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Zinc compound air releases from Toxics Release Inventory facilities and cardiovascular disease mortality rates

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ABSTRACT

Background: Inhaled zinc has been found in association with cardiopulmonary toxicity. However, limited human epidemiologic studies are available. This study analyzed the association between covariate-adjusted cardiovascular (CVD) mortality rates and zinc compound air releases in the United States.
Methods: We conducted an ecological analysis on the association between zinc compound air releases for 1991–2000 using the Toxics Release Inventory database and average age-adjusted CVD mortality for 2006–2010, adjusting for race/ethnicity composition and several health and socioeconomic factors. Models were estimated for males and females and for metropolitan and nonmetropolitan counties.
Results: Zinc compound air releases were positively associated with increased adjusted CVD mortality rates in all four models (β=0.0085, $p<0.0001$ for males in nonmetropolitan counties; β=0.0093, $p<0.0001$ for males in metropolitan counties; β=0.0145, $p<0.0001$ for females in nonmetropolitan counties; and β=0.0098, $p<0.0001$ for females in metropolitan counties). Results were largely robust to various sensitivity analyses.
Conclusion: This study provides epidemiological evidence for possible CVD health impacts of inhaled zinc in the United States. Although the strongest effect was found for females in nonmetropolitan counties, the associations were consistent in nonmetropolitan or metropolitan counties for both genders.

1. Introduction

Cardiovascular diseases (CVD) have remained the top leading cause of death in the United States for more than 20 years (National Center for Health Statistics, 2014). The estimated annual cost of CVD is $315 billion (Go et al., 2014). Individuals can reduce the risk of CVD by eating a healthy diet, doing regular physical activity, and not smoking (Goff et al., 2014). However, individuals have less control over other CVD risk factors-including genetic factors, social structure, and environmental pollution.

Zinc and zinc compounds are widely used chemicals in industrial processes. Zinc is the fourth most widely used metal (US Geological Survey, 2015). One could expect increased use of zinc with advances in medical, textile, and optical electronic applications and production technologies (Becheri et al., 2007; Choi et al., 2014; Hau et al., 2008; Liu et al., 2009; Wang, 2004; Yadav et al., 2006). It is the second most abundant compound among the metals reported in the Speciation Trends Network 2008 after iron (US EPA, 2013). It was also the chemical that had been reported by the largest number of counties in the TRI dataset for 1991–2000. Our choice of zinc for this study was intended to add to the limited evidence base for possible CVD risk from exposure to this widely used industrial chemical.

Exposure to particulate matter (PM) is of major environmental concern in the etiology of CVD (Breysse et al., 2013; Brook et al., 2004; Gold and Mittleman, 2013). Epidemiological studies have documented both long- and short-term health effects of PM exposure (Chang et al., 2011; Gan et al., 2011; Peng et al., 2009; Rich et al., 2012; Weichenthal et al., 2014). PM induced inflammation has been proposed to be responsible for increased CVD risk (Ghio and Devlin, 2001). Some studies had attempted to evaluate whether zinc is part of the risk-bearing PM components. Zinc has inflammatory properties but evidence on its possible links to population CVD is inconclusive. Studies in cell lines, rats, and rabbits had reported profound cardiac and systemic effects of zinc exposure in both cellular and tissue levels (Chuang et al., 2014; Gilmour et al., 2006a, 2006b; Kodavanti et al., 2008; LaGier et al., 2008; Moos et al., 2011), which include alteration in metal homeostasis, up-regulation of inflammatory and coagulation

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related proteins, and cardiac inflammation and fibrosis. Occupational exposure to zinc has been linked to respiratory syndromes and general symptoms like fever and fatigue, although these studies did not follow CVD endpoints and reported that effects generally resolved in days (Freitag and Caduff, 1996; Hartmann et al., 2014; Luo et al., 2009; Malo and Cartier, 1987; Safty et al., 2008). In contrast to an earlier animal study that suggested zinc may be a crucial component in the inflammatory response to PM (Adamson et al., 2000), later epidemiological studies did not fully support this hypothesis. While Ostro et al. (2010) were able to demonstrate consistent associations between nitrate, potassium, iron, silicon, and zinc and mortality risk among California female teachers for 2002–2007, Zanobetti et al. (2009) found that only nickel, arsenic, chromium, bromide, and organic carbon were associated with increased hospital admissions in 26 US metropolitan areas for 2000–2003 among 10 metals, including zinc, and 8 other chemical species. Bell et al. (2009) reported that only vanadium, elemental carbon, and nickel PM2.5 among 20 PM components, including zinc, showed consistent association with hospital admissions in another study among 106 US counties for 2000–2005.

The Toxics Release Inventory database (TRI) hosted by the Environmental Protection Agency has been used for several ecological studies that investigate associations between industrial pollutant releases and health outcomes (Wine et al., 2014). We previously found that higher metal releases to the air from TRI facilities are associated with significantly higher adjusted CVD population mortality rates (Hendryx et al., 2014). However, this study did not investigate which specific metals may be responsible for the elevated mortality rates. We aimed to extend the prior study by evaluating the association between CVD mortality and the compounds of a specific metal, zinc, and to provide epidemiological evidence on the CVD risk of inhaled zinc chemicals. We evaluated the potential associations between long-term exposure to zinc compound industrial releases and CVD mortality, allowing a time-lag and controlling for a set of covariates. We aimed to provide ecological evidence at the national level for the US population.

2. Method

2.1. Design

We conducted a retrospective ecological study including all counties in the United States. The primary outcome variable was age-adjusted CVD mortality per 100,000. The primary independent variable of interest was the area-adjusted cumulative amount of zinc compound air releases reported in the TRI database. Data for the study were gathered from five sources described below: the Environmental Protection Agency's (EPA) TRI database, the EPA AirData dataset, the County Health Rankings Data, the Centers for Disease Control and Prevention (CDC) Mortality Files, and the Area Health Resource File.

2.2. Toxics Release Inventory

The Toxics Release Inventory (TRI) is an administrative dataset that reflects "annual quantities (in pounds) of toxic chemicals released from a facility to the environment, managed by the facility as waste, transferred from the facility to another facility for release or other waste management" (US EPA, 2012). The dataset is compiled by the EPA with reports from more than 53,000 facilities that handle toxic chemicals across the US (US EPA, 2012). Each record contains facility information, chemical information, and columns for amount (in pounds) of chemical releases into air, water, land, and summations of the three, as well as amount of the chemical that was transferred to another facility. There is a separate line of data for each chemical within each facility, each year. We extracted the data using the TRI.net application. The application is available on the EPA website (http://www2.epa.gov/toxics-release-inventory-tri-program/tri-data-and-tools). We compiled a county level dataset that aggregated the air release of zinc compounds for the ten years between 1991 and 2000. For the current study we examined only air releases. We summed the zinc compound air releases for all facilities across the ten years in each county into a single measurement to represent the cumulative release in the county. We aggregated to the county to be able to merge to CVD mortality statistics which are reported at the county level (see below). A county identifier, the Federal Information Processing Standards (FIPS) code, was used to merge with other datasets.

2.3. Cardiovascular diseases mortality

Cardiovascular disease (CVD) mortality data were downloaded from the CDC Wonder website (http://wonder.cdc.gov/mortsql.html). We obtained age-adjusted CVD mortality per 100,000 persons for each US county. All CVD diagnoses were included. It has been shown that CVD mortality differs among age groups (Pagidipati and Gaziano, 2013). We used age-adjusted CVD mortality to adjust for the different age-composition among the counties. The age-adjustment was based on the 2000 US standard population. We used the average annual mortality across 5 years to create a reliable estimate. Data from 2006 to 2010 were chosen to allow a delay between the years of exposure and mortality outcome.

2.4. County health ranking data

County health ranking data were downloaded from the County Health Rankings website (http://www.countyhealthrankings.org/rankings/data). We obtained County Health Rankings National Data and used primarily the records in the "Ranked Measure Data" section. The 2012 data were chosen for the most complete set of potential covariates of interest. The actual year of data collection for the indicators varies from measure to measure, but the county level population estimates tend to be stable from year to year. We examined the following variables as potential covariates in regression analyses to represent significant behavioral and socioeconomic influences on mortality risk: adult smoking rate, obesity rate, percentage of adults who are physically inactive, percentage of population without health insurance, primary care physicians to population ratio, percentage high school graduates, percentage with at least some post-secondary (college) education, unemployment rate, and percentage of children in single-parent households. The adult smoking rate data were missing for 617 counties (20% of total counties). We replaced missing smoking data with an estimate for each county obtained from our examination of state public health department websites. These estimates were based on Behavioral Risk Factor Surveillance System (BRFSS) state-specific survey results and were sometimes specific to a county, sometimes specific to a group of contiguous counties, and in a few cases limited to a state average. This method of estimating missing cases did not change the overall observed percent: before making this estimate the average county smoking percent was 21.2, and after the adjustment the average percent was 21.4.

2.5. Area Health Resource File

Area Health Resource File data were downloaded from the Health Resources and Services Administration website (http://www.hrsa.gov/data-statistics/). We used variables from the 2005