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# Total and cardiovascular mortality rates in relation to discharges from toxics release inventory sites in the United States



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## ABSTRACT

*Background:* This study analyzed Toxics Release Inventory (TRI) discharges in association with covariateadjusted total and cardiovascular mortality rates for males and females in US counties. *Methods:* Average annual county-level reported releases from TRI facilities measured in pounds per square mile which were calculated for the years1990–1999, and tested for associations with age-adjusted mortality rates for 2006–2010. Chemicals were grouped into four categories: 1) carcinogens, 2) metals, 3) hazardous air pollutants, and 4) chemicals in the Comprehensive Environmental Response, Compensation and Liability Act. For each of these chemical groups the reported total, water, and air emissions were measured. Age-adjusted mortality rates were found separately for males and females from the Centers for Disease Control and Prevention for total and cardiovascular disease. Covariates included rates of smoking, obesity, high school and college education, race/ethnicity, poverty, unemployment, percent without health insurance, and urban-rural setting. Data were analyzed using multiple linear regression models.

*Results:* Greater average annual TRI releases in 1990–1999 in all four chemical categories were significantly associated with higher mortality rates in 2006–2010 for both total and cardiovascular mortality, and for both males and females, adjusted for covariates. Associations were stronger for air releases than for water releases.

*Conclusions:* This study provides the first evidence that greater amounts of TRI releases are related to higher population mortality rates for cardiovascular disease. In addition, the study showed that adverse TRI effects were broadly present for both males and females for multiple chemical groups. Further progress is needed to reduce the use and release of harmful chemicals from TRI facilities in the United States.

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## 1. Introduction

Data on chemical releases from industrial sources in the United States have been reported annually since 1988 through the Environmental Protection Agency's Toxics Release Inventory (TRI). A number of recent studies have investigated associations between chemical releases from TRI facilities and human health population outcomes. For example, Boeglin et al. (2006) observed that releases of volatile organic compounds from TRI facilities were associated with higher incidence rates for some types of cancer. Their study employed a county-level ecological design and was limited to releases occurring in facilities in Indiana. Other state-specific studies have observed higher incidence of bladder

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http://dx.doi.org/10.1016/j.envres.2014.05.010 0013-9351/© 2014 Elsevier Inc. All rights reserved. cancer in association with TRI facilities in Utah (Fortunato et al., 2011), and a modest but significant association between maternal residence near TRI facilities in Texas and risk of neural tube birth defects in offspring (Suarez et al., 2007). Most published studies have demonstrated significant associations between TRI sites or releases and health outcome measures of interest, although there are cases where no associations were observed (Langlois et al., 2009).

In addition to state-level studies, nationwide studies of TRI data in relation to population health indicators have also been undertaken. Agarwal et al. (2010) demonstrated that toxic air pollutants, especially carcinogens, were linked to higher infant mortality rates. Ho and Hite (2009) found that greater TRI releases were significantly associated with higher reported number of workdays lost to illness. A study by Hendryx and Luo (2013) found higher hospitalization rates for some cancer types in relationship to carcinogenic releases from TRI facilities. Another study reported significant associations between air releases of carcinogens and lung cancer mortality, but after control for covariates the effect was limited to rural and not urban areas (Luo and Hendryx, 2011). Luo et al. (2011) observed significant associations between lung cancer incidence and release amounts of three specific TRI chemicals (chromium, formaldehyde, and nickel) but no significant associations for three other chemicals (arsenic, 1–3 butadiene and cadmium.)

Most studies examining health impacts of TRI releases have focused on either maternal/infant outcomes, or cancer outcomes. In particular, it appears that no published studies have examined whether or not TRI releases are related to cardiovascular disease. However, evidence from both human and animal studies (Araujo et al., 2008; Belleudi et al., 2010; Delfino et al., 2005; Goldberg et al., 2001; Mastin, 2005; O'Toole et al., 2008; Wellenius et al., 2006; Zhang et al., 2012) suggest that a variety of air pollutants including ozone, dioxins, polychlorinated biphenyls, polyaromatic hydrocarbons, ultrafine particulate matter, PM2.5 and PM10 are related to cardiovascular disease. Studies of water pollution are less common but cardiovascular risk has been linked to arsenic in drinking water (Medrano et al., 2010; Moon et al., 2013; Wu et al., 2012), and potentially to high levels of cadmium and lead in water (Wang et al., 2011). The current study contributes to the evidence base on the effects of TRI releases on health outcomes by conducting an analysis of national mortality rates in relation to releases of various chemical classifications separately for men and women. We investigated associations for total mortality as well as mortality from cardiovascular disease. Within cardiovascular disease we examined all forms combined, as well as the subset of ischemic heart disease diagnoses. We employed a set of covariates to control for confounding influences on population mortality rates. We allowed for temporal effects by associating TRI releases in the years 1990-1999 to mortality occurring in the years 2006-2010: this time period is consistent with exposure periods that have been used to detect associations between ambient air pollution and cardiovascular events (Atkinson et al., 2013; Cesaroni et al., 2014). Our hypothesis is that higher amounts of TRI releases will be significantly associated with higher total and cardiovascular mortality rates after controlling for covariates.

#### 2. Materials and Methods

#### 2.1. Design

The study design was an ecological, county-level retrospective analysis for all US counties. The primary dependent measures of interest were age-adjusted mortality rates. The primary independent measures of interest were reported amounts of TRI chemical releases per county square mile for the years 1990–1999. Population covariates were used to adjust for the relationship between TRI releases and mortality outcomes. Data for the study were gathered from four sources described below: the Environmental Protection Agency's (EPA) TRI, the County Health Rankings Data, the Centers for Disease Control and Prevention (CDC) Mortality Files, and the Area Health Resource File.

#### 2.2. Data sources and variables

#### 2.2.1. TRI chemical classifications

Toxics Release Inventory (TRI) data were taken from the TRI.Net application available on the EPA TRI website (EPA, 2014d). In general, chemicals included in the TRI database are those that cause cancer, other chronic human health effects, significant acute human health effects, or significant adverse environmental effects. The number of chemicals have changed over time; currently 682 chemicals and chemical categories are included (EPA, 2014c). We investigated chemicals found in one or more of four TRI classifications; in many cases a particular chemical will be present in more than one classification:

2.2.1.1. Carcinogens. The TRI includes 198 known or suspected human carcinogens based on Occupational Safety and Health Administration (OSHA) classifications (EPA, 2011). Although the current study investigated cardiovascular outcomes, chemicals that are carcinogenic may also have other adverse health impacts,

including impacts on the cardiovascular system. For example, benzene (Bahadar et al., 2014), vinyl chloride (Gennaro et al., 2008) and polychlorinated biphenyl exposures (Coburn et al., 2007) have been linked to cardiovascular illness.

2.2.1.2. Metals. The TRI includes 17 metals, each with its corresponding metal compound (total of 34 chemicals) including antimony, arsenic, barium, beryllium, cadmium, chromium, cobalt, copper, lead, manganese, mercury, nickel, selenium, silver, thallium, vanadium, and zinc (EPA, 2014b). Some of these metals have been shown to increase the risk of cardiovascular disease (Agarwal et al., 2011; Campen et al., 2001; Mendy et al., 2012; Navas-Acien et al., 2005).

2.2.1.3. Hazardous air pollutants. The TRI includes 190 chemicals recognized as hazardous air pollutants (EPA, 2014a). Hazardous air pollutants (HAPs) include metals, gases, solvents and pesticides that in many cases are thought to have no minimum safe threshold of exposure (Young et al., 2012). They potentially target multiple organ systems and have possible synergistic effects that are not well understood. Although these chemicals may also be released into water, for the present analysis releases into water were not considered within this group.

2.2.1.4. CERCLA (Comprehensive Environmental Response, Compensation and Liability Act) chemicals. This Act provided for the identification of a priority list of hazardous substances. The current list, maintained by the Agency for Toxic Substances and Disease Registry and last updated in 2011, includes 275 chemicals (ATSDR, 2014). Some of these chemicals are also found in the lists of carcinogens, metals, and hazardous air pollutants.

We calculated the releases of all chemicals and chemical compounds in each of the four classifications, measured as pounds of release per county square mile. For each of the classifications, three release measures were calculated: total emissions, total water emissions, and total air emissions. Both on-site and off-site emissions were included. Releases in pounds were summed for each county over the 10 year period and then an annual mean was found for each county for the 10 year period 1990–1999. To correct for county size, release quantities were divided by county land square miles; county size in land square miles was measured using Area Health Resource File data. The resulting distributions of release quantities were positively skewed, so we added 1 to each observation and then found the natural log of release values for purpose of statistical analysis.

#### 2.2.2. Mortality data

Age-adjusted mortality rate data were obtained from the CDC compressed mortality files (CDC, 2013). The age-adjustment used the 2000 US standard population. Age-adjusted rates were found for males and females separately for each county. Rates were collapsed across five years (2006–2010) to obtain more reliable estimates than would be found for a single year. We thus examined the relationship between average TRI releases for 1990–1999 and average annual age-adjusted mortality for 2006–2010, assuming a delay between exposure and health outcomes.

Age-adjusted mortality rates were found for total mortality, for all forms of circulatory diseases, and for ischemic heart disease. Disease classifications were based on ICD-10 codes; circulatory system disease included codes I00-I99, and codes I20-I25 were used for ischemic heart disease.

#### 2.2.3. County health rankings data

The 2012 County health rankings data was used as a source for potential covariates to adjust for confounds in the relationship between TRI discharges and mortality outcomes (County Health Rankings and Roadmaps, 2014). We chose 2012 rather than other years because the 2012 data release offered the most complete set of potential covariates of interest; the actual year of data collection for the indicators varies from measure to measure and may be found by examining the County Health Rankings website. County level population estimates tend to be stable from year to year. The set of covariates included was intended to represent significant behavioral and socioeconomic influences on mortality risk. We initially considered the following variables as potential covariates in the regression analyses: adult smoking percent, adult obesity percent, percent adults who are physically inactive, percent without health insurance, number of primary care physicians per capita, percent high school graduation, percent with at least some post-secondary (college) education, percent unemployed, and percent children in single-parent households. We dropped the number of primary care physicians per capita because it had missing observations and because the direction of effect was inverse to expectation (more physicians per capita at the county level were related to higher mortality rates.) Adult smoking data were missing from 617 counties (20% of total counties). We replaced missing smoking data with an estimate obtained from our examination of state public health department websites; these estimates were based on Behavioral Risk Factor Surveillance System (BRFSS) statespecific 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.

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