal tool to support targeted place-based policy interventions to mitigate air pollution impacts on health.

Keywords: air pollution exposure, atmospheric chemistry, case-crossover study, hospital admission, water-soluble inorganic ions.

1. INTRODUCTION

Changes in the environment have been affecting the functioning of ecosystems and human health. Due to its intrinsic role in the global energy balance and hydrological and nutrient cycles, atmospheric aerosol loading is one of the nine planetary boundaries that have not yet been fully quantified[1–8]. It is also well known that air pollution is the most significant and leading environmental and occupational risk to public health[9,10], which led the World Health Organization (WHO) to tighten its air quality guidelines in 2021 for the first time since 2005[11]. Studies have shown that each air pollutant has different toxicological and physiological effects on human health[12]. Several hazardous elements and compounds bound to particulate matter (PM) have been classified as carcinogens by the International Agency for Research on Cancer

(IARC)[13]. However, air quality standards, guidelines, and legislation treat PM as a homogeneous mixture, reporting it as a total mass without distinguishing variations in chemical composition. A plethora of health studies[14–18] have demonstrated that there is no threshold of PM exposure below which adverse health effects do not occur. Such findings suggest that the impacts of anthropogenic PM should be of concern even in areas that already meet national ambient air quality standards[19]. Thus, the risks associated with finer particles such as $PM_{2.5}$ can no longer be solely attributed to their overall mass concentration, as a wide range of adverse health effects resulting from exposure to $PM_{2.5}$-bound components is already well-documented to be linked to increased mortality and morbidity outcomes[20–22]. Carrying potentially toxic soluble components such as trace metals and gaseous co-pollutants, $PM_{2.5}$ undergoes systemic translocation when inhaled, not only depositing in the pulmonary tract but also crossing the epithelium and entering the systemic circulation[23,24]. As a result, many studies have reported that short-term changes in the concentration of specific fine PM components may trigger respiratory and cardiovascular events[25,26], including respiratory infection[27], exacerbation of asthma and chronic obstructive pulmonary disease (COPD)[28–32], myocardial infarction[33–36], ischemic stroke[37], cardiac arrhythmia[38–41], and heart failure[42,43].

Inconsistent associations between particle components and hospital admissions for cardiovascular and respiratory diseases found by several studies[23,44–46], however, warrant for further examination of this issue. The 2015 guidance statement from the UK Committee on the Medical Effects of Air Pollutants[47], for example, suggests that particulate sulfates are most consistently associated with adverse effects on health, with less evidence, however, for nitrates and other components. On the other hand, in Guangzhou (China), Lin et al.[48] found significant associations of cardiovascular mortality with $PM_{2.5}$ elemental carbon, sulfate, nitrate, and ammonium at moving averages for the current day and the previous 3 days. In the USA, organic carbon and sulfate were also more strongly associated with cardiopulmonary mortality than

other $PM_{2.5}$ constituents, such as iron, potassium, silicon, and zinc[24]. In South Korea, Kim et al.[49] found that transition metals consistently showed associations with all-cause mortality, while the effects of other constituents varied across the cities and for cause of death. These studies highlight the difficulty of identifying the role of one specific $PM_{2.5}$-bound component as driving air pollution-mediated health effects. It has multiple and shared emission sources and even may serve as a proxy of another component[48,50], which in a mixture may be associated with enhanced biological response compared to others[51]. In addition, most findings are limited to the USA and China, with little evidence available from other parts of the world[23], which limits the identification of toxic components of particles and related concentration-response functions. Therefore, from the perspective of exposure prevention, understanding the sources, composition, and spatial and temporal characteristics of $PM_{2.5}$ is of critical importance.

While specific environmental emissions can originate from natural sources, those produced by human activities tend to be more harmful than those found in the natural background[52–54]. Although industrially developed cities can indirectly affect public health due to the manifold effects of their associated air pollution, few studies have focused on the source-specific particulate pollutants carrying potentially toxic substances released from the various activities established in such areas[55,56]. According to Lelieveld et al.[57], 5.13 million deaths per year globally are attributed to long-term exposure to $PM_{2.5}$ and ozone related to fossil fuels emissions, which typically stem from industry (e.g., iron, steel, and aluminum production), the chemical and transformation sectors (e.g., coal and coke production and combustion, petroleum refining), and transportation and power generation (coal, oil, and gas). Among these deaths, nearly 80% are related to cardiometabolic (e.g., ischaemic heart disease, stroke, type 2 diabetes) and respiratory diseases (e.g., chronic obstructive pulmonary disease, lung cancer, lower respiratory infections). In Spain, it was reported that cancer mortality rates were approximately 17% higher in industrial areas compared to other urban areas[58]. Furthermore, although a

decreasing trend of health risks associated with $PM_{2.5}$-bound metals has been observed over the years in highly industrialized cities in Mexico and China, emissions related to vehicles and industry continued to exceed widely acceptable non-carcinogenic and carcinogenic risk levels[55,59]. Therefore, it can be hypothesized that the increased toxicity can be attributed to physical and chemical transformations resulting from a complex nexus between environmental dynamics, anthropogenic processes, and land-use changes that give rise to these emissions. In this context, it is recognized that local emissions play a decisive role in affecting air quality, and therefore, reducing emissions is crucial for its improvement[7,60–64].

Hence, methods capable of quantifying the impact on human health of exposure to different environmental conditions become essential tools for investigating risks and supporting decision-making in public policies. To that end, case-crossover models integrating daily exposure and health data allow us to examine the health effects linked to short-term environmental exposure-response[65]. To our knowledge, few previous studies[66–70] used the same original time-stratified case-crossover study design using conditional logistic regression models' statistical approach as we used in our study but only to analyze health effects associated with extreme air pollution events from wildfires. In Vietnam, for example, a positive association was found between $PM_{2.5}$ and $PM_{1.0}$ exposure and hospital admissions for cardiovascular conditions in industrial and mining cities[71]. In Brazil, an increase in cardiovascular and respiratory hospital admissions of up to 21% and 23%, respectively, was associated with wildfire-related air pollution across the country[70].

Exploring the health impact of a wider range of air pollution sources, a few studies[25–27,42,72], mostly in New York State (NYS), explored the use of source-apportioned $PM_{2.5}$ concentrations combined with a time-stratified case-crossover design[73] similar to the approach suggested in this study. Among their findings, short-term increases in $PM_{2.5}$ from traffic and other combustion sources appear to be a potential risk factor for increased hospitalizations and

emergency department visits for respiratory and cardiovascular diseases. They also explored the fact that despite decreasing $PM_{2.5}$ concentrations reported in recent years due to new air quality policies, increased rates of cardiovascular hospitalizations have been observed in NYS. Changes in $PM_{2.5}$ composition and sources seem to explain such differences, because meanwhile, the triggering of adverse health effects associated with spark-ignition emissions declined, the rate of ST-elevation myocardial infarction (STEMI), a type of heart attack that affects your heart's lower chambers, as associated with increased secondary organic carbon after the Tier 3 light duty vehicle policy is being implemented in NYS. While these studies apply the most common time-stratified case-crossover design fitting a conditional logistic regression model that contrasts ambient air pollutant exposure concentrations on the day on which the health event occurs (case days) to other times when the subject did not have a health event (control days), this study suggests a space-time-stratified case-crossover design based on a binary indicator variable for case/control days to compare the health effects of exposure to episodes of higher source-specific contributions to $PM_{2.5}$ on the day of the health event (hospital admission; case days) with the exposure on non-event days (control days), controlling the bias associated not only with temporal but also spatial variability.

These findings highlight the critical importance of robust methodologies in assessing the health effects of industrial air pollution. Within the context of industrial agglomerations and their consequential impact on public health, the urban locale of Joinville serves as an exemplary case study. It is emblematic of the intricate nexus between urbanization, industrialization, and environmental health. Positioned as a coastal industrial hub in southern Brazil, Joinville hosts a diverse array of industrial sectors, including metallurgical, textile, chemical, and plastics manufacturing. This diversity accentuates environmental concerns and health hazards for its inhabitants, whether they are part of the labor force or the residential population in its immediate surroundings[74].

Therefore, while plenty literature is available on air pollution and its health impacts in urban areas, this study aims to investigate the source-specific health risk of $PM_{2.5}$-bound compounds over a coastal industrial city. In this regard, this study suggests a space-time-stratified case-crossover study design using conditional logistic regression models to quantify the impact of source-related $PM_{2.5}$ on hospital admissions due to cardiorespiratory diseases. To accomplish this, the research design includes a receptor-based source apportionment model to determine the source-specific $PM_{2.5}$ contribution, following a modeled approach proposed by Requia et al.[70] and the source-specific risk assessment logic of Yan et al.[59]. This approach design and exposure assumptions distinguish itself from (traditional) other studies in that it: i) controls the impacts of spatiotemporal variations of air pollution and of people's daily activity environments by using multilocation-specific fixed and disjointed space-time strata instead of averaging individual exposure and assigning PM concentrations to static population distributions; ii) addresses the spatial heterogeneity of personal exposure separating its variable effect from other predictors by allowing different baseline hazards for each space-time stratum instead of using the spatial variable as predictor, which would affect the outcome directly, ; iii) aligns case/control periods with strong/regular episodes of source-specific PM-multipollutant fingerprint contribution rather than only with health outcomes while modelling source-related PM or specific PM-bound components as independent variables. In this way it strengthens the health risk assessment causal inference by controlling for proximity-based exposure-response confounders.

Although air pollutants are regulated individually through limits on emissions or ambient air-quality standards set by governments as spatiotemporally homogeneous substances, the effects of air pollution are driven by pollutant composition. As such, rather than being viewed as causal, these individual constituents might serve as proxy markers for other chemical species or the resulting mixture of multiple components that also might interact with aspects of

the physical environment as well as combine with socioeconomic and biological factors to trigger health effects[24]. Therefore, as a result of heterogeneity in chemical composition and emission sources of the particles, the health impact of heterogeneous pollutants such as $PM_{2.5}$ varies according to time and place and more targeted air quality standards are warranted to incorporate this complex $PM_{2.5}$-health impacts nexus. In this context, this new integrated approach aims to identify the $PM_{2.5}$ -bound components associated with more significant health impacts. This approach strengthens the connection between source-specific air pollution exposure and health outcomes by defining case events based on hospital admissions linked to episodes of higher source-specific contributions to $PM_{2.5}$ and, as such, may provide important reference information for prioritizing source contributions in air quality control actions for future place-based policymaking.

2. MATERIALS AND METHODS

This research aimed to investigate ambient air $PM_{2.5}$-bound components over complex terrain in a coastal industrial city. It also proposes a methodology for prioritizing source contributions in air quality policies through integrated health risk assessments. This was achieved by comparing source contributions to $PM_{2.5}$-related cardiovascular and respiratory hospital admission incidence in the study area.

With this aim in view, the following approach was applied: a) a spatiotemporal characterization of the concentration and characteristics of species bound to $PM_{2.5}$ at the local level was conducted; b) source apportionment was conducted to estimate $PM_{2.5}$ pollution sources and the amount they contribute to ambient air pollution levels; c) a comprehensive understanding of the complex source-specific composition and (trans)formation processes contributing to $PM_{2.5}$ exposure; d) an identification of those sources associated with more significant health risks was performed. More details about these sites, research data, sampling collection, and chemical analysis, including the instruments used, are provided in the Supplementary Material (SM, Sections S1-S3), and in our previous study[75].

2.1 Study area

Located in southern Brazil, Joinville is the largest city in Santa Catarina State, covering an area of 1,125 km² and having a population of about 600,000 inhabitants[76]. The region lies between the eastern edge of the Sea Mountain range (Serra do Mar), which is covered by remnants of the Atlantic Rainforest, and the estuary of Babitonga Bay to the east (Figure 1). Due to regional topography and coastal position, Joinville is characterized by high humidity and prevailing wind directions usually from the east. The city has a subtropical mesothermal humid climate with hot summers (Cfa)[77] in the urban area.

The region has undergone significant industrial development since the 1930s, making it one of the most industrialized regions in southern Brazil. The urban-industrial area expanded from a foundry plant downtown to the east during the 1950s, when a district dominated by a major Metallurgical Industrial Complex was established. This district reached its consolidation as a primarily metallurgical center in the 1970s toward the north, where a separate industrial district (known nowadays as North Industrial District) was delineated, ultimately defining the urban densification seen today.

2.2 Research data

The source-specific health risk was assessed by combining three datasets: i) air pollutant exposure characteristics, which included daily samples' $PM_{2.5}$ concentrations and the profile source contributions quantified by the receptor model (PMF); ii) meteorological conditions, i.e., temperature, relative humidity, wind speed and direction, and precipitation; and iii) the morbidity database for cardiorespiratory diseases. In this study, data were only pre-processed to exclude outliers resulting from measurement or data entry errors. Unlike previous studies that often relied on shorter sampling periods, our research spans over two years. This extended period offers a more robust dataset and provides a clearer understanding of long-term exposure risks. By integrating meteorological data and performing detailed spatiotemporal analysis, our approach not only identifies key pollution sources but also contextualizes their impact within the unique environmental dynamics of Joinville.

The hospital admission data was obtained from publicly available database curated by the Ministry of Health in Brazil, which ensures patient confidentiality. This work was based on open access data and model calculations therefore ethical approval was not required.

2.2.1 Sampling sites

The $PM_{2.5}$ sampling sites were set up in the two urban-industrial districts (Figure 1): one is located about 2 km southwest of the Metallurgical Industrial Complex (26°18'00.1" S/48°49'25.2" W, at 11 m asl, hereafter named MIC), close to a traffic street, on a school courtyard; the other is situated south of the North Industrial District (26°15'10.6" S/48°51'24.2" W at 16 m asl, hereafter NID), on a meteorological station at University of the Region of Joinville Campus. The sites were selected based on accessibility, downwind from both urban-industrial districts, near residential areas, and their representativeness of different environments (near the coast or mountain range, respectively).

2.2.2 Daily $PM_{2.5}$ characterization

Sampling was conducted using low-volume Harvard Impactor samplers equipped with $PM_{2.5}$ fractionating inlet. Daily $PM_{2.5}$ samples were collected at a mean sampling flow rate of 10 L min^{-1} onto 37 mm polycarbonate filter membranes (Whatman® Nuclepore™, USA) with pore size 0.8 µm. Gravimetric analysis was conducted following Method 0500[78]. Twenty-one elements were analyzed using an Energy Dispersive X-Ray Fluorescence (EDXRF) spectrometer. Black carbon (BC) in $PM_{2.5}$ was quantified using a transmissometer. The concentration of ten water-soluble inorganic ions (WSIIs) was determined via ion chromatography.

2.2.3 Meteorological database

Meteorological data were obtained from the Santa Catarina Civil Defense meteorological stations' network and the Joinville-Lauro Carneiro de Loyola Airport station (SBJV) (available on the MESONET website[79]). Precipitation data were also obtained from the CEMADEN's rain gauges' network[80]. Details in Figure 1 and SM, Table S1)

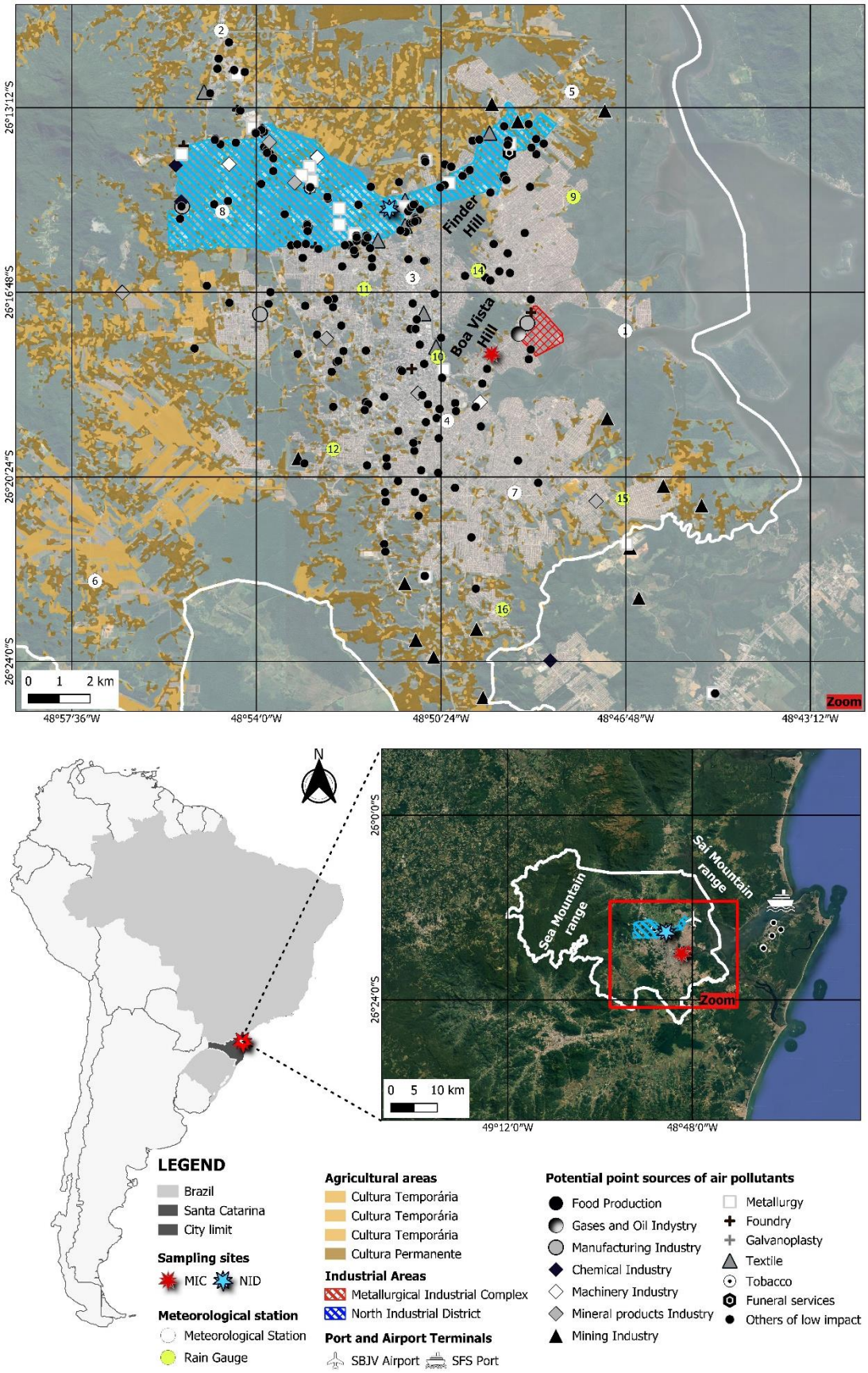


Figure 1. Localization of the study area, sampling sites [Metallurgical Industrial Complex (MIC) and North Industrial District (NID)], potential sources of air pollutants, and meteorological and rain gauge stations

2.2.4 Health and population data

Hospital admissions data were obtained using the "microdatasus"[81] package in R to download files from DATASUS, the Informatics Department of the Brazilian Unified Health System. The following information was selected: the date of hospital admission, sex, number of days of hospitalization, and primary diagnosis according to the International Classification of Diseases, code version 10 (ICD-10), associated with diseases of the circulatory (I00-I99) and respiratory systems (J00-J99). It is essential to highlight that the information comprises only public health data, disregarding data from health insurance and private morbidity.

In this analysis, the study period was defined as March 17, 2020, when the first confirmed case of COVID-19 was registered, to reduce COVID-19-related disruption on hospital admission occurrence, diagnosis, and counting. Therefore, the data include individual hospital admission records in Joinville between August 24, 2018, and March 16, 2020.

2.3 Source apportionment

To apportion the source-specific health risk, a source analysis was conducted. Building upon similar approaches employed in previous studies[53,82–84], we propose a systematic integration of source apportionment and risk estimation. This combined approach aims to elucidate the source-specific contributions to the health risks posed by key components bound to $PM_{2.5}$, ultimately facilitating their effective control. Positive matrix factorization (PMF) is a receptor-based source apportionment model, developed by the U.S. Environmental Protection Agency (EPA), based on a weighted least-squares technique to solve the factor analysis problem by integrating non-negativity constraints in the optimization process and to determine the primary pollution source and its contribution rate[85,86].

As part of this study, the chemically speciated $PM_{2.5}$ dataset was used as input to the EPA's PMF 5.0 receptor model to quantitatively profile source contributions to the analyzed

$PM_{2.5}$-bound components (i.e., based on the composition or fingerprint of the sources)[86]. This model aims to solve the chemical mass balance between measured species concentrations and source profiles, based on the principle of conservation of mass:

$$X_{ij} = \sum_{k=1}^{p} g_{ik} f_{kj} + e_{ij} = C_{ij} + e_{ij} \quad (1)$$

where C_{ij} is the modeled solution of x_{ij} (i.e., the concentration of species j measured on sample i), p is the number of factors contributing to the samples), g_{ik} is the relative contribution of factor k to sample i, f_{kj} is the concentration of species j in factor profile k, and e_{ij} is the residual for each sample/species.

In this analysis, multiple runs – with five to seven factors – were conducted for both sites to identify the optimal factors for source identification. The choice of species to include in the PMF input depended on the percentage of data below the detection limit[87]. Elements with more than 25% of their measured concentration below the minimum detection limit (MDL) were excluded[88–91] unless they were considered important tracers of specific sources. The uncertainty calculation followed the criteria established by Norris et al.[86]. Details of the PMF method and process metrics are provided in the SM, Section S4.

Source contributions were apportioned through multilinear regression analysis (MLRA). To track these sources, a graphical analysis was conducted using the polar plot function in OpenAir package in R-studio, as outlined by Carslaw and Ropkins[92]. This analysis generated bivariate plot graphs using source contributions (obtained by MLRA) and the daily averaged wind data, allowing the visualization of the concentration variation according to wind speed and wind direction. These plots aimed to provide insights into potential source influences at each location and guide the identification of sources on the map charts (Figure 1) which depict their positions within the studied region.

2.4 Source-specific and health risk assessment of $PM_{2.5}$

To evaluate the health risks associated with source-specific chemical contributions to $PM_{2.5}$ population exposure, a case-crossover study was implemented. Our research addresses the gap in quantifying the impacts of source-related $PM_{2.5}$ on hospital admissions due to cardiorespiratory diseases in an industrial coastal city between 2018-2020. This design utilized spatiotemporal stratification and a conditional logistic regression (CLR) model, as outlined by Wu, Li, and Guo[65]. The source-specific health risk approach was modeled based on Requia et al.[70]'s analysis of the impact of wildfire-related air pollution on the health of the Brazilian population. In particular, we investigated the source-specific impact by using a modeled approach that defines potentially hazardous source-related air pollution episodes at two urban-industrial regions, accounting for spatiotemporal heterogeneity on a population sample of more than 600,000 patients.

In a case-crossover study, control days are matched with case days in a reference window, then an appropriated regression model is fitted to investigate whether changes in environmental exposure can explain some of the short-term variations in the outcome[93]. This study design employs a binary indicator variable for case/control days to compare the exposure (to $PM_{2.5}$) on the day of the health event (hospital admission during episodes of higher source-specific contributions to $PM_{2.5}$; case day) with the exposure on non-event days (hospital admission during episodes of regular source-specific contributions to $PM_{2.5}$; control days). We used a space-time-stratified sampling to select the referent exposure days, which were matched for the sampling site, day of the week, month, and calendar year of the hospital admission.

As exposure to events of higher $PM_{2.5}$-related contribution from each source is a episodic event, then such matched analysis could be conducted. A referent episodic source-related $PM_{2.5}$ exposure event is defined as any day when a specific source exceeded its 75th percentile contribution during the studied period. This concept is used to capture periods with

strong episodes of source-specific $PM_{2.5}$ air pollution contribution, a concept similar to that of extreme air pollution events from wildfires defined in previous studies[68,70,94]. To assess source-specific health risk, the matrix g_{ik} (Equation 1) of relative contributions of each pollution source to each sample total $PM_{2.5}$ mass concentration ($\mu g\ m^{-3}$) – quantified by the receptor model (PMF) profiles source contributions values – was used as a threshold to determine exposure events on case days. Minimum values for the source-specific mass concentrations often have small negative values as a result of the uncertainties in the PMF analysis[95]. However, we did not left-censor the values to avoid the potential bias that such truncation would induce[27,95].

The time-stratified design is not subject to bias resulting from time trends because there is no pattern in the placement of controls relative to the case time. In addition, the design can control for season and day of the week by restricting referents to the same day of the week, month, and year as the case day. The time-stratified design is, therefore, a localizable (i.e., it allows to obtain unbiased estimates by making comparisons within referent windows), ignorable (i.e., the control sampling scheme can be ignored in conducting the analysis, and the CLR estimating equations are unbiased) design[96,97].

In this study, we have a unique epidemiological dataset for the total resident population of Joinville while collecting air pollution data at two sampling sites within the city, so a space-time-stratified case-crossover design, as proposed by Wu, Li, and Guo[65], allows to control for the spatial variations related to those multilocation environmental exposure health impacts, to make the results generalizable, credible, and confirmable. It could provide reliable effect estimates through matching 'cases and controls' to control for spatial variation, long-term trend, and seasonality.

Thus, this design is the best approach to controlling the bias associated with temporal trends, spatial variations and adjusting individual characteristics[65]. In summary, this approach incorporates some advantages: i) given that the matching periods were close in time, it reduces

confounding effects related to seasonal trend by controlling for time-dependent risk factors (e.g., day of the week, seasonality, and long-term trends) and reducing spatial variations bias resulting from location-specific fixed exposure and disjointed time strata; ii) in this matching study design, a person whose hospitalization were attributable to certain disease is defined as their own control (i.e., same person for both the case and control periods), which allows, by design, for control of all potential confounding factors at the individual level which are unlikely to undergo changes in a short space of time [such as demographics (e.g., gender, race, socioeconomic status, preexisting illnesses and education) and lifestyle (e.g., smoking or drinking alcoholic beverages)].

However, in air pollution studies, other time-varying confounders such as weather variables are not constant across the time periods and must be included in the analytic models[93,98]. So, the model was adjusted for a series of control/confounding variables, including meteorological variables (temperature, relative humidity, precipitation, wind speed, and wind direction), and health variables indicating the number of days that each patient was admitted to the hospital.

Thus, for each case, a stratum combining two dimensions of time (e.g., month) and space (e.g., study locations). Specifically, within each ID stratum, the case day and control days are matched by day of the week within the same month, in the same year, and in the same location (e.g., sampling site representative of residents' exposure within the same municipality). It is noteworthy that, in this study design, each case period has three or four control periods. Therefore, for each subject (from the daily individual-level hospitalization report), daily average concentrations of $PM_{2.5}$ and daily weather variables measurements (i.e., mean temperature, relative humidity, average wind speed and direction, and total rainfall) were obtained at each $PM_{2.5}$ sampling site and from its nearest weather station (more details can be found in SM, S3), respectively.

In the primary analysis, the conditional logistic model described above was applied for each group of health outcomes – respiratory diseases and cardiovascular diseases for each $PM_{2.5}$ source described above. We accounted for moving averages of higher (i.e., above 75th percentile) source contribution events, air pollutants (total $PM_{2.5}$), and weather variables. Time lags were applied to exposure variables not related to exposure events on case days, i.e., pollutant exposure (total $PM_{2.5}$ mass concentration), and weather variables. The binary indicator variable for case/control days to compare the source-related $PM_{2.5}$ exposure on the day of the health event, and the hospital admissions-related variable (i.e., number of days that each patient was admitted to the hospital due to each selected disease group) remained representative of the case day exposure. Five moving averages were included: from a 1-day moving average to a 5-day moving average.

Additionally, some effect modification and sensitivity analysis were performed by stratifying the analyses by sex, by age (< 60 years old, and >= 60 years old), and by accounting for cardiorespiratory hospital admissions (cardiovascular and respiratory hospital admissions together). To check the goodness-of-fit of our model choice, we compared two case-crossover designs using conditional logistic regression models, one that uses the spatial variable as a predictor in a time-stratified referent and another that includes it in the strata as a space-time-stratified referent selection. The model comparison was done using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). The lower AIC and BIC values of the model we propose indicate that this parsimonious model fits the data better. Results are shown in SM (XLS file).

These analyses were conducted in the R software, using the Survival statistical package (clogit function), referencing the model and code from Requia et al.[70]. Further details are available in the SM, S5.

3. RESULTS AND DISCUSSION

3.1 Atmospheric chemistry balance and air quality – An overview

This study continuously monitored $PM_{2.5}$ concentrations in urban-industrial areas of a medium-sized coastal Brazilian city, from August 24, 2018, to October 28, 2020. Daily $PM_{2.5}$ mean concentrations were 6.1 and 5.2 μg m^{-3} at MIC and NID, respectively. These values appear low compared to other cities influenced by industrial activities such as Athens, Barcelona, Firenze, Milan, and Porto (where $PM_{2.5}$ ranged from 11 to 30 μg m^{-3})[99] or even larger Brazilian cities like Belo Horizonte, Rio de Janeiro, São Paulo, Curitiba, Manaus, and Porto Alegre, where mean $PM_{2.5}$ mass concentrations ranged from 13 to 28 μg m^{-3} [100–102].

To further explore the influence of human-environment dynamics on aerosol air pollution, we analyzed the spatiotemporal variation of the $PM_{2.5}$-bound components (SI, PDF file). Mean BC concentrations (and their contribution to total $PM_{2.5}$ mass) were lower than 1 μg m^{-3} (i.e., 18%) at both sites, extremely low compared to other Brazilian cities[101–105], where a minimum of 2 μg m^{-3} (17%, and usually ranging from 20 – 37%) were observed.

The summed concentration of elemental components varied significantly, ranging from 30 to 4700 ng m^{-3} at MIC and 3 to 7000 ng m^{-3} at NID. Among the analyzed elements, Zn stands out as a $PM_{2.5}$-bound element associated with industrial emissions in several cities worldwide. The highest mean concentration values (440 ng m^{-3}, i.e., up to 26 $ng_{Zn}/\mu g_{PM_{2.5}}$) were observed in China[106], compared to the 114 ng m^{-3} (i.e., 18 $ng_{Zn}/\mu g_{PM_{2.5}}$, at MIC) and 151 ng m^{-3} (i.e., 30 $ng_{Zn}/\mu g_{PM_{2.5}}$, at NID) in Joinville (Figure S1), Globally, however, lower concentrations (and $Zn/PM_{2.5}$ concentration ratio below 4) were found in several cities, among which some of European Mediterranean (from 19 to 77 ng m^{-3})[107], in Turkey (88 ng m^{-3})[108], and in Saudi Arabia (40 ng m^{-3})[109].

WSIIs varied from 60 ng m^{-3} to 3800 ng m^{-3} at MIC and 7200 ng m^{-3} at NID, much less (up to 120-fold) than the total elemental concentration (up to 2000-fold). Among the ionic forms, SO_4^{2-}, in addition to being the most abundant anion, was also the most prevalent inorganic ion, accounting for more than 10% of $PM_{2.5}$ total mass, on average, at both sites. Conversely, Na^+ was the most abundant cation, contributing 2.3% and 3.2% at MIC and NID, respectively.

The acidity of $PM_{2.5}$ was analyzed by the linear relationship between cation and anion equivalents (details in SM, Section S6). Regardless of the season or site, a prevalence of alkaline particles was observed and, consequently, an anion deficiency (Figure S2). This study found lower WSIIs concentrations than those reported in other coastal cities such as Athens, Greece[66], Seoul, South Korea[67], and China[68], where $PM_{2.5}$ aerosols were acidic.

The secondary inorganic components (SO_4^{2-}, NO_3^-, and NH_4^+) accounted for approximately 73% of the WSIIs at both sites. Results of linear regression analysis for NO_3^-, and SO_4^{2-} against NH_4^+ concentrations (Figure S3) suggest ammonia complete (at MIC) and near complete (at NID) neutralization of those anions. Although a good correlation between levels of NH_4^+ with the summed concentrations of SO_4^{2-} and NO_3^- could be observed, the results of correlation analysis between major ions (Table S7) suggest that NH_4^+ was moderately or highly correlated only with SO_4^{2-}. The $[NH_4^+]/[SO_4^{2-}]$ molar ratios < 2 indicate an "ammonia-poor environment"[110,111] at both sites. As such, the neutralization of sulfate precursors by ammonia was the reaction more thermodynamically favorable[110–112], with the formation of NH_4HSO_4 prevailing salts at NID's, and $(NH_4)_2SO_4$ at MIC's $PM_{2.5}$ samples. Overall, there was no correlation between NH_4^+ and NO_3^-, suggesting NH_4NO_3 was not a significant compound in $PM_{2.5}$.

As sulfate is dominating and particulate is alkaline in this coastal region, discerning non-sea-salt sulfate (nss-SO_4^{2-}) content (calculated from measured SO_4^{2-} and Na^+

concentrations[113]) in $PM_{2.5}$ apart from SO_4^{2-} can be useful to analyze the impact of air mass transport of marine aerosols during less and more polluted events. Considering the WHO guideline[20] for short-term (i.e., 24h) $PM_{2.5}$ exposure of 15 μg m^{-3} as a threshold value, $PM_{2.5}$-bound species (Nss-SO_4^{2-}, NO_3^-, and NH_4^+) concentrations were compared between days of "safer" exposure to $PM_{2.5}$ or so-called non-episode days (NEDs) and episode days (EDs). In this study, nss-SO_4^{2-} constituted about 98% of ambient $PM_{2.5}$ sulfate during EDs and 90% during NEDs. Nss-SO_4^{2-}, NO_3^-, and NH_4^+ contribution to $PM_{2.5}$ varied from 13% (MIC, 2.2 μg m^{-3}) to 9% (NID, 1.9 μg m^{-3}) during EDs, up to 19% (MIC, 0.9 μg m^{-3}) and 24% (NID, 1.1 μg m^{-3}) during NEDs. Therefore, meanwhile marine aerosols contributed more to $PM_{2.5}$-sulfate during common NEDs, the non-marine absolute concentrations during EDs were near twice as higher those during NEDs, and their relative contribution was higher during NEDs. An increase of these species by a factor that is more than twice as high in concentration has been associated with increased formation of secondary species and with the recirculation of anthropogenic emissions of precursor chemicals[114–116].

When alkaline material is present, heterogeneous reactions of gaseous species with more alkaline aerosol species, like mineral and sea salt, can impact nitrate aerosol formation[117]. As such, a proportion of these anions was associated with other cations, such as sodium, calcium, and magnesium adding to the alkaline aerosol profile[118–122] observed in Figure S1. This is indicated by the correlation coefficients observed between Na^+, Ca^{2+}, and Mg^{2+} and acid ions (Cl^-, and NO_3^-), suggesting the presence of $Ca(NO_3)$, $Mg(NO_3)_2$[111,123,124]. K^+ and acid ions (SO_4^{2-}) were correlated to each other (> 0.500) during summer and spring at NID, and K_2SO_4 was one of the chemical species in the aerosol particles. Other correlation coefficients between alkaline and acid ions were less significant, and fewer compounds were formed between those ions.

Aerosol acidity health implications have been explored in other studies. Sulfate plays an important role in producing acidic aerosols capable of promoting the dissolution of metals that contribute to aerosol oxidative potential and increased toxicity[125–128]. WSIIs constituents of $PM_{2.5}$ (especially, NO_3^-) might increase stress hormones associated with cardiometabolic risks[129]. Therefore, as a determining factor in particles' alkalinity, ammonia is critically important as it can neutralize acidic species leading to the formation of ammonium salts[128,130].

However, more studies regarding the health risks associated with $PM_{2.5}$-bound WSII are needed. $PM_{2.5}$ nitrate content was also associated with a reduction of location-specific relative mortality risk[131], while interactions of NH_4^+, typically found as ammonium sulfate in $PM_{2.5}$[131], increased mortality risks. Luo et al.[132] have observed that air enriched with nonhazardous levels of nitric acid can increase viruses inactivation in small aerosol particles. Consequently, alkaline aerosol may prolong airborne virus persistence and should be considered in transmission and mitigation strategies.

Secondary inorganic components are major constituents of $PM_{2.5}$ and are linked to aerosol formation processes and atmospheric transformations, as such, influence significatively its physical and chemical properties, affecting the exposure levels of harmful $PM_{2.5}$ species. Therefore, aerosol acidity might affect particle-bound species interactions and the role of $PM_{2.5}$ composition on potential health impacts, ultimately altering its toxicity.

3.2 Receptor surroundings characterization

Joinville, a mid-sized city affectionately nicknamed the Catarinense Manchester is renowned for its extensive industrial sector and similar climate. It is particularly known for its foundry industries and a wide array of metallurgical, textile, chemical, and plastic industries (Figure 1). As illustrated in Figure 1, starting from the north and moving anticlockwise toward

the southwest, the urban area is also surrounded by agricultural land, with increasing natural vegetation closer to the mountains.

Heavy traffic flow during rush hours on major thoroughfares to the east may also significantly contribute to air pollution at these sites. Consequently, $PM_{2.5}$ measurements at the stations are likely to be heavily influenced by traffic-related aerosols. Additionally, shipping emissions could impact $PM_{2.5}$ levels at both sites, as strong easterly winds have potential to transport emissions from the São Francisco port terminal and nearby facilities, located approximately 20 km to the east.

3.3 Chemical fingerprinting of source profiles

Source factors were obtained from the PMF analysis for the two sites using metal and ionic $PM_{2.5}$ concentrations. The results indicated that the solution with seven sources was the most reasonable and robust for both sites (i.e., minor errors, less ambiguity, and variability as well as improved profile interpretability, as shown in Tables S3 and S4).

The chemical source profiles contributing to $PM_{2.5}$ at MIC and NID – and the concentration variation according to wind speed and direction – are depicted in Figures 2 and 3, respectively. The sources were then identified based on input species with the highest loadings in each factor, drawing comparisons with prior research and online datasets[133,134]. Consequently, henceforward all the source descriptions refer to the results presented in Figures 2 (MIC) and 3 (NID).

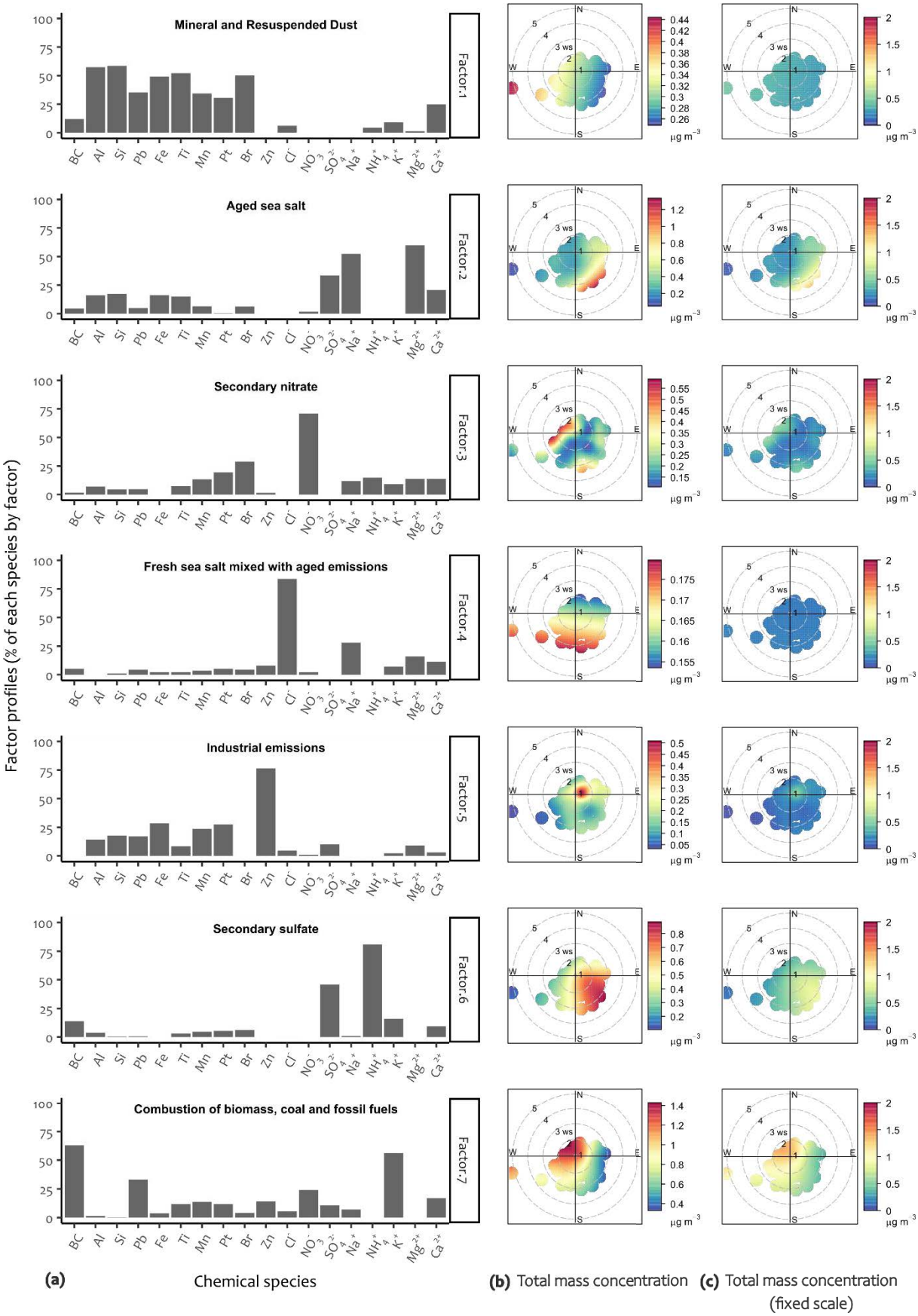


Figure 2 – Factor profiles at MIC sampling site, in (a) percentage of species apportioned to each factor), (b) and (c) polar plots of each source absolute concentration contribution to total mass concentration variation – by wind direction and wind speed (ws) – obtained using PMF source apportionment model, showing a free and a fixed scale, respectively

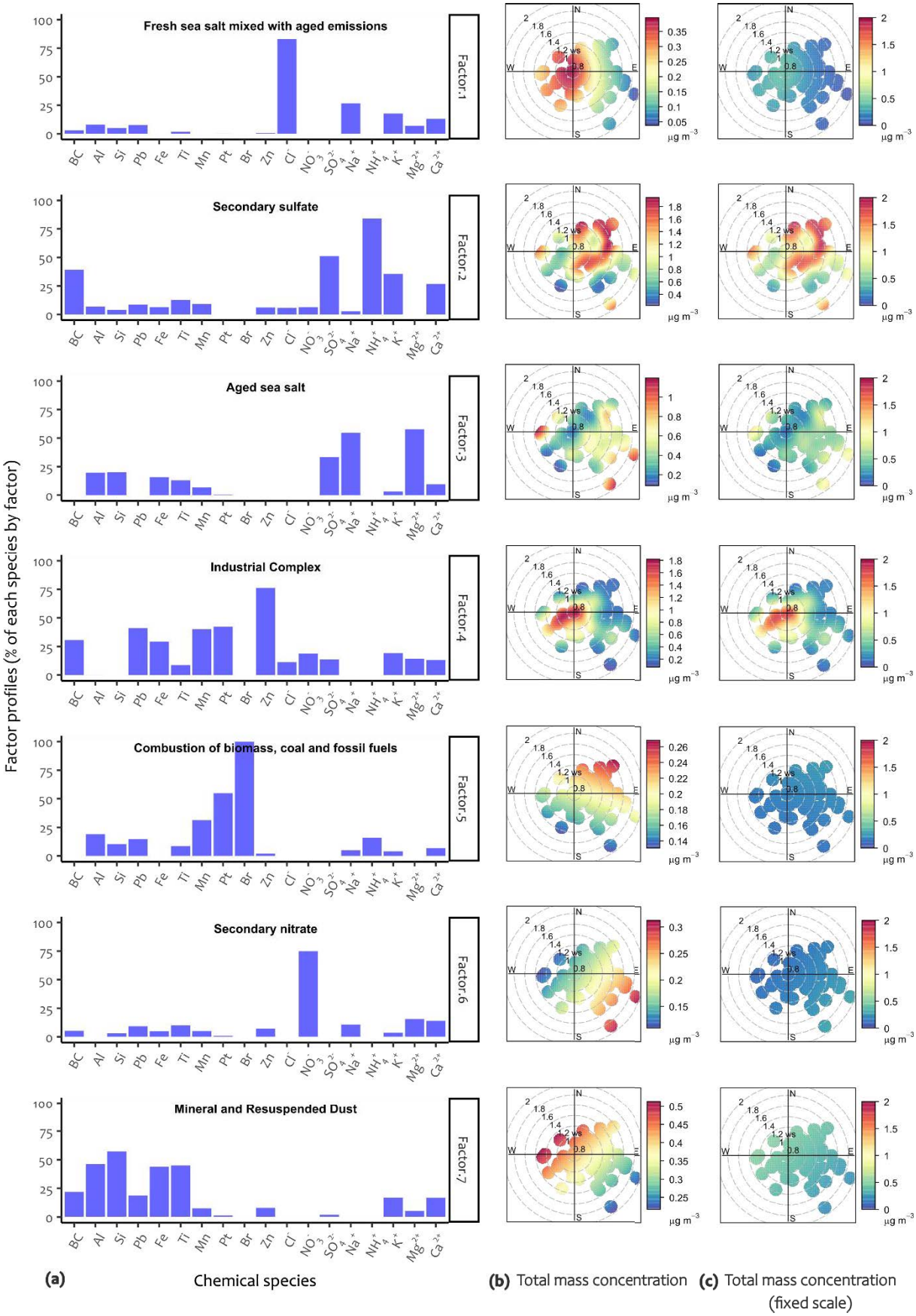


Figure 3 – Factor profiles at NID sampling site, in (a) percentage of species apportioned to each factor), (b) and (c) polar plots of each source absolute concentration contribution to total mass concentration variation – by wind direction and wind speed (ws) – obtained using PMF source apportionment model, showing a free and a fixed scale, respectively

In summary, based on the elemental and ionic composition, the PMF analysis elucidates the source apportionment and its contribution to the chemical composition of $PM_{2.5}$, as detailed in Table 1. Although in varying proportions, the same sources contributed to $PM_{2.5}$ of both sites: secondary sulfate formation, aged sea salt, industrial emissions, combustion of biomass, coal, and fossil fuels, mineral and resuspended dust, secondary nitrate formation, and fresh sea salt mixed with aged emissions. The primary contribution was from secondary sulfate formation (greater at NID), and combustion-derived (at MIC) emissions followed by aged sea salt aerosol at both locations and industrial emissions (more significant than sea salt at NID). Without accounting for black carbon content, the secondary sulfate formation was the largest contributor at both sites, followed by aged sea salt aerosol (greater than the industrial sources at MIC) and industrial emissions (more significant than sea salt at NID) at both locations.

Table 1 – Source contributions percentage estimates for $PM_{2.5}$ derived from the tracer-based PMF solution for each site sampling period. Values within parenthesis indicate each source contribution without black carbon content

Emission Source	**Contribution to estimated $PM_{2.5}$ mass concentration**	
	MIC	**NID**
Secondary sulfate formation	22.7% (26.4%)	31.4% (28.5%)
Aged sea salt	14.9% (20%)	14.5% (20.3%)
Industrial emissions	8.9% (13.4%)	21.9% (17.9%)
Combustion of biomass, coal, and fossil fuels	27.7% (11.2%)	6.4% (9%)
Mineral and resuspended dust	11.1% (10.8%)	12% (8.2%)
Secondary nitrate formation	7% (9.5%)	5.9% (6.4%)
Fresh sea salt mixed with aged emissions	7.7% (8.8%)	7.9% (9.7%)

As dominant as it is in major economies such as North America, Europe, China, and other East Asian countries[135], sulfate was the most abundant species found during sampling. Its main source can be described as secondary sulfate formation (SSF) processes[136] since it was discriminated by its significant contributions of sulfate (approx. 50%) and ammonium (> 80%) ions to $PM_{2.5}$ total mass at both sites.

As the most important alkaline gas, ammonia plays a primary role in forming secondary particulate matter by neutralizing with acidic precursor species, such as SOx and NOx, to form ammonium salts (e.g., particulate sulfate or nitrate ammonium-containing aerosols)[137–140]. The main sources of ammonia are animal excretion, synthetic fertilizers, oceans, biomass burning, agricultural crops, industrial processes, and fossil fuels[141], whilst sulfate aerosol main precursors, sulfur dioxide (SO_2) and dimethyl sulfide (DMS), mainly originate from marine aerosol, vehicular emissions, fossil fuels burning and industrial activities[142,143]. The extent to which particulate sulfate or nitrate is then formed is governed by a thermodynamic equilibrium that favors the neutralization of sulfate precursors by ammonia[110,111,137,144], meanwhile aerosol water, manganese, and sodium chloride content may also promote sulfate formation[145].

Being a coastal city, biogenic sources of sulfate likely contribute significantly to the high sulfate load of this factor as air masses pass over the coastline. The blooming of phytoplankton and sulfate reduction in the anoxic conditions of sediment in mangrove coastal areas can release substantial amounts of biogenic sulfur gases (such as biogenic DMS), which ultimately convert to nss-SO_4^{2-} in the aerosol[146,147], a key regulator of global climate[148].

Since the city is built on previously mangrove-occupied land and intertwined with numerous water features, Joinville's coastal landscape plays a unique role in shaping its aerosol composition. The intertwining roots of plants in the coastal area not only break the wind but also induce waves and reduce the water speed, promoting the production of sea salt aerosols (SSA) from the bursting of air-entrained bubbles during the breaking of waves and the formation of aerosolized wind-blown excreted salts from various halophytic plants and soil microbial activity[146,149].

Traces of Ca^{2+} and PO_4^{3-} (not included in the PMF model but displaying similar wind speed-direction dependent concentration patterns as shown in Figure 4) indicate mixed aerosols of marine, biogenic, and soil origins. Studies of the Sundarban Mangrove Forest in India have

shown similar dynamics, with high concentrations of phosphate aerosol associated with salt particles resulting from the interaction between continental (dust, sea spray, and plant pollen) and coastal ecosystems (nutrient runoff from mangrove estuaries)[146].

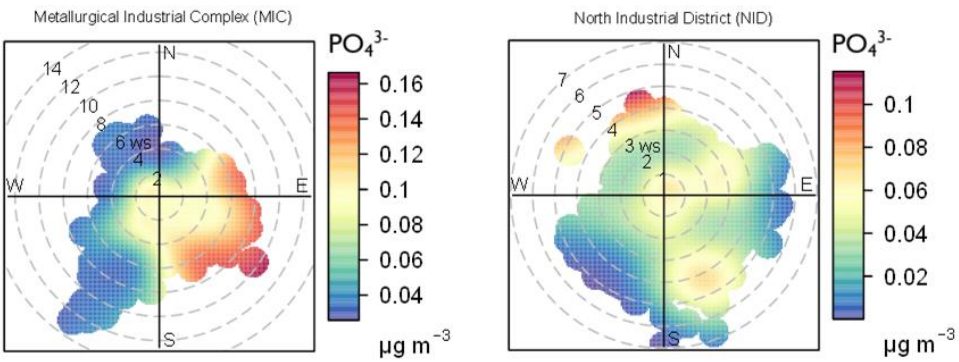


Figure 4 – Bivariate polar plots of phosphate ion (PO_4^{3-}) mass concentration contribution to $PM_{2.5}$, showing the concentration variation by wind direction and wind speed (ws) at the sampling sites (MIC and NID)

These SSF processes seem to be favored by their precursor's emission from fertilizer storages and transportation around port facilities to the east. A significant contribution to BC, K^+, and Ti in $PM_{2.5}$ also characterized these profiles. The greater contribution of these species at NID compared to MIC suggests a more significant impact from agricultural open burning emissions, transported by northerly orographically-oriented winds from the surrounding rural areas of that receptor site. Therefore, while agricultural-related emissions such as fertilizer handling, storage, and application likely contribute to ammonia (NH_3) emissions, the release of trace metals is more commonly linked to coal combustion[56].

Extremely high contributions of NO_3^- (> 70%) to $PM_{2.5}$ characterize another factor profile of both sites. These profiles also contribute to almost all chemical components analyzed, and therefore, can be identified as secondary nitrate formation (SNF). A greater contribution from the SNF apportioned source was observed at the MIC site compared to the NID site. The prevailing wind direction, associated with the higher contributions of NO_3^- to $PM_{2.5}$ at both sites, indicates that these secondary nitrate source profiles are formed in a region between the

sampling sites (i.e., northwest from MIC and southeast from NID), probably downtown, and also from high traffic on major thoroughfares surrounding the sites, from where nitrogen oxides formed by vehicular traffic activities and fossil fuel combustion[150] are transported by wind local recirculation.

Nitrate formation depends on the thermodynamic state of its precursors – usually ammonium and nitrogen oxides – occurring in areas characterized by a high concentration of ammonia, low concentration of sulfate, and under conditions of high relative humidity and low temperature[118]. However, as observed about the alkaline $PM_{2.5}$-bound WSIIs at the sites, a low $[NH_4^+]/[SO_4^{2-}]$ molar ratio of 0.8 at NID suggests SSF in an ammonia-poor environment[110] with high sulfate concentrations, which inhibits the formation of nitrate[118]. An absence of nitrate and a higher $[NH_4^+]/[SO_4^{2-}]$ ratio (of 1.1) was also observed in the SSF source contributing to MIC's $PM_{2.5}$. The SNF source at the MIC site exhibited a molar ratio of $[NH_4^+]/[NO_3^-]$ of 0.97, suggesting the formation of NH_4NO_3[151], meanwhile, the ammonium contribution at NID was absent, indicating an environment favoring SNF with other cations (i.e., Na^+, Ca^{2+}, and Mg^{2+}) present in this source chemical profile. Ultimately, although this *ammonia-poor environment* would be insufficient to neutralize nitrate (shifting it to its gaseous phase), the aerosol alkalinity given by dust and sea salts facilitates the capture of nitrate in coarser particles – that, during transport to the continent, end up having their concentration reduced in the aerosol due to the higher deposition rate[117,152,153] – thus reducing $PM_{2.5}$-SNF contribution to minimal levels.

For coastal cities, sea salts and mineral dust are the main natural contributors to aerosols. The presence of sodium characterizes a sea salt source profile that can be considered fresh when associated with a significant chloride concentration, and aged when chloride is depleted[135]. At both sites, the second largest contributor to $PM_{2.5}$ was characterized by sea salt species (Na^+, Cl^-, Mg^{2+}, and Ca^{2+}), with a high contribution of Cl^- (~ 80%), and a molar $[Na^+]/[Cl^-]$ ratio of 0.88. This ratio can be used to investigate the aging of aerosols[136]. It varies between 1.2 and 2.2

in fine particle aerosols above the sea atmosphere but can be enriched in Cl^-(~ 0.86) as it receives inputs of dust and HCl within the continent[154]. In addition to Pb, this factor also showed a significant mixture with metals from industrial emissions in nearby zones. Therefore, these factors likely represent fresh sea salt mixed with emissions from metallurgical, chemical, and textile industries.

Despite the wind direction associated with the higher contributions in this source (Figures 2–5) appearing contrary to the relative position of marine sources (i.e., to the east), air masses transportation from the southeast (i.e., from ocean areas) contributes directly to the concentration's 0 – 50 percentile range at both sites, as well as to that fraction above the 75th percentile at MIC. However, a significant input coming from the west is possibly associated with orographically-oriented wind direction as a result of specific local geo-environmental constraints reflecting the recirculation dynamics and potential air mass mixture as discussed in our previous study[75].

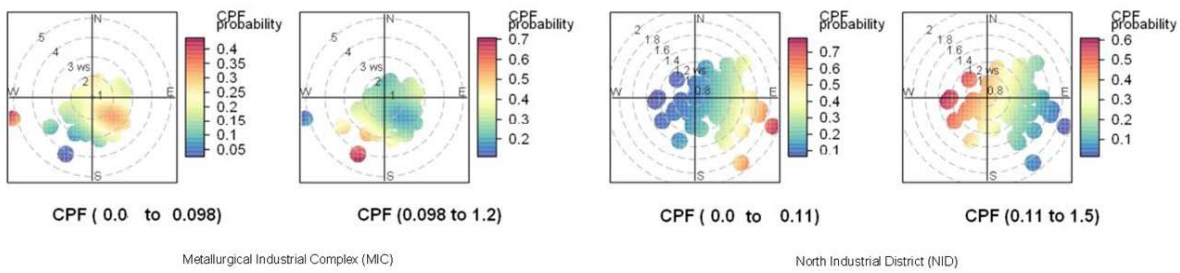


Figure 5 – Bivariate polar plots of fresh sea salt mass concentration contribution to $PM_{2.5}$ at the sampling sites (MIC and NID) based on the Conditional Probability Function (CPF) for the percentile intervals from 0 – 50 (to the left) and 50 – 100 (to the right), showing the probability of such concentrations occurring by wind direction and speed (ws)

Heterogeneous reactions involving SSA significantly affect the atmospheric chemical balance in coastal locations, acting as sink for nitrogen and sulfur oxides, while also a source of halogen gases[152]. Aged sea spray (ASS) aerosol played a similar role at both sites, exhibiting significant sulfate concentration compared to the original fresh sea spray aerosol source and acting as a source of chloride across the atmosphere. Except for the fresh sea salt factor chemical

profiles, $PM_{2.5}$-bound Cl^- depletion exceeded 30% in all other profiles. This occurs because of halogen radicals' formation in chemical reactions between NaCl and acid species (such as nitric acid and sulfuric acid from anthropogenic emission on the continent), producing gaseous $HCl_{(g)}$[155] and enriching the aerosol in other species as it is transported away from the sea surface over land[152,156]. Consequently, at both sites, southeast winds were associated with an ASS factor characterized by ionic tracers like Mg^{2+}, Na^+, and minerals such as Al, Si, and Fe[157].

Alongside those processes involving ionic compounds, during the study period, Northwesterly winds transported $PM_{2.5}$ enriched with typical crustal elements (i.e., Si, Al, Ti, Fe, and Ca^{2+})[136,158–160] to both sites, likely originated from exposed soil in the surrounding mountains and agricultural areas. Furthermore, the abundance of BC, Fe, Pb, Mn, and Pt of these factors' contribution to $PM_{2.5}$ suggests an anthropogenic origin. In industrial areas, atmospheric deposition typically increases the concentration of metallic elements such as Al, Fe, Mn, and Zn in soil, and dust resuspension has been observed to increase atmospheric concentrations up to threefold those of rural[161] or residential[162] areas.

The typical K/Pb ratio in aerosols of mineral origin has been found to vary between 775 – 863[163]. However, in this study, enrichment of Pb in all factors' chemical profiles resulted in K/Pb ratios below 100, consistent with the typical ratio reported for coal-burning[164]. The Fe/Al ratio (~1.5) was more than twice the one observed in the Earth's crust but comparable with the reported for heavy road traffic emissions (range of 0.32 – 1.7)[160,165]. Contributing to this resuspended material composition are exhaust-related emissions compounds deposited on the ground, such as BC and NO_x from tailpipe emission, Ca and Zn as major additives to lubricant oil, and non-exhaust emissions of Cu, Mn, Pb, Zn, and Fe from break wear, tire abrasion, pavement wear, and vehicle corrosion[135,160,166–171]. This source is well-known but unpredictable, as metal concentrations vary according to factors such as traffic volume and patterns, vehicle fleet characteristics, climate, and the geology of the region[160,172]. These

chemical profiles can be identified as both mineral and resuspended dust since although primarily composed of crustal elements reinjected into the atmosphere as windblown aerosols[173] but also resuspended material from nearby roads[135], where the soil has been mixed with anthropogenic emissions from vehicles and industries deposited during transport.

The source apportionment clearly discriminated a chemical profile of industrial sources with high loadings of Zn, Pt, Mn, Fe, and Pb, elements typically associated with metallurgic industry $PM_{2.5}$ emissions[56,136,174–176] and fossil fuel combustion[135] for both sites. The sampling sites are surrounded by numerous iron (MIC) and aluminum (NID) foundries. The raw materials of foundry processes are characterized by ferrous and non-ferrous elements consumed during high-temperature slag melting. Foundry sand (constituting ~70% of process waste and is used as molds) contains a complex mix of sand compounds, organic materials (e.g., mineral coal dust and tar), inorganic additives, and binding agents. These can contribute to the content of several metals and species like SO_4^{2-}, and NH_4^+ in aerosols[177–180]. The wind profile associated with these compounds' higher concentrations corroborates this identification, as industrial areas are located east of MIC and west of NID. The K/Pb ratio of 12 at NID reinforces this assumption since values between 10.6 and 15.7 have been linked to coal combustion[164], typical of these industrial activities. Additionally, high concentrations of BC, K^+, Mg^{2+}, SO_4^{2-}, NO_3^-, and Ca^{2+} also characterized these factors during low wind speed from the southwest, where significant vehicular traffic-related fossil fuel combustion occurs. Therefore, these chemical profiles likely represent a mixture of multiple industrial and associated combustion emissions resulting from varying degrees of chemical and physical changes as $PM_{2.5}$ is formed during the transport from its sources.

Meanwhile, chemical profiles characterized by a high contribution of BC, K^+, Pb, NO_3^{2-}, Ca^{2+}, Ti, Mn, and Pt at MIC, and by Br, Pt, Mn, Al, Si, Pb, Ti, and NH_4^+ at NID, distinguish the specific emission profiles of industrial and vehicular combustion processes. At

NID, the mix of industrial and both exhaust and non-exhaust traffic emissions appears to be the source of such metallic elements, consistent with the volume of traffic activities and the characteristics of the vehicle fleet in their respective surrounding environments[160,172]. As industrial zones, the fleet composition includes an important amount of regular and heavy vehicles, such as spark-ignition (gasoline and ethanol) and compression-ignition (diesel) vehicles. Notably, at MIC, there is a high contribution of air pollutants from coal and biomass combustion such as BC, Pb, and K emitted by metallurgical processes, local residential and commercial activities surrounding this sampling site.

However, although those sources are characterized by high emissions of BC, a reduced contribution of BC to $PM_{2.5}$ was observed at NID compared to MIC. This phenomenon may be associated with atmospheric chemistry processes related to the higher rainfall index in the surrounding region[75] and longer distances from potential sources. Despite BC's high hydrophobicity[181], during the particulate aging process in the environment, BC can be coated with water-soluble components and become hydrophilic. As a result, particles containing BC can become cloud condensation nuclei and precipitate through humid deposition[182,183]. This makes the transportation of BC uncertain and its suspension in the atmosphere is dependent on aging time (between 12h and 8 days) and of factors that control its deposition rate (i.e., precipitation)[184,185]. Several studies have shown that BC emitted from biomass burning (one of the main sources associated with this factor at NID) is more likely to be coated in such a manner (70%) compared to those from urban areas (9%)[185]. Therefore, this source chemical profile encompasses multiple combustion sources: agricultural burning, industrial coke/coal fuel use, commercial heating/cooking with wood or other biomass (crop residues, dung, etc.), and even fossil fuel combustion exhaust and non-exhaust emissions by vehicles[135].

Hence, as it moves away from the coastline, the SSA undergoes transformations due to atmospheric aging processes[186]. These recirculation events bring fresh marine aerosols into the

urban environment, causing a decrease in Cl^- content and an increase in anthropogenic emission compounds. At MIC, the chemical feature of the observed aerosol seems to lose its marine character and to acquire a chemical signature dominated by contributions from all the major anthropogenic aerosols due to this phenomenon. Consequently, atmospheric recirculation in coastal areas may contribute to the presence of atmospheric pollutants in these areas due to the occurrence of pollutant feedback mechanisms. The chloride depletion may lead to the enrichment of excess (non-sea-salt) sulfate, nitrate, and nitrite[146]. Finally, this urban-industrial $PM_{2.5}$ composition is strongly dependent on ammonia availability in addition to sea-salt-minerals particulate alkalinity and is regulated by coastal environmental conditions. In such an environment, vertical transport and exchange between sea and land facilitate multiple chemical reactions, leading to the formation of secondary aerosols.

3.4 Environmental Epidemiology

3.4.1 Hospital admissions characteristics

During the study period, Joinville recorded 7,378 hospital admissions for circulatory diseases and 5,027 for respiratory diseases. Of these, 77% matched with $PM_{2.5}$ speciation data (and, thus, were source apportioned). Males comprised most hospitalizations in both disease groups, accounting for approximately 54%. A higher rate of hospital admissions for circulatory diseases (62%) was observed among the elderly (age $\geq$ 60 years old), whereas the opposite was observed among people below 60 years old (i.e., 63% of the hospitalizations for respiratory diseases). Figure 6a shows the monthly distribution of the morbidity database throughout the study period. October witnessed the highest daily morbidity (15 ± 6), while December had the lowest (11 ± 4). The daily number of hospital admissions in Joinville varied from 3 to 29

(average of 13 ± 4.8) for diseases of the circulatory system (ICD-10 I+) and from 1 to 29 (average of 8.8 ± 4.4) for respiratory diseases (ICD-10 J+).

3.4.2 Exposure characteristics

From August 24, 2018, to March 16, 2020 (case study period), the annual mean concentration of ambient $PM_{2.5}$ was 3.9 (n = 117), 6.6 (329), 6.5 (232) μg m^{-3} at MIC and 5.0 (82), 5.1 (253), 3.8 (15) μg m^{-3} at NID – in 2018, 2019, and 2020, respectively – mostly exceeding the World Health Organization (WHO) 24-hour annual air quality guideline of 5 μg/m^3 [20]. Daily mean temperature varied from 13 to 35ºC, relative humidity from 47 to 94%, and total precipitation reached up to 110 mm. A monthly summary of source contributions and meteorological variables is presented in Figures 6b and 6c, respectively.

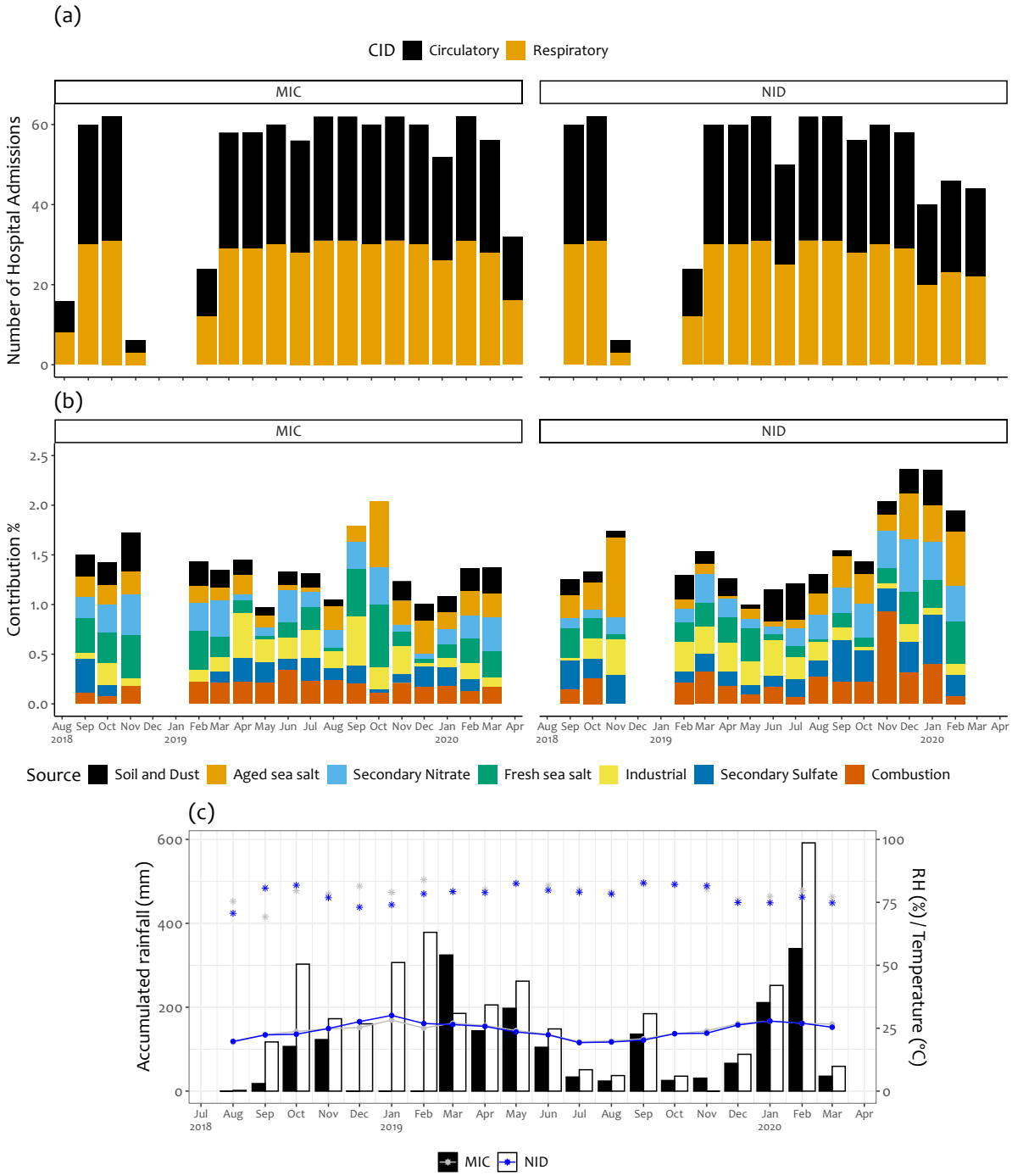


Figure 6 – For the study period, monthly (a) number of hospital admissions for circulatory and respiratory diseases, (b) meteorological conditions, and (c) sources contribution to $PM_{2.5}$

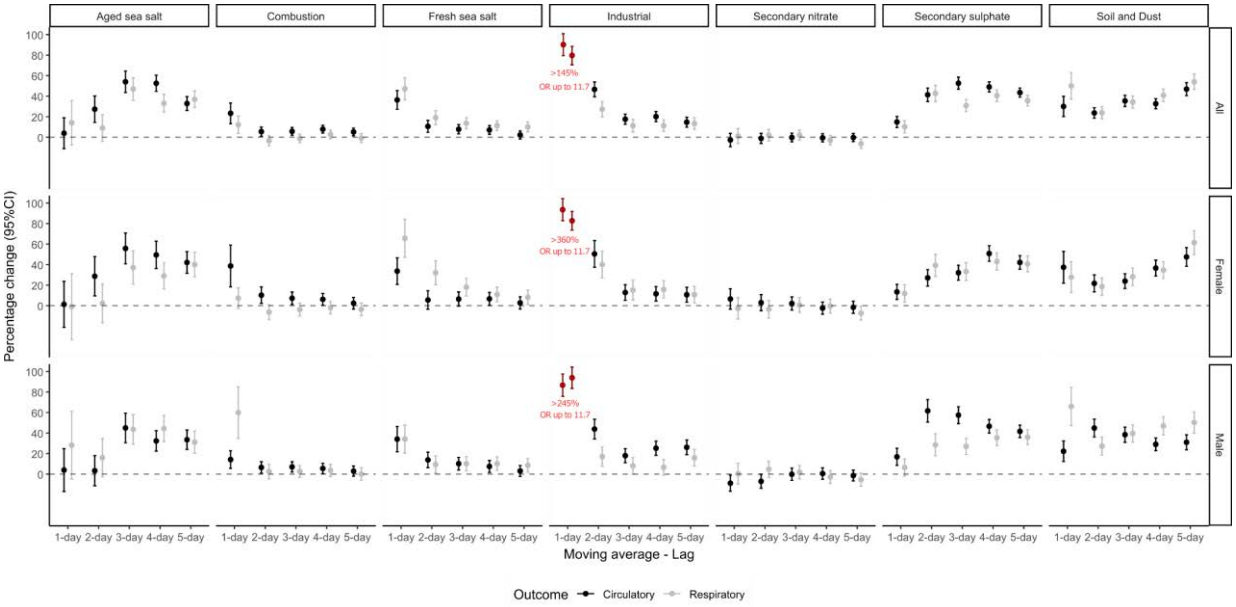


Figure 7 – Association between hospital admissions and source-related $PM_{2.5}$. Percentage increase in risk (and 95% CI) of hospital admissions (black line- respiratory diseases; gray line, circulatory diseases) associated with source-related $PM_{2.5}$ in events with source contributions higher than their own 75th percentile during the study period for the moving averages 1–5 days. Note 1: Numbers in x-axis indicate the moving averages

3.4.3 Source-specific health risk of $PM_{2.5}$

To evaluate the short-term effects of exposure to $PM_{2.5}$ on the health of the resident population, a time-stratified case-crossover study design using a conditional logistic regression model was employed, considering each source's contribution to $PM_{2.5}$ samples.

The percentage increase in risk (and 95% confidence interval, CI) of hospital admissions associated with source-specific $PM_{2.5}$ for the moving averages of 1–5 days by health outcome (circulatory and respiratory disease) is presented in Figure 7. The obtained source-specific odds ratio (OR) of hospital admissions, and each model statistical significance are shown in Table 2 and Table 3. The full results (primary and all sensitivity analysis by sex, and age) can be found in SM (XLS file). The sensitivity analysis revealed substantial differences between men and women for most of the sources and moving averages, as well as the elderly and those aged < 60 years old.

Table 2 – Odds ratio and 95% CI representing the circulatory hospital admissions associated with source-specific $PM_{2.5}$ during episodes of higher source-specific contribution to $PM_{2.5}$ air pollution in Joinville (2018-2020) for 1–5 moving averages.

Source	*Outcome*	*Moving averages*	*Odds ratio*	*Lower 95% CI*	*Upper 95% CI*	*p-value model**	*p-value β $PM_{2.5}$***
Circulatory Hospital Admissions	Aged sea salt	1	1.04	0.89	1.19	$2.02\ 10^{97}$	$6.22\ 10^{-01}$
		2	1.27	1.14	1.40	$1.28\ 10^{172}$	$2.39\ 10^{-04}$
		3	1.54	1.44	1.64	$1.13\ 10^{224}$	$4.68\ 10^{-16}$
		4	1.53	1.45	1.60	$3.87\ 10^{220}$	$8.39\ 10^{-26}$
		5	1.33	1.26	1.40	$1.28\ 10^{208}$	$2.07\ 10^{-16}$
	Combustion of biomass, coal and fossil fuels	1	1.23	1.13	1.33	$2.90\ 10^{55}$	$4.46\ 10^{-05}$
		2	1.05	1.01	1.10	$1.08\ 10^{65}$	$2.00\ 10^{-02}$
		3	1.06	1.02	1.10	$1.10\ 10^{55}$	$4.39\ 10^{-03}$
		4	1.08	1.04	1.12	$7.68\ 10^{72}$	$9.65\ 10^{-05}$
		5	1.05	1.01	1.09	$1.08\ 10^{57}$	$8.99\ 10^{-03}$
	Fresh sea salt mixed with aged emissions	1	1.36	1.27	1.45	$2.25\ 10^{56}$	$2.51\ 10^{-11}$
		2	1.11	1.05	1.16	$6.52\ 10^{61}$	$6.52\ 10^{-04}$
		3	1.08	1.03	1.12	$6.17\ 10^{71}$	$1.13\ 10^{-03}$
		4	1.07	1.03	1.11	$2.78\ 10^{62}$	$1.60\ 10^{-03}$
		5	1.02	0.98	1.06	$9.79\ 10^{55}$	$2.81\ 10^{-01}$
	Industrial emissions	1	3.90	3.75	4.05	$8.21\ 10^{103}$	$3.65\ 10^{-69}$
		2	1.47	1.39	1.54	$2.61\ 10^{82}$	$2.50\ 10^{-25}$
		3	1.18	1.13	1.22	$2.87\ 10^{105}$	$1.21\ 10^{-10}$
		4	1.20	1.15	1.25	$1.66\ 10^{64}$	$2.77\ 10^{-13}$
		5	1.15	1.10	1.19	$1.80\ 10^{51}$	$3.38\ 10^{-08}$
	Mineral dust and soil ressuspension	1	1.30	1.20	1.40	$6.37\ 10^{84}$	$2.22\ 10^{-07}$
		2	1.24	1.19	1.29	$6.93\ 10^{113}$	$1.88\ 10^{-16}$
		3	1.35	1.30	1.41	$5.25\ 10^{176}$	$6.95\ 10^{-28}$
		4	1.33	1.28	1.38	$8.34\ 10^{187}$	$1.50\ 10^{-29}$
		5	1.47	1.41	1.53	$2.97\ 10^{261}$	$1.28\ 10^{-32}$
	Secondary nitrate	1	0.97	0.91	1.04	$1.36\ 10^{71}$	$4.06\ 10^{-01}$
		2	0.99	0.94	1.04	$5.44\ 10^{126}$	$6.40\ 10^{-01}$
		3	1.00	0.96	1.04	$5.55\ 10^{136}$	$8.97\ 10^{-01}$
		4	0.99	0.95	1.03	$1.97\ 10^{119}$	$7.65\ 10^{-01}$
		5	1.00	0.96	1.04	$2.89\ 10^{101}$	$8.75\ 10^{-01}$
	Secondary sulfate	1	1.15	1.09	1.20	$3.20\ 10^{123}$	$4.16\ 10^{-07}$
		2	1.41	1.35	1.48	$3.27\ 10^{164}$	$3.73\ 10^{-25}$
		3	1.53	1.47	1.58	$1.44\ 10^{190}$	$2.39\ 10^{-45}$
		4	1.49	1.44	1.54	$1.06\ 10^{170}$	$2.05\ 10^{-57}$
		5	1.43	1.39	1.48	$1.42\ 10^{167}$	$7.51\ 10^{-57}$

*Use the log-rank test to compare survival between groups. Statistical significance was defined as $p < 0.05$ (i.e., $5\ 10^{-2}$). From Wald test, all p-values << 0.01.

**This p-value indicates whether the particular $PM_{2.5}$ variable, which coefficient has been used to calculate the Odds Ratio, contributes significantly to the occurrence of the outcome or not.

Table 3 – Odds ratio and 95% CI representing the respiratory hospital admissions associated with source-specific $PM_{2.5}$ during episodes of higher source-specific contribution to $PM_{2.5}$ air pollution in Joinville (2018-2020) for 1–5 moving averages.

Source	*Outcome*	*Moving averages*	*Odds ratio*	*Lower 95% CI*	*Upper 95% CI*	*p-value model**	*p-value β $PM_{2.5}$*
Respiratory Hospital Admissions	Aged sea salt	1	1.14	0.92	1.36	$9.57\ 10^{45}$	$2.33\ 10^{-01}$
		2	1.09	0.96	1.22	$2.46\ 10^{71}$	$1.98\ 10^{-01}$
		3	1.47	1.36	1.58	$2.37\ 10^{119}$	$5.04\ 10^{-12}$
		4	1.33	1.24	1.42	$2.02\ 10^{93}$	$8.92\ 10^{-11}$
		5	1.37	1.29	1.45	$9.14\ 10^{89}$	$1.35\ 10^{-14}$
	Combustion of biomass, coal and fossil fuels	1	1.12	1.04	1.21	$2.41\ 10^{30}$	$7.95\ 10^{-03}$
		2	0.97	0.92	1.01	$2.12\ 10^{28}$	$1.67\ 10^{-01}$
		3	0.99	0.95	1.03	$6.59\ 10^{21}$	$5.73\ 10^{-01}$
		4	1.03	0.98	1.07	$3.59\ 10^{32}$	$2.21\ 10^{-01}$
		5	0.99	0.95	1.03	$1.12\ 10^{25}$	$7.11\ 10^{-01}$
	Fresh sea salt mixed with aged emissions	1	1.47	1.36	1.58	$5.74\ 10^{31}$	$1.29\ 10^{-12}$
		2	1.19	1.12	1.26	$6.93\ 10^{33}$	$5.58\ 10^{-07}$
		3	1.14	1.08	1.19	$1.55\ 10^{26}$	$1.47\ 10^{-06}$
		4	1.11	1.06	1.16	$1.68\ 10^{26}$	$1.31\ 10^{-05}$
		5	1.10	1.05	1.15	$4.24\ 10^{27}$	$8.88\ 10^{-05}$
	Industrial emissions	1	4.82	4.50	5.14	$1.23\ 10^{65}$	$3.22\ 10^{-22}$
		2	1.27	1.20	1.35	$9.97\ 10^{37}$	$3.49\ 10^{-10}$
		3	1.11	1.05	1.17	$1.03\ 10^{65}$	$5.78\ 10^{-04}$
		4	1.11	1.06	1.17	$1.66\ 10^{35}$	$1.99\ 10^{-04}$
		5	1.13	1.08	1.19	$9.32\ 10^{25}$	$1.38\ 10^{-05}$
	Mineral dust and soil ressuspension	1	1.50	1.37	1.63	$1.21\ 10^{44}$	$8.14\ 10^{-10}$
		2	1.24	1.18	1.30	$1.88\ 10^{48}$	$1.72\ 10^{-12}$
		3	1.34	1.28	1.40	$1.64\ 10^{93}$	$1.23\ 10^{-22}$
		4	1.41	1.35	1.47	$1.52\ 10^{121}$	$1.60\ 10^{-29}$
		5	1.54	1.47	1.62	$8.19\ 10^{159}$	$2.26\ 10^{-29}$
	Secondary nitrate	1	1.01	0.94	1.08	$2.80\ 10^{30}$	$7.68\ 10^{-01}$
		2	1.02	0.96	1.08	$1.18\ 10^{65}$	$4.94\ 10^{-01}$
		3	1.02	0.97	1.07	$5.39\ 10^{68}$	$4.09\ 10^{-01}$
		4	0.97	0.92	1.02	$5.54\ 10^{61}$	$1.97\ 10^{-01}$
		5	0.94	0.89	0.98	$3.28\ 10^{53}$	$4.94\ 10^{-03}$
	Secondary sulfate	1	1.10	1.04	1.16	$3.20\ 10^{76}$	$1.49\ 10^{-03}$
		2	1.43	1.35	1.51	$2.96\ 10^{108}$	$2.01\ 10^{-18}$
		3	1.31	1.25	1.37	$1.83\ 10^{90}$	$2.29\ 10^{-19}$
		4	1.41	1.35	1.46	$1.57\ 10^{93}$	$8.11\ 10^{-32}$
		5	1.36	1.31	1.41	$2.69\ 10^{88}$	$1.85\ 10^{-31}$

*Use the log-rank test to compare survival between groups. Statistical significance was defined as $p < 0.05$ (i.e., $5\ 10^{-2}$). From Wald test, all p-values << 0.01.
**This p-value indicates whether the particular $PM_{2.5}$ variable, which coefficient has been used to calculate the Odds Ratio, contributes significantly to the occurrence of the outcome or not.

The results indicate that high $PM_{2.5}$ contributions from anthropogenic activities, specifically from combustion and industrial activities, are associated with increased hospital

admissions for both disease groups. These increases were approximately 23% (95% CI: 15.3%–31.1%) for combustion and >145% (95% CI: 135%–155%) for industrial activities, based on a 1-day moving average. Air pollution attributed to industrial sources was noted to have an excessive risk of more than 2.5 (up to 13.7) of both disease groups' hospital admissions when considering a 1-day moving average. The highest risks were associated with industrial activities, leading to an OR of 4.8 for respiratory disease admissions, and a risk of 3.9 for circulatory disease admissions. Meanwhile, combustion sources were estimated to increase these risks by 12.2%, and 23.2%, respectively.

However, aged sea salt aerosol, crustal material (associated with soil resuspension and mineral dust), and secondary sulfate formation containing trace elements from anthropogenic sources, were associated with high health risks. These risks manifested as an increase exceeding 50% in the likelihood of hospitalizations for both respiratory and circulatory system diseases. Specifically, secondary sulfate formation was associated with the highest increase in risk (53%, based on a 3-day moving average) for circulatory diseases. Meanwhile, mineral dust and soil resuspension were associated with a 54% increase in the risk of hospital admissions for respiratory diseases (considering a 5-day moving average). Overall, mineral dust and soil resuspension (increases in hospital admissions ranged between 24 – 54%), secondary sulfate formation (between 10 – 53%), and aged sea salt (up to 54% increase) sources were consistently associated with the highest risks across all moving averages. By gender group, these sources were associated with increases up to 66% in hospital admissions.

Secondary nitrate and combustion sources showed the lowest increased risk, possibly due to the distance from the sources and their minimal contributions to the total $PM_{2.5}$ observed. Industrial emissions had an immediate impact (based on a 1-day moving average) on increasing the incidence of hospital admissions for both disease groups across the total population. This may occur because exposure to industrial emissions is higher near the source. As pollutants

disperse and undergo atmospheric changes, they return as aged sea salt and soil resuspension sources, which correlate with higher hospital admissions during subsequent exposure lags. Secondary sulfate, significantly influenced by marine aerosols, exhibits a similar trend. This rationale is supported by the fact that the percentage change in hospital admissions related to fresh sea salt mixed with industrial emissions shows transitional or intermediate values; this reflects the diminishing influence of industrial sources as environmental constraints disperse and transport air pollutants. It is noteworthy that dust and soil contribution-related risks, in turn, resulted in a higher increase in hospitalization, displaying a U-shaped curve in terms of moving average response, which indicates a higher risk of both immediate and prolonged exposure. In addition, unlike the general tendency of higher risks for circulatory diseases observed for the majority of source-specific $PM_{2.5}$ exposure across all moving averages, fresh sea salt seems to pose a higher exposure risk for respiratory diseases.

These intriguing findings demonstrate that feedback mechanisms resulting from the particularities of local recirculation conditions (as shown in our previous study[75]) may be reloading the environment with anthropogenic pollutants that pose a significant risk of toxicity. For example, the geochemical profile of the aged marine aerosol source indicates high concentrations of sulfate combined with elements of anthropogenic origin. According to the California Air Resources Board[187], exposure to sulfate is associated with several adverse health effects, such as reduced lung function, worsening of asthma symptoms, and even death in individuals with chronic heart and lung diseases. As a main component of PM, several studies have evidenced the increased health risks and mortality associated with sulfate exposure and the enhanced oxidative potential and toxicity given by its role in the acid dissolution of metals commonly found in ambient particles[128–131]. Rich et al.[25] observed larger odds of myocardial infarction associated with increased mass fractions of sulfate, nitrate, and ammonium at a lower elemental carbon mass fraction. The explicit biological mechanisms of sulfate association are

still undescribed[188]. However, some plausible theories to explain the positive association of sulfate with adverse health effects include: i) the particle acidity by sulfate may change the pulmonary toxicity of other $PM_{2.5}$ constituents or physical properties from their own toxicity[189], and ii) the catalyzation of metals into more bioavailable forms is another possible explanation for the strong association of sulfate with health effects[190].

The same observations can be discussed about the mineral and dust resuspension source, since although crustal soil particles might not appear to play a major role in the toxicity of $PM_{2.5}$, several studies reported significant associations between its constituents – such as transition metals (e.g., Ni, Fe, Mn and Zn), enriched from anthropogenic sources activities – that can induce oxidative stress, and cardiovascular[191–195] and respiratory diseases[196–199]. Studies have indicated that high levels of Cu and Fe may induce oxidative stress and chronic inflammation in asthma cases[200], while Pb is considered a risk factor for asthma due to its role in promoting immune responses[201], and industrial-related species such as Zn and Cr may lead higher inflammatory responses[202,203]. In Xiamen City, a typical low-pollution area in China, Wang et al.[204] investigated the health effects of low-level exposure, especially the $PM_{2.5}$-bound trace elements. They observed that an increase in the concentration of $PM_{2.5}$-bound components such as Si, and Ni would have adverse health effects, such as promoting in the prevalence of COPD, and also that Ca, Fe, Mn, and Ti had a significant health effect on asthma diagnosis rates. Such elements were associated with industrial emissions and crustal material (both mineral and resuspended soil enriched with material from anthropogenic sources). These findings suggest the role of spark ignition and diesel vehicle emissions, non-traffic emissions such as tire and brake wear, and industrial emissions air pollutant deposition in the triggering of acute cardiovascular and respiratory events.

There have been a relatively limited number of prior epidemiological studies using source-specific PM obtained from the application of receptor models combined with time-

stratified case-crossover study design with conditional logistic regression models[25–27,135,205–213], but with a different model design: using source-specific or element-specific concentration as an independent variable rather than as a referent for a health outcome-dependent event. In the United States, studies assessing hospitalizations due to cardiovascular diseases[25,26,214] reported no obvious association with secondary sulfate, road dust, and biomass burning. Contradictorily, as well as in our study, secondary sulfate and biomass burning were associated with increased rates of emergency department visits and hospitalizations for respiratory diseases, particularly influenza[27]. As such, these and our study findings are in line with the suggested by the 2015 guidance statement from the UK Committee on the Medical Effects of Air Pollutants, that particulate sulfates are most consistently associated with adverse effects on health, with less evidence for nitrates and other components[24,47]. In addition, both diseases groups were associated with short-term increases in $PM_{2.5}$ from traffic and other combustion sources by these studies. Vehicle emissions, diesel emissions, and biomass burning $PM_{2.5}$ has been frequently associated with pneumonia, influenza, and other respiratory infections across the U.S. cities[27,215,216]. On the other hand, contrary to those and our findings, Zhao et al.[26] found no association with road dust and biomass burning sources. According to them, this may be related to their heterogeneities since road dust mostly represents non-exhaust traffic emissions, contains deposited soil and road surface material. In our study, as previously discussed, the dust and soil emissions also contained elements from industrial-related emissions. Thus, road dust effects on health may differ by deposition rates, variability in reactivity, and environmental factors. Likewise, combustion-related PM compositional patterns may be due to various fuels consumed. For asthma emergency visits, biomass burning, secondary nitrate, and road dust showed consistent positive associations with road dust having significant values for most lag times[28]. In a suburban site of central Taiwan, Bell et al.[217] found that individual chemical species were better indicators than the resolved source-specific PM. Jung et al.[218] observed that

exposure to nitrate, black carbon, and potassium derived from industry-related combustion or motor-vehicles emission sources may increase the risk of asthma outpatient visits. In California, Ostro et al.[219] observed the same nitrate-asthma association in children. In London, a positive correlation between nitrate levels and the increased number of respiratory admissions in individuals above 65 years old was reported by Atkinson et al.[220]. Unlike these epidemiological studies, our results are consistent with evidence reported from toxicological studies as it seems that nitrate has little biological potency to induce health effects[221,222]. Berger et al.[214] and Rich et al.[25] also found no clear association with secondary nitrate. This has been related to the fact that secondary nitrate, being an unreactive particle, would not provide oxidative potential or the resulting reactive oxygen species and oxidative stress[25–27].

Increased rates of respiratory diseases/events were associated with increased concentrations of $PM_{2.5}$ road dust, and sea salt, as well as crustal species aluminum, calcium, silicon, and titanium, sea salt elements (chlorine), residual oil combustion markers (nickel and vanadium), and black carbon (typically used as a marker of traffic). Black carbon and potassium, key components of PM arising from biomass burning and incomplete combustion processes have been associated with respiratory symptoms such as wheeze, shortness of breath and chest[223] as well as with several respiratory diseases, including incident asthma, asthma symptoms, and rhinitis[224].

Although these source-specific and species-specific exposure-response hypotheses seem biologically plausible, epidemiological and toxicological studies are still needed to further explore $PM_{2.5}$-bound species toxicity profile, both for single- and multipollutant synergic health effects. Ultimately, controlling these emissions sources should be a priority for related governmental agencies, and the combination of studying health and source apportionment is highly recommended for future studies.

Hence, to our knowledge, few previous studies have applied the time-stratified case-crossover study design with conditional logistic regression models as used in this study [68,70,225–228], to assess air pollution health risks. Even fewer studies have considered this approach regarding the human health impacts of $PM_{2.5}$ source-specific emissions, except for studies on wildfire events. In Australia, an increase of 10% in cardiovascular mortality[68], and of ~7% in the risk of out-of-hospital cardiac arrests[67] were associated with air pollution events from wildfires. Additionally, Gan et al.[66] found an 8% increase in hospital admissions for asthma, while Jones et al.[69] reported an increase in the risk of out-of-hospital cardiac arrest on the second lag day following exposure to wildfire-related $PM_{2.5}$ in the United States.

In the nationwide meta-analysis of the health impacts of wildfire-related air pollution in Brazil, Requia et al.[70] reported an increase in cardiovascular hospital admissions ranging from 14.9% (95% CI: 9–18%) for a 1-day moving average to 21% (95% CI: 8–35%) for a 2-day moving average. Similarly, they found a 23% (95% CI: 12–33%) increase in respiratory hospital admissions with a 5-day moving average. In a primary analysis stratified by Brazilian regions, they identified the North and Midwest as the regions with the highest risk of hospital admissions, respectively. The results showed a 38% increase in respiratory hospital admissions (with a 5-day moving average) and a 56% increase in circulatory hospital admissions 2 days following the event (i.e., 2-day moving average). Among the five regions, the South was the third most affected, experiencing increased hospital admissions due to air pollution exposure during wildfires events[70]. Overall, except for secondary nitrate, our study identified higher source-specific health risks compared to those related to air pollution from wildfire events[70] – although based upon a broader geographical and for a different time period (2008–2018) – both nationwide and at a regional level (i.e, across the South of Brazil).

Several epidemiological studies have explored how individual susceptibility to the effects of air pollution varies based on characteristics such as sex and race[12,229]. Both in

Australia[67] and Brazil[70], stratification by sex and/or age revealed significant variations in the impact of $PM_{2.5}$ exposure on cardiovascular health outcomes during wildfires. Ignotti et al.[230] estimated an 8% increase in hospital admissions for respiratory diseases among children and a 10% increase among the elderly, both associated with $PM_{2.5}$ from fires in the Amazon. For the subgroup analysis by age, overall, our results were similar to those found by Requia et al.[70], and indicate a higher risk of respiratory hospital admissions for those aged < 60 years old compared with older patients. Meanwhile, a higher risk of circulatory hospital admissions for those aged > 60 years old. It's worth noticing differences associated with mineral dust and soil mostly affected the elderly, while combustion and secondary sulfate, the children for both disease groups. Admissions related to circulatory diseases were higher among women, while those for respiratory diseases were more common among men. Our study found more robust and consistent associations for the female population. Our results are consistent with the observed by Bell et al.[231]. Their findings indicate that increased $PM_{2.5}$ is associated with a higher relative (i.e., percentage) increase in hospitalizations for women than men. More significant differences were observed concerning exposure to marine aerosols, which seem to pose greater risks to the female population. Further studies are needed to explore the influence of such characteristics on the effects of air pollution. It is essential to consider that this is a generalized study based on discrete $PM_{2.5}$ measurements, which limits the estimating of individual exposure of residents in different areas of the municipality.

Short-term changes in the concentration of source-specific PM components may trigger respiratory and cardiovascular events accordingly. Given that, more epidemiological evidence focusing on the spatiotemporal chemical heterogeneity of fine particulate matter is greatly needed worldwide, both from scientific standpoints, ESG practices, and regulatory perspectives. From the perspective of exposure prevention, understanding the sources, composition, and spatial and temporal characteristics of $PM_{2.5}$ is of critical importance to

promote the re-evaluation of traditional air quality standards for ambient particulate matter as well as of whether a specific land-use anthropogenic activity may produce similar exposure health risks according to individual (i.e., age, and sex) or community-level (i.e., microclimatic or socioeconomic variables in other locations or regional configuration) factors and in face of climate change extreme weather conditions.

Therefore, while detailing the risk of specific $PM_{2.5}$ sources is important, our findings indicate that understanding the chemistry occurring between components of pollution mixtures is an important area for research, as it can clarify $PM_{2.5}$-mediated potentially hazardous mechanisms associated with: i) the toxicity of source-specific particulate matter single- and multi-components; ii) the exposure-response relationship between $PM_{2.5}$-bound components as well as source-specific $PM_{2.5}$ chemical fingerprint (i.e., recognizing particulate matter as a multipollutant mixture) and health outcomes; iii) the effect of exposure timing on the risk of respiratory and cardiovascular events; iv) the interactions between pathogens and particles; v) source-specific PM components that may change according to the development of new source-specific processes and technological changes, air pollution control policies, and climate change-related environmental conditions.

Finally, our findings suggest that the health effects of ambient fine particulate air pollution exposure, even at the lowest levels observed in this study area, are a result of a complex intertwined array of source-specific chemical species reallocated among environments by land-use activities and climate elements and factors, and as such should be taken into account when designing urban planning and development zoning regulations.

3.4.4 Study design strengths and limitations

The case-crossover design is well accepted in environmental epidemiology and can be considered an effective alternative to conventional time-series regression design to examine the acute health effects due to short-term environmental exposure[65,93]. This design is most suitable for studying relations with the following characteristics 1) the individual exposure varies within a short time-interval; 2) the disease has abrupt onset and short latency for detection; and 3) the induction period is short[232–234].

Although several environmental exposure covariates, bias, and spatiotemporal variability may affect the analysis results, this innovative combined approach design aims to provide valuable information to guidepost protective policies for safeguarding residents' health. The purpose of this approach is to conduct a source-specific risk assessment by screening $PM_{2.5}$-bound elements and environmental conditions in an attempt to identify air pollution sources (i.e., land-use activities) with the potential for increasing hospitalizations related to acute cardiorespiratory health risks, and that should be examined further in regulatory decision-making. This innovative combined approach integrates: i) the exposure to air pollutants at receptor level (i.e., ground-based data); ii) the multiple weather factors modulating air quality and influencing a person's susceptibility to air pollution exposure; iii) the acute health effects at low-exposure concentrations; and iv) the cause specific acute health effects attributable to (short-term exposure to) several $PM_{2.5}$-bound species profiles from typical land use primary and secondary source-related air pollution.

This design is implemented to study individual health outcomes related to stronger source-specific $PM_{2.5}$-related air pollution events, focusing on adjusting covariates and investigating effect modification using CLR. Here, instead of averaging observations from these two sites' measurements of exposure for the region, like other studies[45,235,236] do to perform a time-stratified case-crossover design, we suggest the use of a space-time-

stratification, introducing a second dimension (space) and using it as a duplicated measurement of exposure event within the same study region. Therefore, some assumptions to compensate for the lack of more specific data were considered: (1) the assumptions and input parameters used might adequately represent the population; (2) in accordance with the expected to a city developed from industrial plants, we assume from previous results that the residents' exposure to the source-specific $PM_{2.5}$ ambient at both sampling data can reflect the resident-specific hospital admission data at city-level, as a good portion of residents are either part of the labor force or of the residential population in these sampling sites immediate surroundings; (3) the city residents were potentially exposed to the same daily variations in ambient $PM_{2.5}$ concentrations and weather conditions observed at the monitoring locations; (4) the source-specific exposure explored here is restricted to the analyzed elements included in this source apportionment; (5) a source-specific air pollution episodic event is given by source contribution concentration above its 3rd quartile.

Meanwhile, the space-time-stratified case-crossover design offers a flexible framework to properly account for a wide range of covariates and allows simultaneous control of confounders by: (1) allowing the use of routinely monitored air pollution information and at the same time makes it possible to study individuals rather than days as the unit of observation (compared with studies based on daily counts and air pollution levels), (2) considering time-invariant covariates at the subpopulation level by using the time-series health data set into a long format and conditioning out the covariates in the expanded stratum set; (3) adding information on individual characteristics such as age, sex, health status and behavioral factors make it possible to study effect modification i.e. to identify individuals susceptible to the effects of air pollution; (4) the time-stratified approach for selecting referent control periods as per day-of-week within-month and year ensures least biased estimates by accounting for time trends in the environmental exposure; (5) directly adjusting the time-varying confounders in the CLR

when accounting for the adequate lagged exposure function; (6) as the source-specific $PM_{2.5}$ exposure data are available at geographical units, the stratum set combine time and spatial dimensions.

This study has several strengths, including i) a well-defined study population data treated by the Ministry of Health; ii) the use of a case-crossover study design to control for non-time-varying factors and interactions between them, thereby reducing confounding by these factors; iii) although only $PM_{2.5}$-bound inorganic species were included in this analysis, this approach assess risks associated to air pollution events of higher source-specific contribution, which reduce bias associated with source-specific mass concentrations usually used by models to estimate increase in health risks. However, there are several limitations to be considered when interpreting our results: i) due to the use of ambient air pollution levels and weather conditions for all patients within a 50 km radius of each monitoring stations, there is an element of exposure misclassification, which likely led to the underestimation of relative rates; ii) the imprecision in this study could be attributable to the limited sample size of the present study since $PM_{2.5}$ sources and components were only measured randomly every other day, the number of subjects for whom exposure data were available decreased, thus reducing statistical power and precision; iii) all cases were assigned the same values of $PM_{2.5}$ sources contribution for a specific day from a single monitoring site without considering individual-specific differences, such as the distance from the emission source and/or the monitoring site, outdoor exposure duration, and protective measures – however, this error is not likely to be different on case days than control days, which likely led to non-differential exposure misclassification and underestimated effects associated with each source-specific PM; iv) still, the amount of error and therefore the amount of underestimation of the excess rates by source category may differ, as there is likely more spatial variability in some source-specific PM concentrations (e.g., industrial) than others (e.g., secondary sulfate); v) it is difficult for case-crossover designs

combined with CLR to fully adjust for possible overdispersion[237], which may cause larger confidence intervals than reported.

Finally, this work approach may be a valuable tool to evaluate the impact and effectiveness of air quality policies implementation as it provides a further examination of PM sources, components and/or mixtures on triggering hospitalizations since there is no well-defined time window for policies and emission changes. Working with a health outcome case associated with source-specific events of stronger air pollution potential rather than using source-specific air pollution concentration as an independent variable in the model, allows to explore all natural and anthropogenic sources contributing to such a pollutant composition, thus going beyond the limitations given by the group of species analyzed here, and of all environmental conditions leading to such source-specific $PM_{2.5}$ contribution. As such, it embodies a better approach for land-use planning to evaluate the region's capacity to support an increase in land-use design pressure in the environment and public health, which makes it a valuable, universally adaptable tool, specifically useful in complex environments.

3.4.5 Challenges of the air pollution health risks assessment and management

Air pollution is a global problem that does not recognize borders and, thus, disproportionately burdens low- and middle-income countries. These countries suffer from 91% of the premature deaths related to air pollution estimated to occur worldwide as they are typically home to more vulnerable populations[238]. This issue is prevalent in developing countries like Brazil[120], a country that despite having a National Air Pollution Control Program (PRONAR) relies on outdated national air quality standards and flexible emission limits for a limited number of pollutants (e.g., PM, CO, SO_x, NO_x, and Pb). Moreover, environmental agencies often fail to enforce, monitor, and report on these standards. Consequently, although residents living near emission sources have longstanding health concerns regarding exposure

to pollutants such as $PM_{2.5}$, both short- and long-term monitoring and risk assessments of PM total concentration or composition remain limited to studies conducted in a few large cities.

The dynamic involving the emission, transport, reactions with other chemical species under different environmental conditions, dispersion, and deposition of atmospheric aerosols is complex. This complexity leads to variations in concentrations and compositions based on time and location, challenging air quality management. In this context, as a source-dependent problem, air pollution may vary according to local land-use configurations such as the spatial structure and distribution of industries, the design of roads, and other public thoroughfares (as well as parameters such as vehicle fleet characteristics, and traffic volume and patterns). It also varies with the types of business activities, raw materials, and processes used, as well as their goods and services productivity. This distribution shapes urban design, thus linking land use, transportation, economic activities, and housing.

Our findings demonstrate the influence of such complexity through source-apportioned chemical fingerprints—characterized by major chemical species markers of each emission source profile—blending $PM_{2.5}$-bound elements from multiple anthropogenic and natural emissions. These results provide evidence of the modulating role of local environmental conditions in atmospheric chemistry, ultimately governing air pollution exposure risks at the receptor level and prolonging the lagged effects of air pollutants on hospital admissions after exposure.

Air pollution monitoring networks are becoming more widespread in urban areas globally. This expansion can promote public awareness of air pollution through public air quality alert systems. Although personal measures—such as staying indoors, using air filters indoors, wearing protective gear, and avoiding intense activities near pollution sources—may be effective in helping reduce exposure and associated health risks, implementing robust

policies that target emission reductions at their source is undoubtedly a more effective strategy to mitigate these risks[239].

Public policies face constant challenges to balance economic, social, and environmental needs. Air pollution is particularly concerning in a changing natural environment due to the associated environmental limitations and persistent risks, demanding greater attention to territorial and demographic inequalities. Therefore, it is crucial to emphasize that air pollution may be unevenly distributed across neighborhoods, leading to:

- Disproportionate environmental burdens for susceptible individuals with chronic diseases, vulnerable populations, and minoritized groups, as well as those facing socioeconomic disadvantage.
- Combined indoor and outdoor exposure: as both an indoor and outdoor hazard, air pollution poses a serious risk not only to residents but even more to local workers.

Most pollution control policies are "place-blind", disregarding local complexities. This approach may jeopardize decisions regarding which areas to prioritize and hinder the effective provision of environmental services – a public good with benefits and trade-offs that extend across regional boundaries[240]. Moreover, research indicates that weather-related feedback mechanisms play a significant role in either mitigating or exacerbating air pollutants at the regional scale in Brazil[241]. As climate change intensifies, many existing policies lack the necessary adaptation to regional specificities. Consequently, they are likely to fail to address the expected changes in the frequency and severity of extreme weather events, their environmental impacts, and the required adaptation and resilience measures.

Place-based policymaking, informed by the health risks of exposure to source-specific air pollutants, can guide tailored interventions to reduce people's exposure and associated health problems. This approach involves: i) identifying sources of air pollution, their types, and

locations; ii) determining air pollutant emissions variation over time and space, considering local environmental factors; iii) hazard identification; iv) exposure assessment; v) dose-response assessment; vi) risk characterization; vii) evaluating the likelihood of the risk occurring; viii) evaluating the degree of harm that might result; and, ultimately, ix) determining the suitability of control measures.

Consequently, the risk assessment approach explored in this study serves as a valuable policy instrument. Its results contribute to the identification of more hazardous emission sources and local environmental conditions' influence on them. It helps define the scope and scale of place-based interventions designed to effectively support land-use planning within zoning regulations. This approach ensures respect for local environmental limitations, planetary boundaries, and the protection of both the environment and human health in the present and future context.

4. CONCLUSIONS

This study demonstrates the significant health risks posed by source-specific $PM_{2.5}$-bound components in a typical coastal industrial city. By employing a novel approach combining receptor-based source apportionment and a space-time-stratified case-crossover design, we have provided a comprehensive framework for evaluating the short-term effects of $PM_{2.5}$ on cardiorespiratory hospital admissions. Seven major $PM_{2.5}$ sources were identified, including secondary sulfate, industrial emissions, and aged sea salt, with industrial activities contributing most significantly to air pollution and associated health outcomes. The findings underscore that specific $PM_{2.5}$-bound components, rather than overall mass concentrations, drive the increased health risks, particularly among vulnerable populations.

In summary, our study added comparative evidence for increased cardiovascular and respiratory risks associated with short-term exposure to source-specific $PM_{2.5}$-chemical

heterogeneity. Primary anthropogenic emissions (i.e., industrial and combustion sources) were associated with higher immediate (i.e., 1-day moving average) PM-induced risks, meanwhile, natural-related sources [i.e., fresh (and aged) sea salt aerosol and dust and soil resuspension] and secondary sulfate formation were consistently associated with stronger and higher health risks after 1 to 5-days since exposure. Furthermore, aged sea salt aerosol can serve as a sink for pollutants, thereby influencing air quality in coastal urban environments. Therefore, our results suggest that natural processes may promote chemical mixtures enhanced with specific particle components from anthropogenic sources, that may be a trigger to larger biologic response than others.

By identifying these source-specific contributions, the study not only offers a robust assessment of immediate health risks but also emphasizes the broader importance of source-targeted air quality management. Industrial emissions, sea salt, and the interaction of natural and anthropogenic activities highlight the complex nature of $PM_{2.5}$ pollution in coastal regions. The methodology employed here allows for controlling confounding factors such as weather conditions and spatial variability, thereby strengthening causal inferences between air pollution sources and health outcomes.

Although our database has some temporal and spatial limitations, the results obtained have shown that the proposed approach is reliable and suitable for the reality in regions of limited air quality monitoring networks, and may become an important tool: i) for building a comprehensive understanding of PM composition, formation processes, and the complex exposure-response health risks; ii) to identify the areas of highest priority for health effects research on pollutants, technological advancements, and air pollution control strategies; iii) to conduct, as needed, reanalysis of studies, datasets, and methods required by important policy decisions; iv) to stimulate broader research on the health effects of a pollutant, sources, land-use design or technology; and v) to outline source-specific air pollution implications for public

health, policy priorities and key actions for air quality management, by providing a guidepost for setting air quality standards and to evaluate their progress on health benefits.

In light of these findings, this research contributes to the ongoing discourse on air quality and public health, calling for place-based policy interventions that address the specific sources of pollution in industrial areas. Our approach can be applied in various environments to better understand the intrinsic health risks to the population and act as a preventative tool. Future studies should focus on long-term exposure risks, further exploring the interplay between source-specific $PM_{2.5}$ components, environmental conditions, and human health to optimize pollution control strategies globally.

Supplementary Material: Additional experimental details, materials, and methods (DOC) as well as additional results: summary statistics of $PM_{2.5}$ chemical analysis (PDF), and summary results from the case-crossover study (XLS).

Data availability: Datasets related to this article can be found at doi:10.17632/98gg4jzbkb.1, hosted at Mendeley data. R Scripts (code) developed in this study can be found at doi: 10.5281/zenodo.12707699, hosted at Zenodo repository.

Acknowledgement

This study was supported in part by the Coordenação de Aperfeiçoamento e Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001. The authors gratefully acknowledge the Santa Catarina Civil Defense for the meteorological data used in this publication, and the Escola de Educação Básica Presidente Médici authorizing the collection of samples on its property.

REFERENCES

(1) Kaufman, Y. J.; Tanré, D.; Boucher, O. A Satellite View of Aerosols in the Climate System. *Nature* **2002**, *419* (6903), 215–223. https://doi.org/10.1038/nature01091.

(2) Pauliquevis, T.; Artaxo, P.; Oliveira, P. H.; Paixão, M. O Papel Das Partículas de Aerossol No Funcionamento Do Ecossistema Amazônico. *Cienc Cult* **2007**, *59* (3), 48–50. https://doi.org/10.1029/2001JD000666.

(3) Buseck, P. R.; Adachi, K. Nanoparticles in the Atmosphere. *Elements* **2008**, *4* (6), 389–394. https://doi.org/10.2113/gselements.4.6.389.

(4) Fowler, D.; Pilegaard, K.; Sutton, M. A.; Ambus, P.; Raivonen, M.; Duyzer, J.; Simpson, D.; Fagerli, H.; Fuzzi, S.; Schjoerring, J. K.; Granier, C.; Neftel, A.; Isaksen, I. S. A.; Laj, P.; Maione, M.; Monks, P. S.; Burkhardt, J.; Daemmgen, U.; Neirynck, J.; Personne, E.; Wichink-Kruit, R.; Butterbach-Bahl, K.; Flechard, C.; Tuovinen, J. P.; Coyle, M.; Gerosa, G.; Loubet, B.; Altimir, N.; Gruenhage, L.; Ammann, C.; Cieslik, S.; Paoletti, E.; Mikkelsen, T. N.; Ro-Poulsen, H.; Cellier, P.; Cape, J. N.; Horváth, L.; Loreto, F.; Niinemets, Ü.; Palmer, P. I.; Rinne, J.; Misztal, P.; Nemitz, E.; Nilsson, D.; Pryor, S.; Gallagher, M. W.; Vesala, T.; Skiba, U.; Brüggemann, N.; Zechmeister-Boltenstern, S.; Williams, J.; O'Dowd, C.; Facchini, M. C.; de Leeuw, G.; Flossman, A.; Chaumerliac, N.; Erisman, J. W. Atmospheric Composition Change: Ecosystems–Atmosphere Interactions. *Atmos Environ* **2009**, *43* (33), 5193–5267. https://doi.org/10.1016/j.atmosenv.2009.07.068.

(5) Burns, D. A.; Aherne, J.; Gay, D. A.; Lehmann, C. M. B. Acid Rain and Its Environmental Effects: Recent Scientific Advances. *Atmos Environ* **2016**, *146*, 1–4. https://doi.org/10.1016/j.atmosenv.2016.10.019.

(6) Wei, H.; Liu, W.; Zhang, J.; Qin, Z. Effects of Simulated Acid Rain on Soil Fauna Community Composition and Their Ecological Niches. *Environmental Pollution* **2017**, *220*, 460–468. https://doi.org/10.1016/j.envpol.2016.09.088.

(7) IPCC. *Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change*; Cambridge United Kingdom and New York, 2021. https://policycommons.net/artifacts/2679314/climate-change-2022/3702620 (accessed 2022-11-17).

(8) World Health Organization (WHO). *WHO Review of evidence on health aspects of air pollution – REVIHAAP Project.* . https://www.euro.who.int/__data/assets/pdf_file/0004/193108/REVIHAAP-Final-technical-report-final-version.pdf (accessed 2022-04-09).

(9) Landrigan, P. J.; Fuller, R.; Acosta, N. J. R.; Adeyi, O.; Arnold, R.; Basu, N. (Nil); Baldé, A. B.; Bertollini, R.; Bose-O'Reilly, S.; Boufford, J. I.; Breysse, P. N.; Chiles, T.; Mahidol, C.; Coll-Seck, A. M.; Cropper, M. L.; Fobil, J.; Fuster, V.; Greenstone, M.; Haines, A.; Hanrahan, D.; Hunter, D.; Khare, M.; Krupnick, A.; Lanphear, B.; Lohani, B.; Martin, K.; Mathiasen, K. V.; McTeer, M. A.; Murray, C. J. L.; Ndahimananjara, J. D.; Perera, F.; Potočnik, J.; Preker, A. S.; Ramesh, J.; Rockström, J.; Salinas, C.; Samson, L. D.; Sandilya, K.; Sly, P. D.; Smith, K. R.; Steiner, A.; Stewart, R. B.; Suk, W. A.; van Schayck, O. C. P.; Yadama, G. N.; Yumkella, K.; Zhong, M. The Lancet Commission on Pollution and Health. *The Lancet* **2018**, *391* (10119), 462–512. https://doi.org/10.1016/S0140-6736(17)32345-0.

(10) Lelieveld, J.; Klingmüller, K.; Pozzer, A.; Pöschl, U.; Fnais, M.; Daiber, A.; Münzel, T. Cardiovascular Disease Burden from Ambient Air Pollution in Europe Reassessed Using

Novel Hazard Ratio Functions. *Eur Heart J* **2019**, *40* (20), 1590–1596. https://doi.org/10.1093/EURHEARTJ/EHZ135.

(11) *What are the WHO Air quality guidelines?* https://www.who.int/news-room/feature-stories/detail/what-are-the-who-air-quality-guidelines (accessed 2023-10-21).

(12) Brook, R. D.; Rajagopalan, S.; Pope, C. A.; Brook, J. R.; Bhatnagar, A.; Diez-Roux, A. V.; Holguin, F.; Hong, Y.; Luepker, R. V.; Mittleman, M. A.; Peters, A.; Siscovick, D.; Smith, S. C.; Whitsel, L.; Kaufman, J. D. Particulate Matter Air Pollution and Cardiovascular Disease. *Circulation* **2010**, *121* (21), 2331–2378. https://doi.org/10.1161/CIR.0b013e3181dbece1.

(13) International Agency for Research on Cancer. Outdoor air pollution (IARC). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 109.*; Lyon, 2013. https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Outdoor-Air-Pollution-2015 (accessed 2019-10-27).

(14) Pope, C. A.; Dockery, D. W. Health Effects of Fine Particulate Air Pollution: Lines That Connect. *J Air Waste Manage Assoc* **2006**, *56* (6), 709–742. https://doi.org/10.1080/10473289.2006.10464485.

(15) European Environment Agency (EEA). *Health impacts of air pollution in Europe, 2022*. https://www.eea.europa.eu/publications/air-quality-in-europe-2022/health-impacts-of-air-pollution (accessed 2024-01-27).

(16) World Health Organization (WHO). *Air quality, energy and health*. https://www.who.int/teams/environment-climate-change-and-health/air-quality-energy-and-health/health-impacts (accessed 2024-01-27).

(17) Cassee, F. R.; Héroux, M.-E.; Gerlofs-Nijland, M. E.; Kelly, F. J. Particulate Matter beyond Mass: Recent Health Evidence on the Role of Fractions, Chemical Constituents and Sources of Emission. *Inhal Toxicol* **2013**, *25* (14), 802–812. https://doi.org/10.3109/08958378.2013.850127.

(18) Stafoggia, M.; Oftedal, B.; Chen, J.; Rodopoulou, S.; Renzi, M.; Atkinson, R. W.; Bauwelinck, M.; Klompmaker, J. O.; Mehta, A.; Vienneau, D.; Andersen, Z. J.; Bellander, T.; Brandt, J.; Cesaroni, G.; de Hoogh, K.; Fecht, D.; Gulliver, J.; Hertel, O.; Hoffmann, B.; Hvidtfeldt, U. A.; Jöckel, K.-H.; Jørgensen, J. T.; Katsouyanni, K.; Ketzel, M.; Kristoffersen, D. T.; Lager, A.; Leander, K.; Liu, S.; Ljungman, P. L. S.; Nagel, G.; Pershagen, G.; Peters, A.; Raaschou-Nielsen, O.; Rizzuto, D.; Schramm, S.; Schwarze, P. E.; Severi, G.; Sigsgaard, T.; Strak, M.; van der Schouw, Y. T.; Verschuren, M.; Weinmayr, G.; Wolf, K.; Zitt, E.; Samoli, E.; Forastiere, F.; Brunekreef, B.; Hoek, G.; Janssen, N. A. H. Long-Term Exposure to Low Ambient Air Pollution Concentrations and Mortality among 28 Million People: Results from Seven Large European Cohorts within the ELAPSE Project. *Lancet Planet Health* **2022**, *6* (1), e9–e18. https://doi.org/10.1016/S2542-5196(21)00277-1.

(19) Kotchenruther, R. A. A Regional Assessment of Marine Vessel PM2.5 Impacts in the U.S. Pacific Northwest Using a Receptor-Based Source Apportionment Method. *Atmos Environ* **2013**, *68*, 103–111. https://doi.org/10.1016/j.atmosenv.2012.11.067.

(20) World Health Organization (WHO). *WHO Global Air Quality Guidelines: Particulate Matter (PM2.5 and PM10), Ozone, Nitrogen Dioxide, Sulfur Dioxide and Carbon Monoxide*; 2021. https://apps.who.int/iris/handle/10665/345329 (accessed 2022-04-09).

(21) Hao, H.; Wang, Y.; Zhu, Q.; Zhang, H.; Rosenberg, A.; Schwartz, J.; Amini, H.; van Donkelaar, A.; Martin, R.; Liu, P.; Weber, R.; Russel, A.; Yitshak-sade, M.; Chang, H.; Shi, L. National Cohort Study of Long-Term Exposure to $PM_{2.5}$ Components and Mortality in Medicare American Older Adults. *Environ Sci Technol* **2023**, *57* (17), 6835–6843. https://doi.org/10.1021/acs.est.2c07064.

(22) Li, B.; Ma, Y.; Zhou, Y.; Chai, E. Research Progress of Different Components of PM2.5 and Ischemic Stroke. *Sci Rep* **2023**, *13* (1), 15965. https://doi.org/10.1038/s41598-023-43119-5.
(23) Lu, F.; Xu, D.; Cheng, Y.; Dong, S.; Guo, C.; Jiang, X.; Zheng, X. Systematic Review and Meta-Analysis of the Adverse Health Effects of Ambient PM2.5 and PM10 Pollution in the Chinese Population. *Environ Res* **2015**, *136*, 196–204. https://doi.org/10.1016/j.envres.2014.06.029.
(24) Al-Kindi, S. G.; Brook, R. D.; Biswal, S.; Rajagopalan, S. Environmental Determinants of Cardiovascular Disease: Lessons Learned from Air Pollution. *Nat Rev Cardiol* **2020**, *17* (10), 656–672. https://doi.org/10.1038/s41569-020-0371-2.
(25) Rich, D. Q.; Zhang, W.; Lin, S.; Squizzato, S.; Thurston, S. W.; van Wijngaarden, E.; Croft, D.; Masiol, M.; Hopke, P. K. Triggering of Cardiovascular Hospital Admissions by Source Specific Fine Particle Concentrations in Urban Centers of New York State. *Environ Int* **2019**, *126*, 387–394. https://doi.org/10.1016/j.envint.2019.02.018.
(26) Zhao, T.; Hopke, P. K.; Utell, M. J.; Croft, D. P.; Thurston, S. W.; Lin, S.; Ling, F. S.; Chen, Y.; Yount, C. S.; Rich, D. Q. A Case-Crossover Study of ST-Elevation Myocardial Infarction and Organic Carbon and Source-Specific PM2.5 Concentrations in Monroe County, New York. *Front Public Health* **2024**, *12*. https://doi.org/10.3389/fpubh.2024.1369698.
(27) Croft, D. P.; Zhang, W.; Lin, S.; Thurston, S. W.; Hopke, P. K.; van Wijngaarden, E.; Squizzato, S.; Masiol, M.; Utell, M. J.; Rich, D. Q. Associations between Source-Specific Particulate Matter and Respiratory Infections in New York State Adults. *Environ Sci Technol* **2020**, *54* (2), 975–984. https://doi.org/10.1021/acs.est.9b04295.
(28) Hopke, P. K.; Croft, D. P.; Zhang, W.; Lin, S.; Masiol, M.; Squizzato, S.; Thurston, S. W.; van Wijngaarden, E.; Utell, M. J.; Rich, D. Q. Changes in the Hospitalization and ED Visit Rates for Respiratory Diseases Associated with Source-Specific PM2.5 in New York State from 2005 to 2016. *Environ Res* **2020**, *181*, 108912. https://doi.org/10.1016/j.envres.2019.108912.
(29) Anenberg, S. C.; Henze, D. K.; Tinney, V.; Kinney, P. L.; Raich, W.; Fann, N.; Malley, C. S.; Roman, H.; Lamsal, L.; Duncan, B.; Martin, R. V.; van Donkelaar, A.; Brauer, M.; Doherty, R.; Jonson, J. E.; Davila, Y.; Sudo, K.; Kuylenstierna, J. C. I. Estimates of the Global Burden of Ambient PM2.5, Ozone, and NO2 on Asthma Incidence and Emergency Room Visits. *Environ Health Perspect* **2018**, *126* (10). https://doi.org/10.1289/EHP3766.
(30) Tsai, S.-S.; Chang, C.-C.; Yang, C.-Y. Fine Particulate Air Pollution and Hospital Admissions for Chronic Obstructive Pulmonary Disease: A Case-Crossover Study in Taipei. *Int J Environ Res Public Health* **2013**, *10* (11), 6015–6026. https://doi.org/10.3390/ijerph10116015.
(31) Faustini, A.; Stafoggia, M.; Colais, P.; Berti, G.; Bisanti, L.; Cadum, E.; Cernigliaro, A.; Mallone, S.; Scarnato, C.; Forastiere, F. Air Pollution and Multiple Acute Respiratory Outcomes. *European Respiratory Journal* **2013**, *42* (2), 304–313. https://doi.org/10.1183/09031936.00128712.
(32) Yang, L.; Li, C.; Tang, X. The Impact of PM2.5 on the Host Defense of Respiratory System. *Front Cell Dev Biol* **2020**, *8*. https://doi.org/10.3389/fcell.2020.00091.
(33) Pope, C. A.; Muhlestein, J. B.; Anderson, J. L.; Cannon, J. B.; Hales, N. M.; Meredith, K. G.; Le, V.; Horne, B. D. Short-Term Exposure to Fine Particulate Matter Air Pollution Is Preferentially Associated With the Risk of ST-Segment Elevation Acute Coronary Events. *J Am Heart Assoc* **2015**, *4* (12). https://doi.org/10.1161/JAHA.115.002506.
(34) Mustafić, H.; Jabre, P.; Caussin, C.; Murad, M. H.; Escolano, S.; Tafflet, M.; Périer, M.-C.; Marijon, E.; Vernerey, D.; Empana, J.-P.; Jouven, X. Main Air Pollutants and

Myocardial Infarction. *JAMA* **2012**, *307* (7), 713. https://doi.org/10.1001/jama.2012.126.

(35) Gardner, B.; Ling, F.; Hopke, P. K.; Frampton, M. W.; Utell, M. J.; Zareba, W.; Cameron, S. J.; Chalupa, D.; Kane, C.; Kulandhaisamy, S.; Topf, M. C.; Rich, D. Q. Ambient Fine Particulate Air Pollution Triggers ST-Elevation Myocardial Infarction, but Not Non-ST Elevation Myocardial Infarction: A Case-Crossover Study. *Part Fibre Toxicol* **2014**, *11* (1), 1. https://doi.org/10.1186/1743-8977-11-1.

(36) Evans, K. A.; Hopke, P. K.; Utell, M. J.; Kane, C.; Thurston, S. W.; Ling, F. S.; Chalupa, D.; Rich, D. Q. Triggering of ST-Elevation Myocardial Infarction by Ambient Wood Smoke and Other Particulate and Gaseous Pollutants. *J Expo Sci Environ Epidemiol* **2017**, *27* (2), 198–206. https://doi.org/10.1038/jes.2016.15.

(37) Shah, A. S. V; Lee, K. K.; McAllister, D. A.; Hunter, A.; Nair, H.; Whiteley, W.; Langrish, J. P.; Newby, D. E.; Mills, N. L. Short Term Exposure to Air Pollution and Stroke: Systematic Review and Meta-Analysis. *BMJ* **2015**, h1295. https://doi.org/10.1136/bmj.h1295.

(38) Link, M. S.; Luttmann-Gibson, H.; Schwartz, J.; Mittleman, M. A.; Wessler, B.; Gold, D. R.; Dockery, D. W.; Laden, F. Acute Exposure to Air Pollution Triggers Atrial Fibrillation. *J Am Coll Cardiol* **2013**, *62* (9), 816–825. https://doi.org/10.1016/j.jacc.2013.05.043.

(39) Rich, D. Q.; Mittleman, M. A.; Link, M. S.; Schwartz, J.; Luttmann-Gibson, H.; Catalano, P. J.; Speizer, F. E.; Gold, D. R.; Dockery, D. W. Increased Risk of Paroxysmal Atrial Fibrillation Episodes Associated with Acute Increases in Ambient Air Pollution. *Environ Health Perspect* **2006**, *114* (1), 120–123. https://doi.org/10.1289/ehp.8371.

(40) Rich, D. Q.; Kim, M. H.; Turner, J. R.; Mittleman, M. A.; Schwartz, J.; Catalano, P. J.; Dockery, D. W. Association of Ventricular Arrhythmias Detected by Implantable Cardioverter Defibrillator and Ambient Air Pollutants in the St Louis, Missouri Metropolitan Area. *Occup Environ Med* **2006**, *63* (9), 591–596. https://doi.org/10.1136/oem.2005.023457.

(41) Rich, D. Q.; Schwartz, J.; Mittleman, M. A.; Link, M.; Luttmann-Gibson, H.; Catalano, P. J.; Speizer, F. E.; Dockery, D. W. Association of Short-Term Ambient Air Pollution Concentrations and Ventricular Arrhythmias. *Am J Epidemiol* **2005**, *161* (12), 1123–1132. https://doi.org/10.1093/aje/kwi143.

(42) Zhang, W.; Lin, S.; Hopke, P. K.; Thurston, S. W.; van Wijngaarden, E.; Croft, D.; Squizzato, S.; Masiol, M.; Rich, D. Q. Triggering of Cardiovascular Hospital Admissions by Fine Particle Concentrations in New York State: Before, during, and after Implementation of Multiple Environmental Policies and a Recession. *Environmental Pollution* **2018**, *242*, 1404–1416. https://doi.org/10.1016/j.envpol.2018.08.030.

(43) Shah, A. S.; Langrish, J. P.; Nair, H.; McAllister, D. A.; Hunter, A. L.; Donaldson, K.; Newby, D. E.; Mills, N. L. Global Association of Air Pollution and Heart Failure: A Systematic Review and Meta-Analysis. *The Lancet* **2013**, *382* (9897), 1039–1048. https://doi.org/10.1016/S0140-6736(13)60898-3.

(44) Cao, J.; Xu, H.; Xu, Q.; Chen, B.; Kan, H. Fine Particulate Matter Constituents and Cardiopulmonary Mortality in a Heavily Polluted Chinese City. *Environ Health Perspect* **2012**, *120* (3), 373–378. https://doi.org/10.1289/ehp.1103671.

(45) Peng, R. D.; Bell, M. L.; Geyh, A. S.; McDermott, A.; Zeger, S. L.; Samet, J. M.; Dominici, F. Emergency Admissions for Cardiovascular and Respiratory Diseases and the Chemical Composition of Fine Particle Air Pollution. *Environ Health Perspect* **2009**, *117* (6), 957–963. https://doi.org/10.1289/ehp.0800185.

(46) Mar, T. F.; Norris, G. A.; Koenig, J. Q.; Larson, T. V. Associations between Air Pollution and Mortality in Phoenix, 1995-1997. *Environ Health Perspect* **2000**, *108* (4), 347–353. https://doi.org/10.1289/ehp.00108347.
(47) Committee on the Medical Effects of Air Pollutants (COMEAP). *Statement on the differential toxicity of particulate matter according to source or constituents: 2022*. gov.uk. https://www.gov.uk/government/publications/particulate-air-pollution-health-effects-of-exposure/statement-on-the-differential-toxicity-of-particulate-matter-according-to-source-or-constituents-2022 (accessed 2024-09-24).
(48) Lin, H.; Tao, J.; Du, Y.; Liu, T.; Qian, Z.; Tian, L.; Di, Q.; Rutherford, S.; Guo, L.; Zeng, W.; Xiao, J.; Li, X.; He, Z.; Xu, Y.; Ma, W. Particle Size and Chemical Constituents of Ambient Particulate Pollution Associated with Cardiovascular Mortality in Guangzhou, China. *Environmental Pollution* **2016**, *208*, 758–766. https://doi.org/10.1016/j.envpol.2015.10.056.
(49) Kim, S.; Yang, J.; Park, J.; Song, I.; Kim, D.-G.; Jeon, K.; Kim, H.; Yi, S.-M. Health Effects of PM2.5 Constituents and Source Contributions in Major Metropolitan Cities, South Korea. *Environmental Science and Pollution Research* **2022**, *29* (55), 82873–82887. https://doi.org/10.1007/s11356-022-21592-1.
(50) Atkinson, R. W.; Mills, I. C.; Walton, H. A.; Anderson, H. R. Fine Particle Components and Health—a Systematic Review and Meta-Analysis of Epidemiological Time Series Studies of Daily Mortality and Hospital Admissions. *J Expo Sci Environ Epidemiol* **2015**, *25* (2), 208–214. https://doi.org/10.1038/jes.2014.63.
(51) Rich, D. Q.; Özkaynak, H.; Crooks, J.; Baxter, L.; Burke, J.; Ohman-Strickland, P.; Thevenet-Morrison, K.; Kipen, H. M.; Zhang, J.; Kostis, J. B.; Lunden, M.; Hodas, N.; Turpin, B. J. The Triggering of Myocardial Infarction by Fine Particles Is Enhanced When Particles Are Enriched in Secondary Species. *Environ Sci Technol* **2013**, *47* (16), 9414–9423. https://doi.org/10.1021/es4027248.
(52) Tchounwou, P. B.; Yedjou, C. G.; Patlolla, A. K.; Sutton, D. J. Heavy Metal Toxicity and the Environment; 2012; pp 133–164. https://doi.org/10.1007/978-3-7643-8340-4_6.
(53) Hsu, C.-Y.; Chi, K.-H.; Wu, C.-D.; Lin, S.-L.; Hsu, W.-C.; Tseng, C.-C.; Chen, M.-J.; Chen, Y.-C. Integrated Analysis of Source-Specific Risks for PM2.5-Bound Metals in Urban, Suburban, Rural, and Industrial Areas. *Environmental Pollution* **2021**, *275*, 116652. https://doi.org/10.1016/j.envpol.2021.116652.
(54) Hsu, C.-Y.; Chiang, H.-C.; Lin, S.-L.; Chen, M.-J.; Lin, T.-Y.; Chen, Y.-C. Elemental Characterization and Source Apportionment of PM 10 and PM 2.5 in the Western Coastal Area of Central Taiwan. *Science of The Total Environment* **2016**, *541*, 1139–1150. https://doi.org/10.1016/j.scitotenv.2015.09.122.
(55) Vega, E.; López-Veneroni, D.; Ramírez, O.; Chow, J. C.; Watson, J. G. Particle-Bound PAHs and Chemical Composition, Sources and Health Risk of PM2.5 in a Highly Industrialized Area. *Aerosol Air Qual Res* **2021**, *21* (10), 210047. https://doi.org/10.4209/aaqr.210047.
(56) Yadav, M.; Singh, N. K.; Sahu, S. P.; Padhiyar, H. Investigations on Air Quality of a Critically Polluted Industrial City Using Multivariate Statistical Methods: Way Forward for Future Sustainability. *Chemosphere* **2022**, *291*, 133024. https://doi.org/10.1016/j.chemosphere.2021.133024.
(57) Lelieveld, J.; Haines, A.; Burnett, R.; Tonne, C.; Klingmüller, K.; Münzel, T.; Pozzer, A. Air Pollution Deaths Attributable to Fossil Fuels: Observational and Modelling Study. *BMJ* **2023**, e077784. https://doi.org/10.1136/bmj-2023-077784.
(58) Fernández-Navarro, P.; García-Pérez, J.; Ramis, R.; Boldo, E.; López-Abente, G. Industrial Pollution and Cancer in Spain: An Important Public Health Issue. *Environ Res* **2017**, *159*, 555–563. https://doi.org/10.1016/j.envres.2017.08.049.

(59) Yan, R.-H.; Peng, X.; Lin, W.; He, L.-Y.; Wei, F.-H.; Tang, M.-X.; Huang, X.-F. Trends and Challenges Regarding the Source-Specific Health Risk of $PM_{2.5}$ -Bound Metals in a Chinese Megacity from 2014 to 2020. *Environ Sci Technol* **2022**, *56* (11), 6996–7005. https://doi.org/10.1021/acs.est.1c06948.

(60) Zhou, C.; Wei, G.; Zheng, H.; Russo, A.; Li, C.; Du, H.; Xiang, J. Effects of Potential Recirculation on Air Quality in Coastal Cities in the Yangtze River Delta. *Science of The Total Environment* **2019**, *651*, 12–23. https://doi.org/10.1016/j.scitotenv.2018.08.423.

(61) Candanosa, R. M. *Reducing Emissions to Lessen Climate Change Would Yield Dramatic Health Benefits by 2030*. NASA's Earth Science News Team. https://climate.nasa.gov/news/3134/reducing-emissions-to-lessen-climate-change-would-yield-dramatic-health-benefits-by-2030/ (accessed 2024-01-27).

(62) Erickson, L. E. Reducing Greenhouse Gas Emissions and Improving Air Quality: Two Global Challenges. *Environ Prog Sustain Energy* **2017**, *36* (4), 982–988. https://doi.org/10.1002/ep.12665.

(63) Zhang, J. P.; Zhu, T.; Zhang, Q. H.; Li, C. C.; Shu, H. L.; Ying, Y.; Dai, Z. P.; Wang, X.; Liu, X. Y.; Liang, A. M.; Shen, H. X.; Yi, B. Q. The Impact of Circulation Patterns on Regional Transport Pathways and Air Quality over Beijing and Its Surroundings. *Atmos Chem Phys* **2012**, *12* (11), 5031–5053. https://doi.org/10.5194/acp-12-5031-2012.

(64) Zhang, Y.; Guo, Y.; Li, G.; Zhou, J.; Jin, X.; Wang, W.; Pan, X. The Spatial Characteristics of Ambient Particulate Matter and Daily Mortality in the Urban Area of Beijing, China. *Science of The Total Environment* **2012**, *435–436*, 14–20. https://doi.org/10.1016/j.scitotenv.2012.06.092.

(65) Wu, Y.; Li, S.; Guo, Y. Space-Time-Stratified Case-Crossover Design in Environmental Epidemiology Study. *Health Data Science* **2021**, *2021*. https://doi.org/10.34133/2021/9870798.

(66) Gan, R. W.; Ford, B.; Lassman, W.; Pfister, G.; Vaidyanathan, A.; Fischer, E.; Volckens, J.; Pierce, J. R.; Magzamen, S. Comparison of Wildfire Smoke Estimation Methods and Associations with Cardiopulmonary-related Hospital Admissions. *Geohealth* **2017**, *1* (3), 122–136. https://doi.org/10.1002/2017GH000073.

(67) Haikerwal, A.; Akram, M.; Del Monaco, A.; Smith, K.; Sim, M. R.; Meyer, M.; Tonkin, A. M.; Abramson, M. J.; Dennekamp, M. Impact of Fine Particulate Matter ($PM_{2.5}$) Exposure During Wildfires on Cardiovascular Health Outcomes. *J Am Heart Assoc* **2015**, *4* (7). https://doi.org/10.1161/JAHA.114.001653.

(68) Johnston, F.; Hanigan, I.; Henderson, S.; Morgan, G.; Bowman, D. Extreme Air Pollution Events from Bushfires and Dust Storms and Their Association with Mortality in Sydney, Australia 1994–2007. *Environ Res* **2011**, *111* (6), 811–816. https://doi.org/10.1016/j.envres.2011.05.007.

(69) Jones, C. G.; Rappold, A. G.; Vargo, J.; Cascio, W. E.; Kharrazi, M.; McNally, B.; Hoshiko, S. Out-of-Hospital Cardiac Arrests and Wildfire-Related Particulate Matter During 2015–2017 California Wildfires. *J Am Heart Assoc* **2020**, *9* (8). https://doi.org/10.1161/JAHA.119.014125.

(70) Requia, W. J.; Amini, H.; Mukherjee, R.; Gold, D. R.; Schwartz, J. D. Health Impacts of Wildfire-Related Air Pollution in Brazil: A Nationwide Study of More than 2 Million Hospital Admissions between 2008 and 2018. *Nat Commun* **2021**, *12* (1), 6555. https://doi.org/10.1038/s41467-021-26822-7.

(71) Nhung, N. T. T.; Schindler, C.; Chau, N. Q.; Hanh, P. T.; Hoang, L. T.; Dien, T. M.; Thanh, N. T. N.; Künzli, N. Exposure to Air Pollution and Risk of Hospitalization for Cardiovascular Diseases amongst Vietnamese Adults: Case-Crossover Study. *Science of The Total Environment* **2020**, *703*, 134637. https://doi.org/10.1016/j.scitotenv.2019.134637.

(72) Hopke, P. K.; Croft, D.; Zhang, W.; Lin, S.; Masiol, M.; Squizzato, S.; Thurston, S. W.; van Wijngaarden, E.; Utell, M. J.; Rich, D. Q. Changes in the Acute Response of Respiratory Diseases to PM2.5 in New York State from 2005 to 2016. *Science of The Total Environment* **2019**, *677*, 328–339. https://doi.org/10.1016/j.scitotenv.2019.04.357.
(73) Levy, D.; Lumley, T.; Sheppard, L.; Kaufman, J.; Checkoway, H. Referent Selection in Case-Crossover Analyses of Acute Health Effects of Air Pollution. *Epidemiology* **2001**, *12* (2), 186–192. https://doi.org/10.1097/00001648-200103000-00010.
(74) Secretaria de Planejamento Urbano e Desenvolvimento Sustentável (SEPUD). *Joinville Cidade Em Dados 2020*; Joinville, 2020. https://www.joinville.sc.gov.br/publicacoes/joinville-cidade-em-dados-2020 (accessed 2021-05-09).
(75) dos Santos-Silva, J. C.; Potgieter-Vermaak, S.; Medeiros, S. H. W.; da Silva, L. V.; Ferreira, D. V.; Moreira, C. A. B.; de Souza Zorzenão, P. C.; Pauliquevis, T.; Godoi, A. F. L.; de Souza, R. A. F.; Yamamoto, C. I.; Godoi, R. H. M. A New Strategy for Risk Assessment of PM<inf>2.5</Inf>-Bound Elements by Considering the Influence of Wind Regimes. *Science of the Total Environment* **2023**, *872*. https://doi.org/10.1016/j.scitotenv.2023.162131.
(76) *IBGE | Cidades@ | Santa Catarina | Joinville | Panorama*. https://cidades.ibge.gov.br/brasil/sc/joinville/panorama (accessed 2024-01-24).
(77) Köppen, W. Climatologia: Com Um Estúdio de Los Climas de La Tierra. *Climatology* **1948**.
(78) NIOSH. *CAS Number Listing - No CAS number - NMAM 4th Edition | NIOSH | CDC*. NIOSH 0500 Manual of Analytical Methods 881 (NMAM), Fourth Edition. https://www.cdc.gov/niosh/docs/2003-154/method-cas0.html (accessed 2023-12-12).
(79) MESONET. *ASOS-AWOS-METAR Data Download.* . https://mesonet.agron.iastate.edu/request/download.phtml?network=BR__ASOS (accessed 2022-03-01).
(80) CEMADEN. *Baixar dados. Pluviômetros.* http://www2.cemaden.gov.br/mapainterativo/download/downpluv.php (accessed 2022-03-01).
(81) Saldanha, R. de F.; Bastos, R. R.; Barcellos, C. Microdatasus: Pacote Para Download e Pré-Processamento de Microdados Do Departamento de Informática Do SUS (DATASUS). *Cad Saude Publica* **2019**, *35* (9). https://doi.org/10.1590/0102-311x00032419.
(82) Chen, R.; Jia, B.; Tian, Y.; Feng, Y. Source-Specific Health Risk Assessment of PM2.5-Bound Heavy Metals Based on High Time-Resolved Measurement in a Chinese Megacity: Insights into Seasonal and Diurnal Variations. *Ecotoxicol Environ Saf* **2021**, *216*, 112167. https://doi.org/10.1016/j.ecoenv.2021.112167.
(83) Liu, S.; Zhan, C.; Zhang, J.; Guo, J.; Liu, H.; Liu, T.; Zheng, J.; Yao, R.; Liu, X.; Xing, X.; Cao, J.; Qi, S. Source-Specific Health Risk Assessment of PM2.5 Bound Heavy Metal in Re-Suspended Fugitive Dust: A Case Study in Wuhan Metropolitan Area, Central China. *J Clean Prod* **2022**, *379*, 134480. https://doi.org/10.1016/j.jclepro.2022.134480.
(84) Yan, R.-H.; Peng, X.; Lin, W.; He, L.-Y.; Wei, F.-H.; Tang, M.-X.; Huang, X.-F. Trends and Challenges Regarding the Source-Specific Health Risk of $PM_{2.5}$ -Bound Metals in a Chinese Megacity from 2014 to 2020. *Environ Sci Technol* **2022**, *56* (11), 6996–7005. https://doi.org/10.1021/acs.est.1c06948.
(85) Paatero, P.; Tapper, U. Positive Matrix Factorization: A Non-negative Factor Model with Optimal Utilization of Error Estimates of Data Values. *Environmetrics* **1994**, *5* (2), 111–126. https://doi.org/10.1002/env.3170050203.

(86) Norris, G. *EPA Positive Matrix Factorization 5.0 Fundamentals and User Guide | US EPA*. Prepared for the US Environmental Protection Agency Office of Research and Development. https://www.epa.gov/air-research/epa-positive-matrix-factorization-50-fundamentals-and-user-guide (accessed 2024-01-24).
(87) Polissar, A. V.; Hopke, P. K.; Paatero, P.; Malm, W. C.; Sisler, J. F. Atmospheric Aerosol over Alaska: 2. Elemental Composition and Sources. *Journal of Geophysical Research: Atmospheres* **1998**, *103* (D15), 19045–19057. https://doi.org/10.1029/98JD01212.
(88) Feng, W.; Wang, X.; Shao, Z.; Liao, H.; Wang, Y.; Xie, M. Time-Resolved Measurements of $PM_{2.5}$ Chemical Composition and Brown Carbon Absorption in Nanjing, East China: Diurnal Variations and Organic Tracer-Based PMF Analysis. *Journal of Geophysical Research: Atmospheres* **2023**, *128* (18). https://doi.org/10.1029/2023JD039092.
(89) Zhang, T.; Su, Y.; Debosz, J.; Noble, M.; Munoz, A.; Xu, X. Sensitivity of Source Apportionment of Ambient PM2.5-Bound Elements to Input Concentration Data. *Atmosphere (Basel)* **2023**, *14* (8), 1269. https://doi.org/10.3390/atmos14081269.
(90) Xie, M.; Hannigan, M. P.; Dutton, S. J.; Milford, J. B.; Hemann, J. G.; Miller, S. L.; Schauer, J. J.; Peel, J. L.; Vedal, S. Positive Matrix Factorization of $PM_{2.5}$: Comparison and Implications of Using Different Speciation Data Sets. *Environ Sci Technol* **2012**, *46* (21), 11962–11970. https://doi.org/10.1021/es302358g.
(91) Farnham, I. M.; Singh, A. K.; Stetzenbach, K. J.; Johannesson, K. H. Treatment of Nondetects in Multivariate Analysis of Groundwater Geochemistry Data. *Chemometrics and Intelligent Laboratory Systems* **2002**, *60* (1–2), 265–281. https://doi.org/10.1016/S0169-7439(01)00201-5.
(92) Carslaw, D. C.; Ropkins, K. Openair - An r Package for Air Quality Data Analysis. *Environmental Modelling and Software* **2012**, *27–28*, 52–61. https://doi.org/10.1016/J.ENVSOFT.2011.09.008.
(93) Tobias, A.; Kim, Y.; Madaniyazi, L. Time-Stratified Case-Crossover Studies for Aggregated Data in Environmental Epidemiology: A Tutorial. *Int J Epidemiol* **2024**, *53* (2). https://doi.org/10.1093/ije/dyae020.
(94) Liu, J. C.; Wilson, A.; Mickley, L. J.; Dominici, F.; Ebisu, K.; Wang, Y.; Sulprizio, M. P.; Peng, R. D.; Yue, X.; Son, J.-Y.; Anderson, G. B.; Bell, M. L. Wildfire-Specific Fine Particulate Matter and Risk of Hospital Admissions in Urban and Rural Counties. *Epidemiology* **2017**, *28* (1), 77–85. https://doi.org/10.1097/EDE.0000000000000556.
(95) Paatero, P.; Eberly, S.; Brown, S. G.; Norris, G. A. Methods for Estimating Uncertainty in Factor Analytic Solutions. *Atmos Meas Tech* **2014**, *7* (3), 781–797. https://doi.org/10.5194/amt-7-781-2014.
(96) Janes, H.; Sheppard, L.; Lumley, T. Case-Crossover Analyses of Air Pollution Exposure Data. *Epidemiology* **2005**, *16* (6), 717–726. https://doi.org/10.1097/01.ede.0000181315.18836.9d.
(97) Janes, H.; Sheppard, L.; Lumley, T. Overlap Bias in the Case-Crossover Design, with Application to Air Pollution Exposures. *Stat Med* **2005**, *24* (2), 285–300. https://doi.org/10.1002/sim.1889.
(98) Buckley, J. P.; Samet, J. M.; Richardson, D. B. Commentary. *Epidemiology* **2014**, *25* (2), 242–245. https://doi.org/10.1097/EDE.0000000000000051.
(99) Amato, F.; Alastuey, A.; Karanasiou, A.; Lucarelli, F.; Nava, S.; Calzolai, G.; Severi, M.; Becagli, S.; Gianelle, V. L.; Colombi, C.; Alves, C.; Custódio, D.; Nunes, T.; Cerqueira, M.; Pio, C.; Eleftheriadis, K.; Diapouli, E.; Reche, C.; Minguillón, M. C.; Manousakas, M.-I.; Maggos, T.; Vratolis, S.; Harrison, R. M.; Querol, X. AIRUSE-LIFE+: A Harmonized PM Speciation and Source Apportionment in Five Southern

European Cities. *Atmos Chem Phys* **2016**, *16* (5), 3289–3309. https://doi.org/10.5194/acp-16-3289-2016.
(100) de Miranda, R. M.; de Fatima Andrade, M.; Fornaro, A.; Astolfo, R.; de Andre, P. A.; Saldiva, P. Urban Air Pollution: A Representative Survey of PM2.5 Mass Concentrations in Six Brazilian Cities. *Air Qual Atmos Health* **2012**, *5* (1), 63–77. https://doi.org/10.1007/s11869-010-0124-1.
(101) Brum, D. R. Estudo Da Composição Química Do Material Particulado Fino (MP2,5) Em Porto Alegre e Belo Horizonte. Tese de Doutorado, Universidade de São Paulo, São Paulo, 2010.
(102) Barbosa, C. G. G. Monitoramento de Material Particulado Fino Na Cidade de Manaus Para Avaliação de Potenciais Riscos à Saúde Da População e Caracterização de Material Particulado Em Ambiente de Florestas (Atto-Amazonian Tall Tower Observatory) - Amazonas, Brasil. . Dissertação de Mestrado, Universidade Federal do Paraná, Curitiba, 2014.
(103) Andrade, M. de F.; de Miranda, R. M.; Fornaro, A.; Kerr, A.; Oyama, B.; de Andre, P. A.; Saldiva, P. Vehicle Emissions and PM2.5 Mass Concentrations in Six Brazilian Cities. *Air Qual Atmos Health* **2012**, *5* (1), 79–88. https://doi.org/10.1007/s11869-010-0104-5.
(104) de Miranda, R. M.; de Fatima Andrade, M.; Fornaro, A.; Astolfo, R.; de Andre, P. A.; Saldiva, P. Urban Air Pollution: A Representative Survey of PM2.5 Mass Concentrations in Six Brazilian Cities. *Air Qual Atmos Health* **2012**, *5* (1), 63–77. https://doi.org/10.1007/s11869-010-0124-1.
(105) Polezer, G. Materiais Antropogênicos Suspensos Na Atmosfera de Curitiba. Dissertação de Mestrado, Universidade Federal do Paraná, Curitiba, 2015.
(106) Zhou, S.; Yuan, Q.; Li, W.; Lu, Y.; Zhang, Y.; Wang, W. Trace Metals in Atmospheric Fine Particles in One Industrial Urban City: Spatial Variations, Sources, and Health Implications. *Journal of Environmental Sciences* **2014**, *26* (1), 205–213. https://doi.org/10.1016/S1001-0742(13)60399-X.
(107) Salameh, D.; Detournay, A.; Pey, J.; Pérez, N.; Liguori, F.; Saraga, D.; Bove, M. C.; Brotto, P.; Cassola, F.; Massabò, D.; Latella, A.; Pillon, S.; Formenton, G.; Patti, S.; Armengaud, A.; Piga, D.; Jaffrezo, J. L.; Bartzis, J.; Tolis, E.; Prati, P.; Querol, X.; Wortham, H.; Marchand, N. PM2.5 Chemical Composition in Five European Mediterranean Cities: A 1-Year Study. *Atmos Res* **2015**, *155*, 102–117. https://doi.org/10.1016/j.atmosres.2014.12.001.
(108) Pekey, B.; Bozkurt, Z. B.; Pekey, H.; Doğan, G.; Zararsız, A.; Efe, N.; Tuncel, G. Indoor/Outdoor Concentrations and Elemental Composition of PM10/PM2.5 in Urban/Industrial Areas of Kocaeli City, Turkey. *Indoor Air* **2010**, *20* (2), 112–125. https://doi.org/10.1111/j.1600-0668.2009.00628.x.
(109) Shaltout, A. A.; Boman, J.; Al-Malawi, D. R.; Shehadeh, Z. F. Elemental Composition of PM2.5 Particles Sampled in Industrial and Residential Areas of Taif, Saudi Arabia. *Aerosol Air Qual Res* **2013**, *13* (4), 1356–1364. https://doi.org/10.4209/aaqr.2012.11.0320.
(110) Alves, C.; Pio, C.; Campos, E.; Barbedo, P. Size Distribution of Atmospheric Particulate Ionic Species at a Coastal Site in Portugal. *Quim Nova* **2007**, *30* (8), 1938–1944. https://doi.org/10.1590/S0100-40422007000800027.
(111) Gluščić, V.; Čačković, M.; Pehnec, G.; Bešlić, I. Ionic Composition of PM2.5 Particle Fraction at a Coastal Urban Background Site in Croatia. *Atmos Pollut Res* **2020**, *11* (12), 2202–2214. https://doi.org/10.1016/j.apr.2020.07.004.

(112) He, Q.; Yan, Y.; Guo, L.; Zhang, Y.; Zhang, G.; Wang, X. Characterization and Source Analysis of Water-Soluble Inorganic Ionic Species in PM2.5 in Taiyuan City, China. *Atmos Res* **2017**, *184*, 48–55. https://doi.org/10.1016/j.atmosres.2016.10.008.
(113) Millero, F. J. *Chemical Oceanography*, 4th ed.; CRC Press, Boca Raton: FL, 2013.
(114) Buczyńska, A. J.; Krata, A.; Van Grieken, R.; Brown, A.; Polezer, G.; De Wael, K.; Potgieter-Vermaak, S. Composition of PM2.5 and PM1 on High and Low Pollution Event Days and Its Relation to Indoor Air Quality in a Home for the Elderly. *Science of The Total Environment* **2014**, *490*, 134–143. https://doi.org/10.1016/j.scitotenv.2014.04.102.
(115) Ram, K.; Sarin, M. M.; Sudheer, A. K.; Rengarajan, R. Carbonaceous and Secondary Inorganic Aerosols during Wintertime Fog and Haze over Urban Sites in the Indo-Gangetic Plain. *Aerosol Air Qual Res* **2012**, *12* (3), 359–370. https://doi.org/10.4209/aaqr.2011.07.0105.
(116) Kang, J.; Cho, B. C.; Lee, C.-B. Atmospheric Transport of Water-Soluble Ions (NO3−, NH4+ and Nss-SO42−) to the Southern East Sea (Sea of Japan). *Science of The Total Environment* **2010**, *408* (11), 2369–2377. https://doi.org/10.1016/j.scitotenv.2010.02.022.
(117) Bauer, S. E.; Koch, D.; Unger, N.; Metzger, S. M.; Shindell, D. T.; Streets, D. G. Nitrate Aerosols Today and in 2030: A Global Simulation Including Aerosols and Tropospheric Ozone. *Atmos Chem Phys* **2007**, *7* (19), 5043–5059. https://doi.org/10.5194/acp-7-5043-2007.
(118) Bauer, S. E.; Koch, D.; Unger, N.; Metzger, S. M.; Shindell, D. T.; Streets, D. G. Nitrate Aerosols Today and in 2030: A Global Simulation Including Aerosols and Tropospheric Ozone. *Atmos Chem Phys* **2007**, *7* (19), 5043–5059. https://doi.org/10.5194/acp-7-5043-2007.
(119) Harrison, R. M.; Msibi, M. I.; Kitto, A.-M. N.; Yamulki, S. Atmospheric Chemical Transformations of Nitrogen Compounds Measured in the North Sea Experiment, September 1991. *Atmos Environ* **1994**, *28* (9), 1593–1599. https://doi.org/10.1016/1352-2310(94)90305-0.
(120) Wakamatsu, S.; Utsunomiya, A.; Jin Suk Han; Mori, A.; Uno, I.; Uehara, K. Seasonal Variation in Atmospheric Aerosols Concentration Covering Northern Kyushu, Japan and Seoul, Korea. *Atmos Environ* **1996**, *30* (13), 2343–2354. https://doi.org/10.1016/1352-2310(95)00421-1.
(121) Querol, X. PM10 and PM2.5 Source Apportionment in the Barcelona Metropolitan Area, Catalonia, Spain. *Atmos Environ* **2001**, *35* (36), 6407–6419. https://doi.org/10.1016/S1352-2310(01)00361-2.
(122) Jacobson, M. Z. Studying the Effects of Calcium and Magnesium on Size-Distributed Nitrate and Ammonium with EQUISOLV II. *Atmos Environ* **1999**, *33* (22), 3635–3649. https://doi.org/10.1016/S1352-2310(99)00105-3.
(123) Wang, H.; Wang, X.; Yang, X.; Li, W.; Xue, L.; Wang, T.; Chen, J.; Wang, W. Mixed Chloride Aerosols and Their Atmospheric Implications: A Review. *Aerosol Air Qual Res* **2017**, *17* (4), 878–887. https://doi.org/10.4209/aaqr.2016.09.0383.
(124) Pan, Y.; Luo, L.; Xiao, H.; Zheng, N.; Fang, X.; Zhang, Z.; Xiao, H. A One-Year Comprehensive Characteristics of Water Soluble Inorganic Ions in PM2.5 from a Typical Mountainous City. *Atmos Pollut Res* **2020**, *11* (11), 1883–1890. https://doi.org/10.1016/j.apr.2020.08.006.
(125) Sánchez, L. F.; Villacura, L.; Catalán, F.; Araya, R. T.; Guzman, M. A. L. The Oxidative Potential of Airborne Particulate Matter Research Trends, Challenges, and Future Perspectives—Insights from a Bibliometric Analysis and Scoping Review. *Antioxidants* **2024**, *13* (6), 640. https://doi.org/10.3390/antiox13060640.

(126) Park, M.; Joo, H. S.; Lee, K.; Jang, M.; Kim, S. D.; Kim, I.; Borlaza, L. J. S.; Lim, H.; Shin, H.; Chung, K. H.; Choi, Y.-H.; Park, S. G.; Bae, M.-S.; Lee, J.; Song, H.; Park, K. Differential Toxicities of Fine Particulate Matters from Various Sources. *Sci Rep* **2018**, *8* (1), 17007. https://doi.org/10.1038/s41598-018-35398-0.

(127) Yang, A.; Jedynska, A.; Hellack, B.; Kooter, I.; Hoek, G.; Brunekreef, B.; Kuhlbusch, T. A. J.; Cassee, F. R.; Janssen, N. A. H. Measurement of the Oxidative Potential of PM2.5 and Its Constituents: The Effect of Extraction Solvent and Filter Type. *Atmos Environ* **2014**, *83*, 35–42. https://doi.org/10.1016/j.atmosenv.2013.10.049.

(128) Fang, T.; Guo, H.; Zeng, L.; Verma, V.; Nenes, A.; Weber, R. J. Highly Acidic Ambient Particles, Soluble Metals, and Oxidative Potential: A Link between Sulfate and Aerosol Toxicity. *Environ Sci Technol* **2017**, *51* (5), 2611–2620. https://doi.org/10.1021/acs.est.6b06151.

(129) Niu, Y.; Chen, R.; Xia, Y.; Cai, J.; Ying, Z.; Lin, Z.; Liu, C.; Chen, C.; Peng, L.; Zhao, Z.; Zhou, W.; Chen, J.; Wang, D.; Huo, J.; Wang, X.; Fu, Q.; Kan, H. Fine Particulate Matter Constituents and Stress Hormones in the Hypothalamus–Pituitary–Adrenal Axis. *Environ Int* **2018**, *119*, 186–192. https://doi.org/10.1016/j.envint.2018.06.027.

(130) Karydis, V. A.; Tsimpidi, A. P.; Pozzer, A.; Lelieveld, J. How Alkaline Compounds Control Atmospheric Aerosol Particle Acidity. *Atmos Chem Phys* **2021**, *21* (19), 14983–15001. https://doi.org/10.5194/acp-21-14983-2021.

(131) Masselot, P.; Sera, F.; Schneider, R.; Kan, H.; Lavigne, É.; Stafoggia, M.; Tobias, A.; Chen, H.; Burnett, R. T.; Schwartz, J.; Zanobetti, A.; Bell, M. L.; Chen, B.-Y.; Guo, Y.-L. L.; Ragettli, M. S.; Vicedo-Cabrera, A. M.; Åström, C.; Forsberg, B.; Íñiguez, C.; Garland, R. M.; Scovronick, N.; Madureira, J.; Nunes, B.; De la Cruz Valencia, C.; Hurtado Diaz, M.; Honda, Y.; Hashizume, M.; Ng, C. F. C.; Samoli, E.; Katsouyanni, K.; Schneider, A.; Breitner, S.; Ryti, N. R. I.; Jaakkola, J. J. K.; Maasikmets, M.; Orru, H.; Guo, Y.; Valdés Ortega, N.; Matus Correa, P.; Tong, S.; Gasparrini, A. Differential Mortality Risks Associated With PM2.5 Components. *Epidemiology* **2022**, *33* (2), 167–175. https://doi.org/10.1097/EDE.0000000000001455.

(132) Luo, B.; Schaub, A.; Glas, I.; Klein, L. K.; David, S. C.; Bluvshtein, N.; Violaki, K.; Motos, G.; Pohl, M. O.; Hugentobler, W.; Nenes, A.; Krieger, U. K.; Stertz, S.; Peter, T.; Kohn, T. Expiratory Aerosol PH: The Overlooked Driver of Airborne Virus Inactivation. *Environ Sci Technol* **2023**, *57* (1), 486–497. https://doi.org/10.1021/acs.est.2c05777.

(133) SPECIEUROPE. *Source profiles for Europe database*. Disponível em: <https://source-apportionment.jrc.ec.europa.eu/Specieurope/profiles.aspx?size=PM2.5 (accessed 2022-10-12).

(134) The United States Environmental Protection Agency (US EPA). SPECIATE: Air Emissions Modeling. 2020. https://www.epa.gov/air-emissions-modeling/speciate-0 (accessed 2022-03-23).

(135) Hopke, P. K.; Dai, Q.; Li, L.; Feng, Y. Global Review of Recent Source Apportionments for Airborne Particulate Matter. *Science of The Total Environment* **2020**, *740*, 140091. https://doi.org/10.1016/j.scitotenv.2020.140091.

(136) Chow, W. S.; Huang, X. H. H.; Leung, K. F.; Huang, L.; Wu, X.; Yu, J. Z. Molecular and Elemental Marker-Based Source Apportionment of Fine Particulate Matter at Six Sites in Hong Kong, China. *Science of The Total Environment* **2022**, *813*, 152652. https://doi.org/10.1016/j.scitotenv.2021.152652.

(137) Behera, S. N.; Sharma, M. Investigating the Potential Role of Ammonia in Ion Chemistry of Fine Particulate Matter Formation for an Urban Environment. *Science of The Total Environment* **2010**, *408* (17), 3569–3575. https://doi.org/10.1016/j.scitotenv.2010.04.017.

(138) Updyke, K. M.; Nguyen, T. B.; Nizkorodov, S. A. Formation of Brown Carbon via Reactions of Ammonia with Secondary Organic Aerosols from Biogenic and Anthropogenic Precursors. *Atmos Environ* **2012**, *63*, 22–31. https://doi.org/10.1016/j.atmosenv.2012.09.012.
(139) Xie, F.; Su, Y.; Tian, Y.; Shi, Y.; Zhou, X.; Wang, P.; Yu, R.; Wang, W.; He, J.; Xin, J.; Lü, C. The Shifting of Secondary Inorganic Aerosol Formation Mechanisms during Haze Aggravation: The Decisive Role of Aerosol Liquid Water. *Atmos Chem Phys* **2023**, *23* (4), 2365–2378. https://doi.org/10.5194/acp-23-2365-2023.
(140) Wang, S.; Nan, J.; Shi, C.; Fu, Q.; Gao, S.; Wang, D.; Cui, H.; Saiz-Lopez, A.; Zhou, B. Atmospheric Ammonia and Its Impacts on Regional Air Quality over the Megacity of Shanghai, China. *Sci Rep* **2015**, *5* (1), 15842. https://doi.org/10.1038/srep15842.
(141) Bouwman, A. F.; Lee, D. S.; Asman, W. A. H.; Dentener, F. J.; Van Der Hoek, K. W.; Olivier, J. G. J. A Global High-resolution Emission Inventory for Ammonia. *Global Biogeochem Cycles* **1997**, *11* (4), 561–587. https://doi.org/10.1029/97GB02266.
(142) Seinfeld, J. H.; Pandis, S. N. *Atmospheric Chemistry and Physics: From Air Pollution to Climate Change*; John Wiley & Sons, Ed.; 2016.
(143) Zhou, J.; Xing, Z.; Deng, J.; Du, K. Characterizing and Sourcing Ambient PM2.5 over Key Emission Regions in China I: Water-Soluble Ions and Carbonaceous Fractions. *Atmos Environ* **2016**, *135*, 20–30. https://doi.org/10.1016/j.atmosenv.2016.03.054.
(144) Pinder, R. W.; Dennis, R. L.; Bhave, P. V. Observable Indicators of the Sensitivity of PM2.5 Nitrate to Emission Reductions—Part I: Derivation of the Adjusted Gas Ratio and Applicability at Regulatory-Relevant Time Scales. *Atmos Environ* **2008**, *42* (6), 1275–1286. https://doi.org/10.1016/j.atmosenv.2007.10.039.
(145) Wang, W.; Liu, M.; Wang, T.; Song, Y.; Zhou, L.; Cao, J.; Hu, J.; Tang, G.; Chen, Z.; Li, Z.; Xu, Z.; Peng, C.; Lian, C.; Chen, Y.; Pan, Y.; Zhang, Y.; Sun, Y.; Li, W.; Zhu, T.; Tian, H.; Ge, M. Sulfate Formation Is Dominated by Manganese-Catalyzed Oxidation of SO2 on Aerosol Surfaces during Haze Events. *Nat Commun* **2021**, *12* (1), 1993. https://doi.org/10.1038/s41467-021-22091-6.
(146) Chatterjee, A.; Dutta, C.; Sen, S.; Ghosh, K.; Biswas, N.; Ganguly, D.; Jana, T. K. Formation, Transformation, and Removal of Aerosol over a Tropical Mangrove Forest. *Journal of Geophysical Research: Atmospheres* **2006**, *111* (D24). https://doi.org/10.1029/2006JD007144.
(147) Biswas, H.; Mukhopadhyay, S. K.; De, T. K.; Sen, S.; Jana, T. K. Biogenic Controls on the Air—Water Carbon Dioxide Exchange in the Sundarban Mangrove Environment, Northeast Coast of Bay of Bengal, India. *Limnol Oceanogr* **2004**, *49* (1), 95–101. https://doi.org/10.4319/lo.2004.49.1.0095.
(148) Webb, A. L.; van Leeuwe, M. A.; den Os, D.; Meredith, M. P.; J. Venables, H.; Stefels, J. Extreme Spikes in DMS Flux Double Estimates of Biogenic Sulfur Export from the Antarctic Coastal Zone to the Atmosphere. *Sci Rep* **2019**, *9* (1), 2233. https://doi.org/10.1038/s41598-019-38714-4.
(149) Reis, C. R. G.; Nardoto, G. B.; Oliveira, R. S. Global Overview on Nitrogen Dynamics in Mangroves and Consequences of Increasing Nitrogen Availability for These Systems. *Plant Soil* **2017**, *410* (1–2), 1–19. https://doi.org/10.1007/s11104-016-3123-7.
(150) Karar, K.; Gupta, A. K.; Kumar, A.; Biswas, A. K. Characterization and Identification of the Sources of Chromium, Zinc, Lead, Cadmium, Nickel, Manganese and Iron in Pm10 Particulates at the Two Sites of Kolkata, India. *Environ Monit Assess* **2006**, *120* (1–3), 347–360. https://doi.org/10.1007/s10661-005-9067-7.
(151) Wu, S.-P.; Xu, C.; Dai, L.-H.; Zhang, N.; Wei, Y.; Gao, Y.; Yan, J.-P.; Schwab, J. J. Source Apportionment of PM2.5 at Urban and Suburban Sites in a Port City of

Southeastern China. *Aerosol Air Qual Res* **2019**, *19* (9), 2017–2031. https://doi.org/10.4209/aaqr.2019.01.0007.
(152) Bondy, A. L.; Wang, B.; Laskin, A.; Craig, R. L.; Nhliziyo, M. V.; Bertman, S. B.; Pratt, K. A.; Shepson, P. B.; Ault, A. P. Inland Sea Spray Aerosol Transport and Incomplete Chloride Depletion: Varying Degrees of Reactive Processing Observed during SOAS. *Environ Sci Technol* **2017**, *51* (17), 9533–9542. https://doi.org/10.1021/acs.est.7b02085.
(153) Crawford, J.; Cohen, D. D.; Chambers, S. D.; Williams, A. G.; Atanacio, A. Impact of Aerosols of Sea Salt Origin in a Coastal Basin: Sydney, Australia. *Atmos Environ* **2019**, *207*, 52–62. https://doi.org/10.1016/j.atmosenv.2019.03.018.
(154) Möller, D. The Na/Cl Ratio in Rainwater and the Seasalt Chloride Cycle. *Tellus B: Chemical and Physical Meteorology* **1990**, *42* (3), 254. https://doi.org/10.3402/tellusb.v42i3.15216.
(155) Zhang, G.; Ding, C.; Jiang, X.; Pan, G.; Wei, X.; Sun, Y. Chemical Compositions and Sources Contribution of Atmospheric Particles at a Typical Steel Industrial Urban Site. *Sci Rep* **2020**, *10* (1), 7654. https://doi.org/10.1038/s41598-020-64519-x.
(156) Pakkanen, T. A. Study of Formation of Coarse Particle Nitrate Aerosol. *Atmos Environ* **1996**, *30* (14), 2475–2482. https://doi.org/10.1016/1352-2310(95)00492-0.
(157) Manousakas, M.; Papaefthymiou, H.; Diapouli, E.; Migliori, A.; Karydas, A. G.; Bogdanovic-Radovic, I.; Eleftheriadis, K. Assessment of PM2.5 Sources and Their Corresponding Level of Uncertainty in a Coastal Urban Area Using EPA PMF 5.0 Enhanced Diagnostics. *Science of The Total Environment* **2017**, *574*, 155–164. https://doi.org/10.1016/j.scitotenv.2016.09.047.
(158) Chow, J. C. Measurement Methods to Determine Compliance with Ambient Air Quality Standards for Suspended Particles. *J Air Waste Manage Assoc* **1995**, *45* (5), 320–382. https://doi.org/10.1080/10473289.1995.10467369.
(159) Kim, E.-A.; Koh, B. Utilization of Road Dust Chemical Profiles for Source Identification and Human Health Impact Assessment. *Sci Rep* **2020**, *10* (1), 14259. https://doi.org/10.1038/s41598-020-71180-x.
(160) Srivastava, D.; Xu, J.; Vu, T. V.; Liu, D.; Li, L.; Fu, P.; Hou, S.; Moreno Palmerola, N.; Shi, Z.; Harrison, R. M. Insight into PM2.5; Its Sources by Applying Positive Matrix Factorization (PMF) at Urban and Rural Sites of Beijing. *Atmos Chem Phys* **2021**, *21* (19), 14703–14724. https://doi.org/10.5194/acp-21-14703-2021.
(161) Xu, D.-M.; Zhang, J.-Q.; Yan, B.; Liu, H.; Zhang, L.-L.; Zhan, C.-L.; Zhang, L.; Zhong, P. Contamination Characteristics and Potential Environmental Implications of Heavy Metals in Road Dusts in Typical Industrial and Agricultural Cities, Southeastern Hubei Province, Central China. *Environmental Science and Pollution Research* **2018**, *25* (36), 36223–36238. https://doi.org/10.1007/s11356-018-3282-6.
(162) Zhu, Z.; Sun, G.; Bi, X.; Li, Z.; Yu, G. Identification of Trace Metal Pollution in Urban Dust from Kindergartens Using Magnetic, Geochemical and Lead Isotopic Analyses. *Atmos Environ* **2013**, *77*, 9–15. https://doi.org/10.1016/j.atmosenv.2013.04.053.
(163) Dewan, N.; Majestic, B. J.; Ketterer, M. E.; Miller-Schulze, J. P.; Shafer, M. M.; Schauer, J. J.; Solomon, P. A.; Artamonova, M.; Chen, B. B.; Imashev, S. A.; Carmichael, G. R. Tracing Dust Sources Using Stable Lead and Strontium Isotopes in Central Asia; 2015; pp 79–98. https://doi.org/10.1021/bk-2015-1210.ch004.
(164) Yu, J.; Yan, C.; Liu, Y.; Li, X.; Zhou, T.; Zheng, M. Potassium: A Tracer for Biomass Burning in Beijing? *Aerosol Air Qual Res* **2018**, *18* (9), 2447–2459. https://doi.org/10.4209/aaqr.2017.11.0536.
(165) Sun, X.; Luo, X.; Zhao, C.; Zhang, B.; Tao, J.; Yang, Z.; Ma, W.; Liu, T. The Associations between Birth Weight and Exposure to Fine Particulate Matter (PM2.5) and

Its Chemical Constituents during Pregnancy: A Meta-Analysis. *Environmental Pollution* **2016**, *211*, 38–47. https://doi.org/10.1016/j.envpol.2015.12.022.
(166) Sörme, L.; Bergbäck, B.; Lohm, U. Goods in the Anthroposphere as a Metal Emission Source A Case Study of Stockholm, Sweden. *Water, Air and Soil Pollution: Focus* **2001**, *1* (3/4), 213–227. https://doi.org/10.1023/A:1017516523915.
(167) Smichowski, P.; Gómez, D.; Frazzoli, C.; Caroli, S. Traffic-Related Elements in Airborne Particulate Matter. *Appl Spectrosc Rev* **2007**, *43* (1), 23–49. https://doi.org/10.1080/05704920701645886.
(168) Canepari, S.; Perrino, C.; Olivieri, F.; Astolfi, M. L. Characterisation of the Traffic Sources of PM through Size-Segregated Sampling, Sequential Leaching and ICP Analysis. *Atmos Environ* **2008**, *42* (35), 8161–8175. https://doi.org/10.1016/j.atmosenv.2008.07.052.
(169) Pant, P.; Harrison, R. M. Critical Review of Receptor Modelling for Particulate Matter: A Case Study of India. *Atmos Environ* **2012**, *49*, 1–12. https://doi.org/10.1016/j.atmosenv.2011.11.060.
(170) Grigoratos, T.; Martini, G. Brake Wear Particle Emissions: A Review. *Environmental Science and Pollution Research* **2015**, *22* (4), 2491–2504. https://doi.org/10.1007/s11356-014-3696-8.
(171) Piscitello, A.; Bianco, C.; Casasso, A.; Sethi, R. Non-Exhaust Traffic Emissions: Sources, Characterization, and Mitigation Measures. *Science of The Total Environment* **2021**, *766*, 144440. https://doi.org/10.1016/j.scitotenv.2020.144440.
(172) Duong, T. T. T.; Lee, B.-K. Determining Contamination Level of Heavy Metals in Road Dust from Busy Traffic Areas with Different Characteristics. *J Environ Manage* **2011**, *92* (3), 554–562. https://doi.org/10.1016/j.jenvman.2010.09.010.
(173) Alves, C. A.; Vicente, E. D.; Vicente, A. M. P.; Rienda, I. C.; Tomé, M.; Querol, X.; Amato, F. Loadings, Chemical Patterns and Risks of Inhalable Road Dust Particles in an Atlantic City in the North of Portugal. *Science of The Total Environment* **2020**, *737*, 139596. https://doi.org/10.1016/j.scitotenv.2020.139596.
(174) Li, H.-H.; Chen, L.-J.; Yu, L.; Guo, Z.-B.; Shan, C.-Q.; Lin, J.-Q.; Gu, Y.-G.; Yang, Z.-B.; Yang, Y.-X.; Shao, J.-R.; Zhu, X.-M.; Cheng, Z. Pollution Characteristics and Risk Assessment of Human Exposure to Oral Bioaccessibility of Heavy Metals via Urban Street Dusts from Different Functional Areas in Chengdu, China. *Science of The Total Environment* **2017**, *586*, 1076–1084. https://doi.org/10.1016/j.scitotenv.2017.02.092.
(175) Samek, L.; Stegowski, Z.; Furman, L.; Fiedor, J. Chemical Content and Estimated Sources of Fine Fraction of Particulate Matter Collected in Krakow. *Air Qual Atmos Health* **2017**, *10* (1), 47–52. https://doi.org/10.1007/s11869-016-0407-2.
(176) Zhu, X.; Yu, W.; Li, F.; Liu, C.; Ma, J.; Yan, J.; Wang, Y.; Tian, R. Spatio-Temporal Distribution and Source Identification of Heavy Metals in Particle Size Fractions of Road Dust from a Typical Industrial District. *Science of The Total Environment* **2021**, *780*, 146357. https://doi.org/10.1016/j.scitotenv.2021.146357.
(177) Carnin, R. L. P.; Folgueras, M. V.; Luvizão, R. R.; Correia, S. L.; da Cunha, C. J.; Dungan, R. S. Use of an Integrated Approach to Characterize the Physicochemical Properties of Foundry Green Sands. *Thermochim Acta* **2012**, *543*, 150–155. https://doi.org/10.1016/j.tca.2012.05.018.
(178) Siddiqui, Z.; Khillare, P. S.; Jyethi, D. S.; Aithani, D.; Yadav, A. K. Pollution Characteristics and Human Health Risk from Trace Metals in Roadside Soil and Road Dust around Major Urban Parks in Delhi City. *Air Qual Atmos Health* **2020**, *13* (11), 1271–1286. https://doi.org/10.1007/s11869-020-00874-y.

(179) Carnin, R. L. P. Reaproveitamento Do Resíduo de Areia Verde de Fundição Como Agregado Em Misturas Asfálticas. Doctorate, Universidade Federal do Paraná, Curitiba, 2008.
(180) Hermenegildo, M. K. Determinação Da Concentração de Metais Presentes Areia Verde de Fundição: Estudo de Caso Da Fundição TUPY S.A. Bachelor of Engineering, Universidade Federal de Santa Catarina , Florianópolis, 2011.
(181) Laborde, M.; Crippa, M.; Tritscher, T.; Jurányi, Z.; Decarlo, P. F.; Temime-Roussel, B.; Marchand, N.; Eckhardt, S.; Stohl, A.; Baltensperger, U.; Prévôt, A. S. H.; Weingartner, E.; Gysel, M. Black Carbon Physical Properties and Mixing State in the European Megacity Paris. *Atmos Chem Phys* **2013**, *13* (11), 5831–5856. https://doi.org/10.5194/acp-13-5831-2013.
(182) Riemer, N.; West, M.; Zaveri, R.; Easter, R. Estimating Black Carbon Aging Time-Scales with a Particle-Resolved Aerosol Model. *J Aerosol Sci* **2010**, *41* (1), 143–158. https://doi.org/10.1016/j.jaerosci.2009.08.009.
(183) Oshima, N.; Koike, M. Development of a Parameterization of Black Carbon Aging for Use in General Circulation Models. *Geosci Model Dev* **2013**, *6* (2), 263–282. https://doi.org/10.5194/gmd-6-263-2013.
(184) Liu, J.; Fan, S.; Horowitz, L. W.; Levy, H. Evaluation of Factors Controlling Long-Range Transport of Black Carbon to the Arctic. *J Geophys Res* **2011**, *116* (D4), D04307. https://doi.org/10.1029/2010JD015145.
(185) Zhang, J.; Liu, J.; Tao, S.; Ban-Weiss, G. A. Long-Range Transport of Black Carbon to the Pacific Ocean and Its Dependence on Aging Timescale. *Atmos Chem Phys* **2015**, *15* (20), 11521–11535. https://doi.org/10.5194/acp-15-11521-2015.
(186) Su, B.; Wang, T.; Zhang, G.; Liang, Y.; Lv, C.; Hu, Y.; Li, L.; Zhou, Z.; Wang, X.; Bi, X. A Review of Atmospheric Aging of Sea Spray Aerosols: Potential Factors Affecting Chloride Depletion. *Atmos Environ* **2022**, *290*, 119365. https://doi.org/10.1016/j.atmosenv.2022.119365.
(187) *Sulfate & Health | California Air Resources Board*. https://ww2.arb.ca.gov/resources/sulfate-and-health (accessed 2024-01-23).
(188) Ueda, K.; Yamagami, M.; Ikemori, F.; Hisatsune, K.; Nitta, H. Associations Between Fine Particulate Matter Components and Daily Mortality in Nagoya, Japan. *J Epidemiol* **2016**, *26* (5), 249–257. https://doi.org/10.2188/jea.JE20150039.
(189) Dreher, K. L. Particulate Matter Physicochemistry and Toxicology: In Search of Causality—A Critical Perspective. *Inhal Toxicol* **2000**, *12* (sup3), 45–57. https://doi.org/10.1080/08958378.2000.11463230.
(190) Lay, J. C.; Zeman, K. L.; Ghio, A. J.; Bennett, W. D. EFFECTS OF INHALED IRON OXIDE PARTICLES ON ALVEOLAR EPITHELIAL PERMEABILITY IN NORMAL SUBJECTS. *Inhal Toxicol* **2001**, *13* (12), 1065–1078. https://doi.org/10.1080/08958370152647618.
(191) Lippmann, M. Toxicological and Epidemiological Studies of Cardiovascular Effects of Ambient Air Fine Particulate Matter ($PM_{2.5}$) and Its Chemical Components: Coherence and Public Health Implications. *Crit Rev Toxicol* **2014**, *44* (4), 299–347. https://doi.org/10.3109/10408444.2013.861796.
(192) Charrier, J. G.; Anastasio, C. Rates of Hydroxyl Radical Production from Transition Metals and Quinones in a Surrogate Lung Fluid. *Environ Sci Technol* **2015**, *49* (15), 9317–9325. https://doi.org/10.1021/acs.est.5b01606.
(193) Di Pietro, A.; Visalli, G.; Munaò, F.; Baluce, B.; La Maestra, S.; Primerano, P.; Corigliano, F.; De Flora, S. Oxidative Damage in Human Epithelial Alveolar Cells Exposed in Vitro to Oil Fly Ash Transition Metals. *Int J Hyg Environ Health* **2009**, *212* (2), 196–208. https://doi.org/10.1016/j.ijheh.2008.05.005.

(194) Wilson, M. Interactions between Ultrafine Particles and Transition Metals in Vivo and in Vitro. *Toxicol Appl Pharmacol* **2002**, *184* (3), 172–179. https://doi.org/10.1006/taap.2002.9501.
(195) Feng, B.; Song, X.; Dan, M.; Yu, J.; Wang, Q.; Shu, M.; Xu, H.; Wang, T.; Chen, J.; Zhang, Y.; Zhao, Q.; Wu, R.; Liu, S.; Yu, J. Z.; Wang, T.; Huang, W. High Level of Source-Specific Particulate Matter Air Pollution Associated with Cardiac Arrhythmias. *Science of The Total Environment* **2019**, *657*, 1285–1293. https://doi.org/10.1016/j.scitotenv.2018.12.178.
(196) Kazemiparkouhi, F.; Honda, T.; Eum, K.-D.; Wang, B.; Manjourides, J.; Suh, H. H. The Impact of Long-Term PM2.5 Constituents and Their Sources on Specific Causes of Death in a US Medicare Cohort. *Environ Int* **2022**, *159*, 106988. https://doi.org/10.1016/j.envint.2021.106988.
(197) Lipfert, F. W.; Wyzga, R. E.; Baty, J. D.; Miller, J. P. Air Pollution and Survival within the Washington University– EPRI Veterans Cohort: Risks Based on Modeled Estimates of Ambient Levels of Hazardous and Criteria Air Pollutants. *J Air Waste Manage Assoc* **2009**, *59* (4), 473–489. https://doi.org/10.3155/1047-3289.59.4.473.
(198) Yoo, S.-E.; Park, J.-S.; Lee, S. H.; Park, C.-H.; Lee, C.-W.; Lee, S.-B.; Yu, S. Do; Kim, S.-Y.; Kim, H. Comparison of Short-Term Associations between PM2.5 Components and Mortality across Six Major Cities in South Korea. *Int J Environ Res Public Health* **2019**, *16* (16), 2872. https://doi.org/10.3390/ijerph16162872.
(199) Hu, J.; Zhou, R.; Ding, R.; Ye, D.-W.; Su, Y. Effect of PM2.5 Air Pollution on the Global Burden of Lower Respiratory Infections, 1990–2019: A Systematic Analysis from the Global Burden of Disease Study 2019. *J Hazard Mater* **2023**, *459*, 132215. https://doi.org/10.1016/j.jhazmat.2023.132215.
(200) Mao, S.; Wu, L.; Shi, W. Association between Trace Elements Levels and Asthma Susceptibility. *Respir Med* **2018**, *145*, 110–119. https://doi.org/10.1016/j.rmed.2018.10.028.
(201) Gao, D.; Mondal, T. K.; Lawrence, D. A. Lead Effects on Development and Function of Bone Marrow-Derived Dendritic Cells Promote Th2 Immune Responses. *Toxicol Appl Pharmacol* **2007**, *222* (1), 69–79. https://doi.org/10.1016/j.taap.2007.04.001.
(202) Kitamura, N.; Mori, A.; Tatsumi, H.; Nemoto, S.; Hiroi, T.; Kaminuma, O. Zinc Finger Protein, Multitype 1, Suppresses Human Th2 Development via Downregulation of IL-4. *Int Arch Allergy Immunol* **2011**, *155* (Suppl. 1), 53–56. https://doi.org/10.1159/000327292.
(203) Oh, C.-M.; Oh, I.-H.; Lee, J.-K.; Park, Y. H.; Choe, B.-K.; Yoon, T.-Y.; Choi, J.-M. Blood Cadmium Levels Are Associated with a Decline in Lung Function in Males. *Environ Res* **2014**, *132*, 119–125. https://doi.org/10.1016/j.envres.2014.04.008.
(204) Wang, Y.; Wu, Y.; Zheng, F.; Zhang, T.; Wang, M.; Huang, L.; Fan, X.; Chen, J.; Xiao, N. Health Threat of PM2.5-Bound Trace Elements Exposure on Asthma Hospital Admission: A Time-Stratified Case-Crossover Study. *Environ Int* **2022**, *170*, 107604. https://doi.org/10.1016/j.envint.2022.107604.
(205) Ito, K.; Mathes, R.; Ross, Z.; Nádas, A.; Thurston, G.; Matte, T. Fine Particulate Matter Constituents Associated with Cardiovascular Hospitalizations and Mortality in New York City. *Environ Health Perspect* **2011**, *119* (4), 467–473. https://doi.org/10.1289/ehp.1002667.
(206) Laden, F.; Neas, L. M.; Dockery, D. W.; Schwartz, J. Association of Fine Particulate Matter from Different Sources with Daily Mortality in Six U.S. Cities. *Environ Health Perspect* **2000**, *108* (10), 941–947. https://doi.org/10.1289/ehp.00108941.
(207) Mar, T. F.; Ito, K.; Koenig, J. Q.; Larson, T. V; Eatough, D. J.; Henry, R. C.; Kim, E.; Laden, F.; Lall, R.; Neas, L.; Stölzel, M.; Paatero, P.; Hopke, P. K.; Thurston, G. D. PM

Source Apportionment and Health Effects. 3. Investigation of Inter-Method Variations in Associations between Estimated Source Contributions of PM2.5 and Daily Mortality in Phoenix, AZ. *J Expo Sci Environ Epidemiol* **2006**, *16* (4), 311–320. https://doi.org/10.1038/sj.jea.7500465.

(208) Mar, T. F.; Norris, G. A.; Koenig, J. Q.; Larson, T. V. Associations between Air Pollution and Mortality in Phoenix, 1995-1997. *Environ Health Perspect* **2000**, *108* (4), 347–353. https://doi.org/10.1289/ehp.00108347.

(209) Özkaynak, H.; Thurston, G. D. Associations Between 1980 U.S. Mortality Rates and Alternative Measures of Airborne Particle Concentration. *Risk Analysis* **1987**, *7* (4), 449–461. https://doi.org/10.1111/j.1539-6924.1987.tb00482.x.

(210) Thurston, G. D.; Ito, K.; Mar, T.; Christensen, W. F.; Eatough, D. J.; Henry, R. C.; Kim, E.; Laden, F.; Lall, R.; Larson, T. V.; Liu, H.; Neas, L.; Pinto, J.; Stölzel, M.; Suh, H.; Hopke, P. K. Workgroup Report: Workshop on Source Apportionment of Particulate Matter Health Effects—Intercomparison of Results and Implications. *Environ Health Perspect* **2005**, *113* (12), 1768–1774. https://doi.org/10.1289/ehp.7989.

(211) Ebisu, K.; Malig, B.; Hasheminassab, S.; Sioutas, C.; Basu, R. Cause-Specific Stillbirth and Exposure to Chemical Constituents and Sources of Fine Particulate Matter. *Environ Res* **2018**, *160*, 358–364. https://doi.org/10.1016/j.envres.2017.10.015.

(212) Halonen, J. I.; Lanki, T.; Yli-Tuomi, T.; Tiittanen, P.; Kulmala, M.; Pekkanen, J. Particulate Air Pollution and Acute Cardiorespiratory Hospital Admissions and Mortality Among the Elderly. *Epidemiology* **2009**, *20* (1), 143–153. https://doi.org/10.1097/EDE.0b013e31818c7237.

(213) Krall, J. R.; Chang, H. H.; Waller, L. A.; Mulholland, J. A.; Winquist, A.; Talbott, E. O.; Rager, J. R.; Tolbert, P. E.; Sarnat, S. E. A Multicity Study of Air Pollution and Cardiorespiratory Emergency Department Visits: Comparing Approaches for Combining Estimates across Cities. *Environ Int* **2018**, *120*, 312–320. https://doi.org/10.1016/j.envint.2018.07.033.

(214) Berger, K.; Malig, B. J.; Hasheminassab, S.; Pearson, D. L.; Sioutas, C.; Ostro, B.; Basu, R. Associations of Source-Apportioned Fine Particles with Cause-Specific Mortality in California. *Epidemiology* **2018**, *29* (5), 639–648. https://doi.org/10.1097/EDE.0000000000000873.

(215) Krall, J. R.; Mulholland, J. A.; Russell, A. G.; Balachandran, S.; Winquist, A.; Tolbert, P. E.; Waller, L. A.; Sarnat, S. E. Associations between Source-Specific Fine Particulate Matter and Emergency Department Visits for Respiratory Disease in Four U.S. Cities. *Environ Health Perspect* **2017**, *125* (1), 97–103. https://doi.org/10.1289/EHP271.

(216) Lall, R.; Ito, K.; Thurston, G. D. Distributed Lag Analyses of Daily Hospital Admissions and Source-Apportioned Fine Particle Air Pollution. *Environ Health Perspect* **2011**, *119* (4), 455–460. https://doi.org/10.1289/ehp.1002638.

(217) Bell, M. L.; Ebisu, K.; Leaderer, B. P.; Gent, J. F.; Lee, H. J.; Koutrakis, P.; Wang, Y.; Dominici, F.; Peng, R. D. Associations of $PM_{2.5}$ Constituents and Sources with Hospital Admissions: Analysis of Four Counties in Connecticut and Massachusetts (USA) for Persons ≥ 65 Years of Age. *Environ Health Perspect* **2014**, *122* (2), 138–144. https://doi.org/10.1289/ehp.1306656.

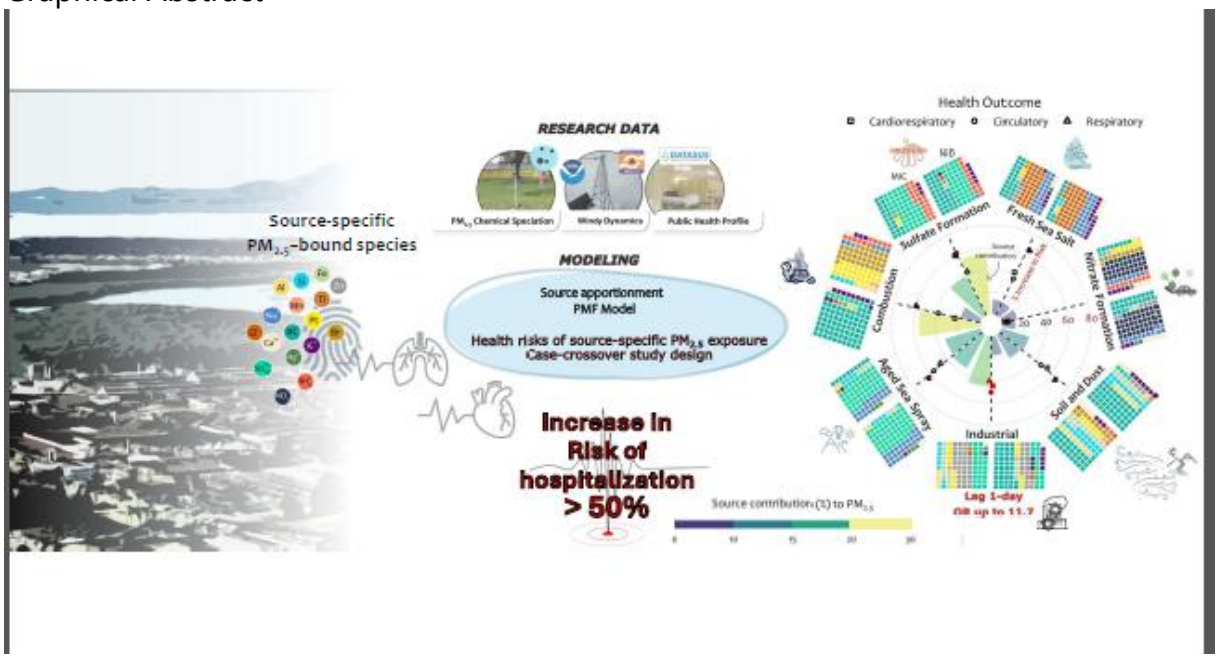
(218) Jung, C.-R.; Young, L.-H.; Hsu, H.-T.; Lin, M.-Y.; Chen, Y.-C.; Hwang, B.-F.; Tsai, P.-J. PM2.5 Components and Outpatient Visits for Asthma: A Time-Stratified Case-Crossover Study in a Suburban Area. *Environmental Pollution* **2017**, *231*, 1085–1092. https://doi.org/10.1016/j.envpol.2017.08.102.

(219) Ostro, B.; Roth, L.; Malig, B.; Marty, M. The Effects of Fine Particle Components on Respiratory Hospital Admissions in Children. *Environ Health Perspect* **2009**, *117* (3), 475–480. https://doi.org/10.1289/ehp.11848.

(220) Atkinson, R. W.; Fuller, G. W.; Anderson, H. R.; Harrison, R. M.; Armstrong, B. Urban Ambient Particle Metrics and Health. *Epidemiology* **2010**, *21* (4), 501–511. https://doi.org/10.1097/EDE.0b013e3181debc88.
(221) Kelly, F. J.; Fussell, J. C. Size, Source and Chemical Composition as Determinants of Toxicity Attributable to Ambient Particulate Matter. *Atmos Environ* **2012**, *60*, 504–526. https://doi.org/10.1016/j.atmosenv.2012.06.039.
(222) Schlesinger, R. B. The Health Impact of Common Inorganic Components of Fine Particulate Matter ($PM_{2.5}$) in Ambient Air: A Critical Review. *Inhal Toxicol* **2007**, *19* (10), 811–832. https://doi.org/10.1080/08958370701402382.
(223) Patel, M. M.; Chillrud, S. N.; Correa, J. C.; Hazi, Y.; Feinberg, M.; KC, D.; Prakash, S.; Ross, J. M.; Levy, D.; Kinney, P. L. Traffic-Related Particulate Matter and Acute Respiratory Symptoms among New York City Area Adolescents. *Environ Health Perspect* **2010**, *118* (9), 1338–1343. https://doi.org/10.1289/ehp.0901499.
(224) Gehring, U.; Beelen, R.; Eeftens, M.; Hoek, G.; de Hoogh, K.; de Jongste, J. C.; Keuken, M.; Koppelman, G. H.; Meliefste, K.; Oldenwening, M.; Postma, D. S.; van Rossem, L.; Wang, M.; Smit, H. A.; Brunekreef, B. Particulate Matter Composition and Respiratory Health. *Epidemiology* **2015**, *26* (3), 300–309. https://doi.org/10.1097/EDE.0000000000000264.
(225) Lee, J. T.; Schwartz, J. Reanalysis of the Effects of Air Pollution on Daily Mortality in Seoul, Korea: A Case-Crossover Design. *Environ Health Perspect* **1999**, *107* (8), 633–636. https://doi.org/10.1289/ehp.99107633.
(226) Carracedo-Martínez, E.; Taracido, M.; Tobias, A.; Saez, M.; Figueiras, A. Case-Crossover Analysis of Air Pollution Health Effects: A Systematic Review of Methodology and Application. *Environ Health Perspect* **2010**, *118* (8), 1173–1182. https://doi.org/10.1289/ehp.0901485.
(227) Santurtún, A.; Sanchez-Lorenzo, A.; Villar, A.; Riancho, J. A.; Zarrabeitia, M. T. The Influence of Nitrogen Dioxide on Arrhythmias in Spain and Its Relationship with Atmospheric Circulation. *Cardiovasc Toxicol* **2017**, *17* (1), 88–96. https://doi.org/10.1007/s12012-016-9359-x.
(228) Slama, A.; Śliwczyński, A.; Woźnica-Pyzikiewicz, J.; Zdrolik, M.; Wiśnicki, B.; Kubajek, J.; Turżańska-Wieczorek, O.; Studnicki, M.; Wierzba, W.; Franek, E. The Short-Term Effects of Air Pollution on Respiratory Disease Hospitalizations in 5 Cities in Poland: Comparison of Time-Series and Case-Crossover Analyses. *Environmental Science and Pollution Research* **2020**, *27* (19), 24582–24590. https://doi.org/10.1007/s11356-020-08542-5.
(229) George, J.; Rapsomaniki, E.; Pujades-Rodriguez, M.; Shah, A. D.; Denaxas, S.; Herrett, E.; Smeeth, L.; Timmis, A.; Hemingway, H. How Does Cardiovascular Disease First Present in Women and Men? *Circulation* **2015**, *132* (14), 1320–1328. https://doi.org/10.1161/CIRCULATIONAHA.114.013797.
(230) Ignotti, E.; Valente, J. G.; Longo, K. M.; Freitas, S. R.; Hacon, S. de S.; Artaxo Netto, P. Impact on Human Health of Particulate Matter Emitted from Burnings in the Brazilian Amazon Region. *Rev Saude Publica* **2010**, *44* (1), 121–130. https://doi.org/10.1590/S0034-89102010000100013.
(231) Bell, M. L.; Son, J.-Y.; Peng, R. D.; Wang, Y.; Dominici, F. Brief Report. *Epidemiology* **2015**, *26* (4), 575–579. https://doi.org/10.1097/EDE.0000000000000310.
(232) Rothman, K. J.; Greenland, S.; Lash, T. L. Case-Control Studies: Overview. In *Wiley StatsRef: Statistics Reference Online*; Wiley, 2014. https://doi.org/10.1002/9781118445112.stat03723.

(233) Maclure, M.; Mittleman, and M. A. Should We Use a Case-Crossover Design? *Annu Rev Public Health* **2000**, *21* (1), 193–221. https://doi.org/10.1146/annurev.publhealth.21.1.193.
(234) Jaakkola, J. J. K. Case-Crossover Design in Air Pollution Epidemiology. *European Respiratory Journal* **2003**, *21* (Supplement 40), 81S – 85s. https://doi.org/10.1183/09031936.03.00402703.
(235) Dominici, F. , , , . Z. A.; Schwartz, J.; Di, Q.; Braun, D.; Choirat, C.; Zanobetti, A. *Assessing Adverse Health Effects of Long-Term Exposure to Low Levels of Ambient Air Pollution: Phase 1.*; Boston, MA, 2019.
(236) Gasparrini, A. A Tutorial on the Case Time Series Design for Small-Area Analysis. *BMC Med Res Methodol* **2022**, *22* (1), 129. https://doi.org/10.1186/s12874-022-01612-x.
(237) Armstrong, B. G.; Gasparrini, A.; Tobias, A. Conditional Poisson Models: A Flexible Alternative to Conditional Logistic Case Cross-over Analysis. *BMC Med Res Methodol* **2014**, *14* (1), 122. https://doi.org/10.1186/1471-2288-14-122.
(238) WHO. *Ambient (outdoor) air pollution*. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health (accessed 2022-03-28).
(239) Laumbach, R.; Meng, Q.; Kipen, H. What Can Individuals Do to Reduce Personal Health Risks from Air Pollution? *J Thorac Dis* **2015**, *7* (1).
(240) Organisation for Economic Co-operation and Development (OECD). *Place-Based Policies for the Future - OECD*. https://www.oecd.org/regional/place-based-policies-for-the-future.htm (accessed 2024-02-18).
(241) Castelhano, F. J.; Pedroso, A. C. N.; Cobelo, I.; Borge, R.; Roig, H. L.; Adams, M.; Amini, H.; Koutrakis, P.; Réquia, W. J. The Impact of Long-Term Weather Changes on Air Quality in Brazil. *Atmos Environ* **2022**, *283*, 119182. https://doi.org/10.1016/j.atmosenv.2022.119182.

Graphical Abstract



Environmental Implications

$PM_{2.5}$ is a heterogeneous mixture of chemicals from multiple sources These fine particles can deeply penetrate the lungs when inhaled, causing a wide range of cardiorespiratory diseases. Their prolonged suspension in the air results in varying toxicity and hazards, influenced by local land use, and weather conditions that affect exposure risks. Our research uses a novel approach, combining receptor-based source apportionment with conditional logistic regression models. This innovative methodology elucidates the source-specific hazardous effects of $PM_{2.5}$-bound species on human health, providing a valuable policy tool to mitigate the environmental and health risks posed by air pollutants.

Declaration of interests

☐ 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.

☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Jessica Caroline dos Santos Silva reports financial support was provided by Coordination of Higher Education Personnel Improvement. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Highlights

- Anthropogenic activities reallocate elements and chemically transform the atmosphere.
- Combined receptor modeling with logistic regression to analyze $PM_{2.5}$ impacts.
- A case-crossover design to assess the health risks of source-specific $PM_{2.5}$ exposure.
- $PM_{2.5}$ from tainted natural sources is linked to increases in hospital admissions > 50%.
- Place-based air quality policies are needed to tackle hazardous sources and hidden risks.