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Effects of long-term exposure to particulate matter and metal components on mortality in the Rome longitudinal study

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A R T I C L E I N F O

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A B S T R A C T

Background: The effect of long-term exposure to metal components in particulate matter on mortality are still controversial.
Objectives: To study the association between long-term exposure to PM_{10}, $PM_{2.5}$, $PM_{2.5}$ absorbance, particulate matter components (copper, iron, zinc, sulfur, silicon, potassium, nickel, and vanadium) and non-accidental, cardiovascular (CVD), and ischemic heart disease (IHD) mortality.
Methods: All 30+ year olds from the Rome Longitudinal Study were followed for vital status from October 2001 until December 2010. We used land use regression models to estimate annual average concentrations at residences and Cox models to estimate the associations between pollutants and cause-specific mortality, adjusting for individual and contextual characteristics. Hazard ratios (HRs) were expressed per increments equal to the 5^{th}–95^{th} percentile range of each pollutant distribution.
Results: We analyzed 1,249,108 residents and found strong associations between all exposure indicators and mortality. We observed higher mortality risk with increasing exposure to $PM_{2.5}$ absorbance (HR = 1.05; 95% CI: 1.03–1.06) and to tracers of non-tailpipe traffic emissions such as tire and brake wear (Cu, Fe, and Zn); for $PM_{2.5}$Zn, we found HR = 1.06 (95% CI: 1.04–1.08) for non-accidental mortality, HR = 1.07 (95% CI: 1.04–1.10) for CVD, and HR = 1.11 (95% CI: 1.06–1.16) for IHD mortality. With increasing levels of nickel in PM_{10}, we found HR = 1.07 (95% CI: 1.05–1.09) for non-accidental mortality, HR = 1.08 (95% CI: 1.05–1.11) for CVD, and HR = 1.13 (95% CI: 1.08–1.18) for IHD mortality. Results were robust when we adjusted for PM mass and for cardiovascular mortality when we adjusted for NO_2.
Conclusions: In addition to vehicular exhaust pollutants, PM related to non-tailpipe emissions and mixed oil burning/industry plays an important role in mortality.

1. Introduction

Particulate matter (PM) is made of a complex mixture of chemical components, depending on the pollution sources. The mass concentrations of $PM_{2.5}$ (particles 2.5 μm or smaller in aerodynamic diameter, largely attributable to combustion processes) and PM_{10} (particles 10 μm or smaller in aerodynamic diameter, which includes larger-sized mechanically generated dust) have been associated with increased mortality and morbidity (Brunekreef and Holgate, 2002; Hoek et al., 2013; Lippmann et al., 2013; WHO, 2013). However, the evidence of the human health effects of the chemical components is still scanty. Several components found in $PM_{2.5}$ and PM_{10} have been considered—copper (Cu), iron (Fe), zinc (Zn), sulfur (S), silicon (Si), potassium (K), nickel (Ni), and vanadium (V) —because they may increase the health risk (Kelly and Fussell, 2012; Stanek et al., 2011). Toxicological evidence about the mechanisms of action of the PM

Abbreviations: CVD, Cardiovascular disease; Cu, Copper; CI, Confidence interval; ESCAPE, European Study of Cohorts for Air Pollution Effects; Fe, Iron; HR, Hazard Ratio; IPW, Inverse probability weighting; IHD, Ischemic heart disease; K, Potassium; LOOCV, Leave-one-out cross validation; LUR, Land-use regression; μg/m^3, Micrograms per cubic meter; Ni, Nickel; ng/m^3, Nanograms per cubic meter; PM, Particulate matter; PM_{10}, Particulate matter with aerodynamic diameter smaller than 10 μm; $PM_{2.5}$, Particulate matter with aerodynamic diameter smaller than 2.5 μm; S, Sulfur; Si, Silicon; TRANSPHORM, Transport-related air pollution and health impacts–integrated methodologies for assessing particulate matter; V, Vanadium; Zn, Zinc

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components is still mixed (Cassee et al., 2013). At least some components have been shown to induce oxidative stress in laboratory test systems, but it is not certain that these mechanisms will also occur at the low ambient concentrations in the environment.

Within the framework of the ESCAPE (European Study of Cohorts for Air Pollution Effects) and TRANSPHORM (transport-related air pollution and health impacts–integrated methodologies for assessing particulate matter) European projects, the relationships between long-term exposure to components of $PM_{2.5}$ and PM_{10} and several health outcomes were analyzed. Beelen et al. found a strong association between natural-cause mortality and $PM_{2.5}$ sulfur, some evidence of association with potassium and nickel components of PM_{10}, and with iron and copper in both PM fractions (Beelen et al., 2015). Long-term exposure to particulate matter components (potassium in $PM_{2.5}$ and PM_{10}, silicon in PM_{10}, and iron in $PM_{2.5}$) has also been associated with higher incidence of coronary events (Wolf et al., 2015). Furthermore, Eeftens et al. detected small adverse effects on lung function related to annual average levels of some elements (particularly, nickel and sulfur) (Eeftens et al., 2014). On the other hand, Wang et al. found no statistically significant association between long-term exposure to eight elemental component particles (Cu, Fe, Zn, S, Si, K, Ni, and V) and cardiovascular mortality (Wang et al., 2014). Various PM components, in particular sulfur and nickel, have been linked to lung cancer incidence (Raaschou-Nielsen et al., 2016). $PM_{2.5}$Cu and PM_{10}Fe were associated with increased levels of inflammation markers (Hampel et al., 2015).

In the US, Ostro et al. reported the association of long-term exposure to 19 components and sources of both $PM_{2.5}$ and ultrafine particles with mortality from all natural causes, cardiovascular disease, ischemic heart disease, and pulmonary disease (Ostro et al., 2015). Among the components investigated, $PM_{2.5}$Cu was associated with an increase of IHD mortality. More recently, Thurston et al. found an association between exposure to iron and zinc in $PM_{2.5}$ and IHD mortality (Thurston et al., 2016). Wang et al. studied 13.1 million Medicare beneficiaries (age ≥ 65) residing in seven southeastern US states and observed that mortality "risk associated with $PM_{2.5}$ increased with relative concentration of elemental carbon, vanadium, copper, calcium, and iron and decreased with nitrate, organic carbon and sulfate" (Wang et al., 2016).

Despite all the literature on the topic, it is still unclear which components of particulate matter are the most deleterious. Moreover, the magnitude of these associations and whether the associations observed between the components and health are independent of PM mass are also unclear. The aim of this study was to evaluate the association between long-term exposure to particulate matter (PM_{10}, $PM_{2.5}$, $PM_{2.5}$ absorbance, and metal components) and non-accidental, cardiovascular (CVD), and ischemic heart disease (IHD) mortality among the adults included in a large cohort, and to investigate which components, independent of PM mass, are associated with mortality.

2. Methods

2.1. The setting and cohort

The study was conducted in Rome, Italy. As of January 1, 2015, the population was about 2.8 million residents over a large 1,285 km^2 area. The study population is from the Rome Longitudinal Study (RoLS), the 2001 census administrative cohort (Italian National Statistical Programme 2011–2016) approved by the Italian Data Protection Authority. The RoLS cohort has been described elsewhere, together with the results of long-term exposure to $PM_{2.5}$ (based on a dispersion model) and to NO_2 (based on a land-use regression model) (Cesaroni et al., 2013). Briefly, all residents aged 30+ years as of October 21, 2001, were included (census reference day), who had lived in Rome for at least 5 years and did not reside in an institution (prisons, hospitals, or nursing homes). The Rome Municipal Register and the Regional Mortality Register were used to determine vital status and causes of death from October 2001 to December 2010. Subjects were followed until December 31, 2010, unless they died or moved outside the city before that date. Those who moved out of Rome during the follow-up were considered lost to follow-up.

2.2. Exposure assessment

We used the LUR models developed in the ESCAPE and TRANSPHORM projects to assess exposure at the baseline residential address of the study subjects (de Hoogh et al., 2013; Eeftens et al., 2012a). For these two European projects, several LUR models were developed to assess particulate matter exposure (PM_{10}, $PM_{2.5}$) absorbance of $PM_{2.5}$ (a proxy of black carbon, representing exhaust emissions) and trace elements in PM_{10} and $PM_{2.5}$, considered a priori indicators of other major anthropogenic sources. Copper (Cu), iron (Fe), and zinc (Zn) were chosen to represent non-tailpipe traffic emissions (particles from brakes, tires, and road surface), sulfur (S) for long-range transportation, silicon (Si) for crustal material, potassium (K) for biomass burning and soil, and nickel (Ni) and vanadium (V), selected for mixed oil burning/industry (de Hoogh et al., 2013; Viana et al., 2008). A particulate matter–monitoring campaign was conducted in Rome for 1 year that started on Jan 28, 2010, and it has been described in detail by Eeftens et al. (Eeftens et al., 2012b). Briefly, particulate matter (PM) was measured at 20 sampling sites, chosen to represent the spatial distribution of residential addresses. Regional background ($N = 2$), urban background ($N = 8$) and traffic sites ($N = 10$) were selected. At each site, PM was measured for 14 days in the cold, warm, and intermediate seasons. A temporal correction was calculated using a background reference site that operated for the entire year (Eeftens et al., 2012b).

Table A1 in the appendix shows all predictor variables with the source of data, predefined variable names, units, and buffer sizes used for the LUR models (Eeftens et al., 2012a; de Hoogh et al., 2013).

Table A2 shows the equations and the performance of the LUR models for all considered pollutants. Overall model performance was evaluated by R^2 and by leave-one-out cross validation (LOOCV). In the LOOCV, each site was sequentially left out from the model while the included variables were left unchanged (Eeftens et al., 2012a).

In this particular study, we used all the LUR models developed in the two projects with an LOOCV-$R^2 > 0.50$ (Table A2); we considered three components for $PM_{2.5}$ (Cu, Fe, Zn), and seven (Cu, Fe, Zn, Si, K, Ni, V) for PM_{10}. The models developed to estimate the PM mass ($PM_{2.5}$ and PM_{10}), $PM_{2.5}$ absorbance, and metals from non-tailpipe vehicular emissions (Cu, Fe, and Zn) had high R^2 (range: 0.71–0.89) and high validation R^2 (range: 0.59–0.79). Models for Si, K, Ni, and V components of PM_{10} performed well (R^2 = 0.64–0.90, and validation R^2 = 0.57–0.86).

2.3. Health outcomes

We analyzed non-accidental mortality, CVD mortality, and IHD mortality. Causes of death were coded according to the International Classification of Disease, 9th Revision (ICD-9) based on codes: < 800, 390–459, and 410–414.

2.4. Covariates

A set of potential individual-level confounders was available from the 2001 census. We included in the analysis sex, date of birth, marital status (married, single, separate/divorced, or widowed), place of birth (Rome or other), education (university, high school, junior high school, or primary), and occupation (high-qualified non-manual: managers, university or high school professors, and researchers; other non-manual employed; manual labor employed; other employed: armed forces and retail sales; housewife; unemployed; retired; or other) (Cesaroni et al.,