Environ Geochem Health
https://doi.org/10.1007/s10653-018-0175-z

ORIGINAL PAPER

Population-based mortality data suggests remediation is modestly effective in two Montana Superfund counties

B. Davis · S. McDermott · M. McCarter · A. Ortaglia

Received: 28 March 2018 / Accepted: 15 August 2018

Abstract The health effects of living in proximity to Superfund sites with ongoing remediation were evaluated for residents of two contiguous Montana counties, Deer Lodge and Silver Bow. Deer Lodge and Silver Bow are home to the Anaconda Smelter and Silver Bow Creek/Butte Area Superfund sites, respectively. Established by the Environmental Protection Agency in 1983, both sites have had ongoing remediation for decades. Employing county level death certificate data obtained from the Centers for Disease Control and Prevention WONDER site, sex and age-adjusted standardized mortality ratios (SMRs) for composite targeted causes of death were calculated using observed versus expected mortality for both counties, and compared to the expected mortality from the remaining Montana counties. Cancers, cerebro- and cardiovascular diseases (CCVD), and organ failure were elevated for the two counties during the study period, 2000–2016, with SMRs of 1.19 (95% CI 1.10, 1.29); 1.36 (95% CI 1.29, 1.43); and 1.24 (95% CI 1.10, 1.38), respectively. Neurological conditions were not elevated for the two counties (SMR = 1.01; 95% CI 0.89, 1.14). Time trend analyses performed using Cox regression models indicate that deaths from cancers (HR = 0.97; $p = 0.0004$), CCVDs (HR = 0.95; $p \leq 0.0001$), and neurological conditions (HR = 0.97; $p = 0.01$) decreased over the study period. While the ecological approach applied limits the interpretation of our results, our study suggests that while mortality is elevated, it is also decreasing over time for these two Superfund sites.

Keywords Superfund site · Heavy metal exposure · Standardized mortality ratio · Directly adjusted mortality rate · Remediation · Open-pit mining

B. Davis · S. McDermott (✉) · M. McCarter · A. Ortaglia
Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA
e-mail: Smcdermo@mailbox.sc.edu

Introduction

The Environmental Protection Agency's (EPA) Superfund program was established in 1980, with the overarching aim of protecting public health and the environment; "the Superfund program focuses on making a visible and lasting difference in communities, ensuring that people can live and work in healthy, vibrant places" (US EPA 2018). Since its inception, thousands of Superfund sites have been established in the United States. One of the largest and longest standing sites lies in Deer Lodge and Silver Bow counties, Montana (EPA 2015, 2016). The city of Butte, in Sliver Bow county, is a mining town established for the exploration of copper, gold, and silver. The Berkeley Pit operated in Butte from 1955 to

Published online: 23 August 2018

1982; the still operating Continental Pit opened in 1986 (EPA 2016). These mines—along with mills, smelters, and concentrators—created millions of cubic yards of mine waste, including mill tailings, slag, waste rock, and dust (EPA 2016; Gammons et al. 2006). Northwest of Silver Bow is a smaller county, Deer Lodge, where the Anaconda Mine Company operated a smelter to refine the copper ore mined in Silver Bow (EPA 2015). The two contiguous counties, Deer Lodge and Silver Bow, are home to the Anaconda Smelter and Silver Bow Creek/Butte Area Superfund sites, respectively. The EPA recently reported they have 'insufficient data' on whether human exposure is under control in Butte, and the agency lists human exposure in the Anaconda site as 'not under control' (EPA 2015, 2016).

In order to determine the exposure risk for the residents, many soil, sediment, and water samples have been collected in the Butte and Anaconda areas as part of the Superfund activities. The EPA lists the following metals in elevated quantities in Butte and Anaconda soil, air, water, or house dust: arsenic, cadmium, copper, lead, and zinc (EPA 2015, 2016), with Butte being additionally exposed to excess aluminum, iron, mercury, and silver (EPA 2016). The Butte Priority Soils Database, created as part of the Remedial Investigation Report for the Butte Priority Soils Operable Unit (BPSOU), contains concentrations of five metals: arsenic, cadmium, copper, lead, and zinc, measured in approximately 2700 soil samples collected in the Butte area, indicated elevated levels for all five levels (Butte GIS 2006). Furthermore, a recent publication reported significantly elevated concentrations of aluminum, arsenic, cadmium, copper, manganese, molybdenum, and uranium within Butte and its residents when compared to Gallatin county, Montana (Hailer et al. 2017). Data collected thus far suggests that previous and current mining practices still expose residents to heavy metals via inhalation, ingestion, and dermal absorption.

Heavy metals are capable of causing harmful human effects because of oxidative reactions (Sharma et al. 2014), disruption of hormonal and metabolic functions (Rana 2014), and accumulation in organ systems (Jaishankar et al. 2014). Specific cancers, heart disease, pulmonary disease, and several neurological conditions have been strongly associated with heavy metal exposure (See Table 2).

Studies investigating the health outcomes of metal exposures for the residents of Butte or Deer Lodge are limited. A series of papers released from 1969 to 2000 followed a cohort of 8047 white male smelter workers from the Anaconda smelter. The original report suggested a threefold excess of respiratory cancer among the smelter workers exposed to arsenic released in the copper smelting process (Lee and Fraumeni 1969). Other studies also reported increased death from lung cancer with environmental arsenic exposure (Welch et al. 1982; Brown and Chu 1983; Lee-Feldstein 1986; Lubin et al. 2000). Another study, reported null findings when analyzing 1980–1986 skin cancer data for Butte and Deer Lodge when compared to Gallatin and Park counties (Wong et al. 1992). However, two additional studies suggested higher than normal rates of cancer (National Cancer Institute 2009) and neurodegenerative disease (Satterly 1995).

The most recent EPA five-year reviews for Anaconda's and Butte's Superfund sites reported seven and five remaining operational units (OU), respectively. According to that report, remediation efforts are complete for six of Butte's OUs. There has been some evidence of progress within the OUs, however these findings need to be verified by routine testing (EPA 2016). The Streamside Tailings OU was reported to have a decline of chemicals of concern (COC); however, surface water, floodplain well water, and weighted mean sediment levels still exceed target COC levels (EPA 2016). The Berkeley Pit/Mine Flooding OU (BMFOU) has routinely tested above acceptable levels of COC since the remediation began. Further, the Berkeley Pit is at risk of exceeding acceptable water levels by 2023; with an expectation for toxic flooding (EPA 2016). Remediation efforts for the Rock and Timber Framing and Treating and Warm Springs Ponds OUs are also problematic, as arsenic levels continues to exceed EPA recommendations (EPA 2016). Lastly, testing for the Butte Priority Soils OU (BPSOU) reveals unacceptable levels of copper and zinc (EPA 2016).

The 5-year EPA review of remediation in Anaconda is ongoing for three of its OUs including the Old Works/East Anaconda Development Area (OW/EADA), Community Soils OU, and the Anaconda Regional Water, Waste and Soils (ARWW&S) OU (EPA 2015). The site-wide activities include ground and surface water remediation in all OUs and remediation efforts have been concluded for over 340 residential properties and more than 11,500 acres of affected land (EPA 2015). Regardless of the latest 5-year updates, an EPA statement in December 2017 listing Anaconda and Butte's Superfund sites as targets for immediate and intense attention (EPA 2017).

Successful remediation efforts for other Superfund sites have been related to improvements in human exposure to toxins (von Lindern et al. 2003) and health outcomes (Currie et al. 2011). One study that examined the effects of Superfund cleanup on infant health reported a 20–25% reduction in birth abnormality incidence (Currie et al. 2011). However, not all remediation efforts have translated to improved health outcomes. The Tar Creek Superfund site in Oklahoma was established in 1983 with remediation beginning soon after (EPA 2015). Excess mortality was found for cerebro- and cardiovascular conditions. Further, within an exposed community, 62.5% of the children under the age of six had excessive blood lead levels (Neuberger et al. 2009).

This study aims to investigate the mortality experience of residents of Deer Lodge and Silver Bow compared to other Montana counties, over the time period of 2000–2015. Using an ecological approach with county level mortality data, we aim to infer the success or failure of remediation efforts. Were remediation efforts for these two Superfund sites effectual, there should be a decline in age and sex adjusted death from select cancers, cerebro- and cardiovascular diseases, neurologic conditions, and organ failure, during the study period. Our study is strengthened by the use of a series of statistical methods that go beyond the typical approach. Cox regression was implemented to estimate our standardized mortality ratios (SMRs). Further, we assessed homogeneity in our age and sex groups, and by time to ensure we display the most accurate and meaningful estimates.

Methods

Our study's aim was to identify any excess mortality from an a priori selection of causes of death associated with heavy metal exposure in Deer Lodge and Silver Bow. Further, our study will evaluate any changes in mortality related to our targeted conditions over our 16-year study period. As remediation has been ongoing for decades, we would expect beneficial remediation to communicate a decrease in adverse health consequences.

The tested hypotheses are:

- There will be significantly higher standardized mortality ratios for a priori selected causes of mortality related to heavy metal exposure, during 2000–2015, for residents of Deer Lodge and Silver Bow compared to the comparison counties.
- There will be significant decreases in the standardized mortality ratios for a priori selected causes of mortality related to heavy metal exposure for residents of Deer Lodge and Silver Bow compared to the comparison counties over the 2000-2015 study period.

Selected metals

A literature search was conducted to identify the metals located in the Deer Lodge and Silver Bow Superfund sites, the exposure route, and relationship to mining (Table 1). Arsenic, cadmium, copper, lead, and zinc have been found in elevated amounts for both case counties (EPA 2015, 2016) with Butte being additionally exposed to excess aluminum, iron, manganese, mercury, molybdenum, silver, and uranium (EPA 2015; Hailer et al. 2017).

Selected causes of death

Targeted causes of death, shown in Table 2, were included when there was strong epidemiological consensus of an association between the heavy metal exposure and disease outcome. The specific diagnoses and associated International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes for select cancers (brain, bladder, breast, bronchus and lung, kidney, liver, pancreas, skin, stomach), cerebro- and cardiovascular diseases (atherosclerosis, cerebrovascular disease, ischemic heart disease, heart failure), neurologic conditions (Alzheimer's disease, motor neuron disease, multiple sclerosis, Parkinson's disease), and organ failures (kidney and liver), are shown (WHO 2015).

Comparison mortality data

The case counties in this study are Deer Lodge and Silver Bow, which have been Superfund locations

Table 1 Known heavy metal exposures for Deer Lodge and Silver Bow counties

Metal	Human exposure identified	Sources of exposure identified	Relationship to mining
Aluminum[a]	Hair	Surface water	Combined with copper to form an alloy-aluminum bronze
Arsenic[b]	Blood	Air	Released during the copper mining process
	Hair	Buildings/structures	
		Ground and surface water	
		Sediment	
		Soil	
		Solid waste	
Cadmium[b]	Hair	Air	Released during the mining and smelting processes
		Buildings/structures	
		Ground and surface water sediment	
		Soil	
		Solid waste	
Copper[b]	Hair	Ground and surface water	Mined from the Berkeley and Continental Pits
		Sediment	
		Soil	
Iron[a]		Ground and surface water	Present in the copper minerals and released in the smelting stage
Lead[b]	Blood	Air	Mined from the Berkeley Pit
		Buildings/structures	
		Ground and surface water	
		Sediment soil	
		Solid waste	
Manganese[a]	Hair	Air	Mined from the Berkeley Pit
		Ground water	
Mercury[a]		Ground and surface water	Used to purify gold mined from the Berkeley Pit
		Sediment	
		Soil	
Molybdenum[a]	Hair		Mined from the Berkeley and Continental Pits
Zinc[a]		Soil	Mined from the Berkeley Pit
		Ground and surface water	
		Sediment	
Uranium[a]	Hair		Unknown
Silver[a]		Surface water	Mined from the Berkeley Pit

[a]Located in Silver Bow county

[b]Located in Silver Bow and Deer Lodge counties

since the mid-1980s. The comparison group consists of the remaining 54 counties of Montana. Further, directly standardized mortality rates for the case counties and the comparison counties were calculated using United States mortality data for standardization. To account for population changes over our study period and to account for demographic differences between the case and comparison populations, population level demographic data for Montana counties were requested from the Behavioral Risk Factor

Table 2 Targeted conditions associated with heavy metal exposure and ICD-10 codes

Type	Condition	ICD-10-CM code	References
Cancers	Stomach	C16, D00.2	Yuan et al. (2016), Arita and Costa (2009)
	Liver and intrahepatic bile ducts	C22, D01.5	Naujokas et al. (2013), Arita and Costa (2009)
	Pancreas	C25, D01.7	Arita and Costa (2009), Garcia-Esquinas et al. (2013)
	Bronchus and lung	C34, D02.20	Nawrot et al. (2015), Naujokas et al. (2013), Smith et al. (2018), Garcia-Esquinas et al. (2013)
	Skin	C43, C44, D03, D04	Naujokas et al. (2013)
	Breast	C50, D05	Byrne (2013)
	Prostate	C61, D07.5	Arita and Costa (2009), Garcia-Esquinas et al. (2013)
	Kidney, except renal pelvis	C64, D09.1	Naujokas et al. (2013), Smith et al. (2018), Arita and Costa (2009), Song et al. (2015)
	Bladder	C67, D09.0	Smith et al. (2018), Naujokas et al. (2013), Arita and Costa (2009)
	Brain	C71	Caffo et al. (2014)
Neurological conditions	Alzheimer's disease	G30	Squitti (2012), Bonda et al. (2010)
	Motor neuron disease*	G12.2	Capozzella et al. (2014), Vinceti et al. (2012), Sutedja et al. (2009)
	Multiple sclerosis	G35	Etemadifar et al. (2016)
	Parkinson's disease	G20	Liu et al. (2013), Campbell (2006), Racette et al. (2017)
Cardio- and cerebrovascular diseases	Ischemic heart diseases	I20–I25	Naujokas et al. (2013), Tellez-Plaza et al. (2013), States et al. (2009), Lee et al. (2011)
	Heart failure	I50	Tellez-Plaza et al. (2013), Borné et al. (2015)
	Cerebrovascular disease	I60–I69	Tellez-Plaza et al. (2013), Agarwal et al. (2011)
	Atherosclerosis	I70	Fagerberg et al. (2015), Solenkova et al. (2014)
Organ failure	Liver failure	K72	Hyder et al. (2013)
	Hepatic fibrosis	K74.0	Hyder et al. (2013)
	Non-alcoholic fatty liver disease (NAFLD)	K76.0	Hyder et al. (2013)
	Non-alcoholic steatohepatitis (NASH)	K75.8	Hyder et al. (2013)
	Renal failure	N17–N19	Sabath and Robles-Osorio (2012), Soderland et al. (2010)

*CDC Wonder doesn't provide data on Amyotrophic lateral sclerosis independently. The ICD-10 code for motor neuron disease was used as a proxy

Surveillance System (BRFSS) for two-time periods, 2000–2005, and 2006–2010. We included two time periods as the population of these two counties is small resulting in unstable annual rates. These data are presented in Table 3 for descriptive purposes; they were not used in the statistical modeling.

Calculation of standardized mortality ratios and rates

Population estimates were obtained from the US Census Bureau for Montana case and comparison counties and the total US population (US Census). For the same case and comparison groups, multiple cause of death (MCOD) mortality data were collected from the Centers for Disease Control and Prevention (CDC) WONDER site (https://wonder.cdc.gov) through the

Table 3 County level self-reported characteristics for case and comparison counties, Behavioral Risk Factor Surveillance System (BRFSS), 2000–2010

	2000–2005				2006–2010			
	Deer Lodge and Silver Bow	95% CI	Other Montana counties	95% CI	Deer Lodge and Silver Bow	95% CI	Other Montana counties	95% CI
Age								
< 35	25.4	20.9–29.9	28.5	27.8–29.3	25.9	22.5–29.4	28.6	27.8–29.4
35–54	38.1	34.2–42.1	39.3	38.6–40.0	35.5	32.8–38.1	35.8	35.1–36.4
55–74	26.2	22.9–29.5	24.3	23.7–24.9	28.4	26.2–30.5	26.4	25.9–26.9
75 +	10.2	8.1–12.4	7.9	7.6–8.3	10.3	9.0–11.5	9.2	8.9–9.5
Race								
Non-hispanic white	97.1*	95.7–98.4	93.2*	93.0–93.5	96.7*	95.3–98.0	92.9*	92.6–93.2
Other	2.9*	1.6–4.3	6.8*	6.5–7.0	3.3*	2.0–4.7	7.1*	6.8–7.4
Income								
< $15,000	16.3	12.8–19.8	12.5	12.0–13.1	15.1	10.8–17.5	10.9	10.5–11.4
$15,000–$24,999	24.8	21.0–28.6	23.0	22.3–23.7	23.6	17.2–25.1	18.3	17.8–18.9
$25,000–$49,999	32.9	28.7–37.1	37.4	36.6–38.1	27.3	25.0–33.9	33.0	32.3–33.7
$50,000–$74,999	16.5	13.1–19.9	15.5	14.9–16.0	15.8	15.1–22.8	18.1	17.5–18.6
$75,000 +	9.5	6.9–12.1	11.6	11.1–12.1	18.2	12.2–20.3	19.6	19.1–20.2
Education								
< High school	7.7	5.1–10.2	8.3	7.9–8.7	8.6	6.7–10.6	7.1	6.7–7.5
High school	34.2	30.1–38.3	33.5	32.8–34.3	33.2	30.4–36.0	32.2	31.5–32.9
Some college	30.2	26.3–34.0	29.1	28.4–29.8	27.0	24.3–29.7	28.6	28.0–29.3
College graduate +	28.0	24.3–31.6	29.1	28.4–29.8	31.2	28.6–33.7	32.0	31.4–32.6
Employment status								
Employed	56.3*	52.1–60.5	65.3*	64.6–66.0	54.6*	51.7–57.5	61.9*	61.2–62.5
Unemployed	43.7*	39.5–47.9	34.7*	34.0–35.4	45.4*	42.5–48.3	38.1*	37.5–38.8
Smoking								
No	74.6	70.9–78.4	78.6	77.9–79.2	76.3*	73.7–78.8	81.5*	80.9–82.0
Yes	25.4	21.6–29.1	21.4	20.8–22.1	23.7*	21.2–26.3	18.5*	18.0–19.1
Alcohol consumption								
Heavy drinking	5.9	3.8–8.0	5.9	5.5–6.2	4.9	3.6–6.2	6.2	5.8–6.5
Binge drinking	17.2	13.9–20.5	18.9	18.2–19.5	18.6	16.1–21.1	18.1	17.5–18.7

*Statistically significant difference between case and comparison county

2000–2015 study period. Since the number of deaths for each ICD-10 coded condition was small, we grouped the causes of death into four composite categories: cancers, cerebro- and cardiovascular conditions, neurological conditions, and organ failures (Table 2). Mortality data were obtained by sex and four age strata: less than 35 years, 35–54 years, 55–74 years, and 75 years and older. Cox regression models were used to estimate SMRs. Further, these models were used to assess homogeneity across age groups and sex, since groups used for standardization need to be homogenous, to accurately describe the mortality experience for the population (Tsai and Wen 1986; Oliveira and Bevan 2003). Additionally, to illustrate changes in case and comparison counties' mortality experiences, directly standardized mortality ratios were generated for Deer Lodge and Silver Bow versus the remaining Montana counties using US mortality data for standardization.

Testing for statistical significance of time trends

Using Cox regression models, homogeneity by age and sex were assessed to test for homogeneity amongst the age and sex groups. Time trend, as well as age and sex specific analyses would need to be done if there was significant heterogeneity. For those composite conditions where the SMRs were homogenous by age and sex, homogeneity over time period, 2000–2015, was assessed for the whole population. Conversely, for those composite conditions where the SMRs were heterogeneous by age or sex, homogeneity over the years, 2000–2015, for specific age or sex groups were assessed.

All statistical analyses were performed using SAS 9.4

Results

County level demographic comparisons

We studied the mortality experiences of residents of Deer Lodge and Silver Bow counties during the period 2000–2015, with the aim to identify elevated causes of death and any monotonic trends of mortality over time. We compared the mortality experiences for these two counties to the remaining Montana counties, during the same period. To illuminate demographic differences between the underlying case and comparison populations, population level demographic data for Montana counties were requested from the Behavioral Risk Factor Surveillance System (BRFSS) for two-time periods, 2000–2005 and 2006–2010. Per Table 3, there were no statistically significant differences between our cause and comparison counties in regard to age, income, education, or alcohol use in either time period. Residents of Deer Lodge and Silver Bow differed from the rest of Montana in their racial demographics and employment status, having a higher proportion of non-Hispanic white residents and higher rates of unemployment. Smoking status differed in the 2006–2010 period for case and comparison counties, with Deer Lodge and Silver Bow having a higher proportion of smokers compared to the remaining Montana counties.

Standardized mortality rates and ratios

Sex and age adjusted SMRs as well as age and sex-specific SMRs are reported in Table 4. For three of the four composite causes of death, Deer Lodge and Silver Bow experienced significantly higher mortality when compared to the rest of Montana. Cancers, CCVDs, and organ failure were elevated for the two counties during the study period, 2000–2016, with SMRs of 1.19 (95% CI 1.10, 1.29); 1.36 (95% CI 1.29, 1.43) and 1.24 (95% CI 1.10, 1.38), respectively. Neurological conditions were not elevated for the two counties (SMR = 1.01; 95% CI 0.89, 1.14).

Using Cox regression models, homogeneity by age and sex were assessed with only CCVDs demonstrating statistically significant heterogeneity by age. Thus, the overall SMR for CCVDs is not meaningful. Age and sex specific SMRs were generated to account for causes of death illustrating heterogeneity by age and to further understand SMRs. Cancer SMRs were significantly elevated for males and females age 55–74, and females aged 75 and older. CCVD SMRs were elevated for both males and females, over all age categories over 35 years. SMRs for organ failure were elevated for males aged 55–74 years of age.

Time trend analysis

Illustrated in Fig. 1, compared to the rest of Montana, Deer Lodge and Silver Bow experienced elevated mortality for the 2000–2001, 2004–2005, and 2006–2015 biennial, cancer-related mortality estimates. Deer Lodge and Silver Bow, experienced elevated mortality related to CCVDs, compared to the rest of Montana for all years within the study period, seen in Fig. 2. Figure 3 demonstrates changes in mortality related to neurological conditions. Only two

Table 4 Mortality Statistics-Standardized mortality ratios for Deer Lodge and Silver Bow compared to Montana, 2000–2015

	Cancer	CCVD	Neurological conditions	Organ failure
Observed deaths, *n*	1245	3463	486	678
Expected deaths, *n*	1041.96	2542.59	478.98	545.91
Overall mortality, SMR (95% CI)	**1.19 (1.10, 1.29)**[a]	**1.36 (1.29, 1.43)**	1.01 (0.89, 1.14)[a]	**1.24 (1.10, 1.38)**[a]
Age and sex specific mortality, SMR (95% CI)				
Male				
< 35	2.11 (0.51, 8,66)	1.13 (0.35, 3.63)	–	0.65 (0.11, 3.82)
35–54	1.21 (0.78, 1.87)	**1.71 (1.30, 2.26)**	1.69 (0.46, 6.29)	1.45 (0.89, 2.36)
55–74	**1.29 (1.09, 1.53)**	**1.46 (1.28, 1.67)**	1.20 (0.73, 1.96)	**1.59 (1.21, 2.10)**
75 +	1.08 (0.93, 1.27)	**1.28 (1.16, 1.40)**	0.95 (0.76, 1.20)	1.19 (0.97, 1.45)
Female				
< 35	0.40 (0.04, 4.10)	0.92 (0.19, 4.39)	–	0.74 (0.12, 4.58)
35–54	0.82 (0.51, 1.31)	**1.62 (1.03, 2.55)**	0.88 (0.23, 3.36)	1.28 (0.70, 2.35)
55–74	**1.31 (1.08, 1.58)**	**1.67 (1.38, 1.97)**	1.27 (0.77, 2.11)	1.34 (0.96, 1.86)
75 +	**1.19 (1.00, 1.41)**	**1.30 (1.20, 1.41)**	0.99 (0.83, 1.17)	1.07 (0.87, 1.30)
Trend analysis, hazard ratio for each additional 2 years (*p* value)	**0.97 (0.0004)**	**0.95 (< 0.0001)**[b]	**0.97 (0.01)**	0.98 (0.16)

Bolded text indicates statistically significant results

[a]Homogenous by age and sex, overall SMR is meaningful

[b]The trend analysis was performed for 55–74 year olds as there was heterogeneity amongst age groups

of the biennial mortality rate estimates were significantly elevated in Deer Lodge and Silver Bow compared to Montana, 2006–2007 and 2010–2011. Our final figure (Fig. 4), illustrates changes in mortality related to organ failure. Residents of Deer Lodge and Silver Bow experienced significantly elevated mortality rates in 2002–2011 and in 2014–2015.

We assessed the SMRs over the 16-year time period, in 2 year intervals, for the presence or absence of any monotonic trends. There were significant decreases in mortality for cancers, CCVD, and neurological conditions with hazard ratios (HR) and related p values of 0.97 (0.0004), 0.95 (< 0.0001), and 0.97 (0.01), respectively. There were no significant changes in organ failure mortality for the 16-year study period (HR = 0.98; p value = 0.16).

Discussion

While the Berkeley Pit closed following EPA Superfund designation in 1983, mining in the Continental Pit and other related mining activities has continued in Silver Bow county throughout the study period (EPA 2016). Further, even though the Anaconda smelter was decommissioned soon after National Priority Listing by the EPA, the smelter was in use, contributing to toxic heavy metal contamination, for almost a century (EPA 2015). While remediation has been reported at the two sites, they are still both heavily contaminated with a number of toxic heavy metals (EPA 2015, 2016), which are associated with cancer, cardiovascular disease, neurologic conditions, and organ failure (see Table 2).

Many of the OUs within both Superfund sites continue to see elevated levels of COC including but not limited to the Streamside Tailings OU, BMFOU, the Rock and Timber Framing and Treating and Warm Springs Ponds OUs, BPSOU (EPA 2016). Moreover, remediation in Anaconda is ongoing for three of its OUs including the OW/EADA, the Community Soils OU, and the ARWW&SOU (EPA 2015). Regardless of the latest 5-year updates, an EPA statement in December 2017 listing Anaconda and Butte's Superfund sites as targets for immediate and intense attention (EPA 2017). Our study suggests that while remediation is conveying some reduction in negative health consequences, these efforts have not protected

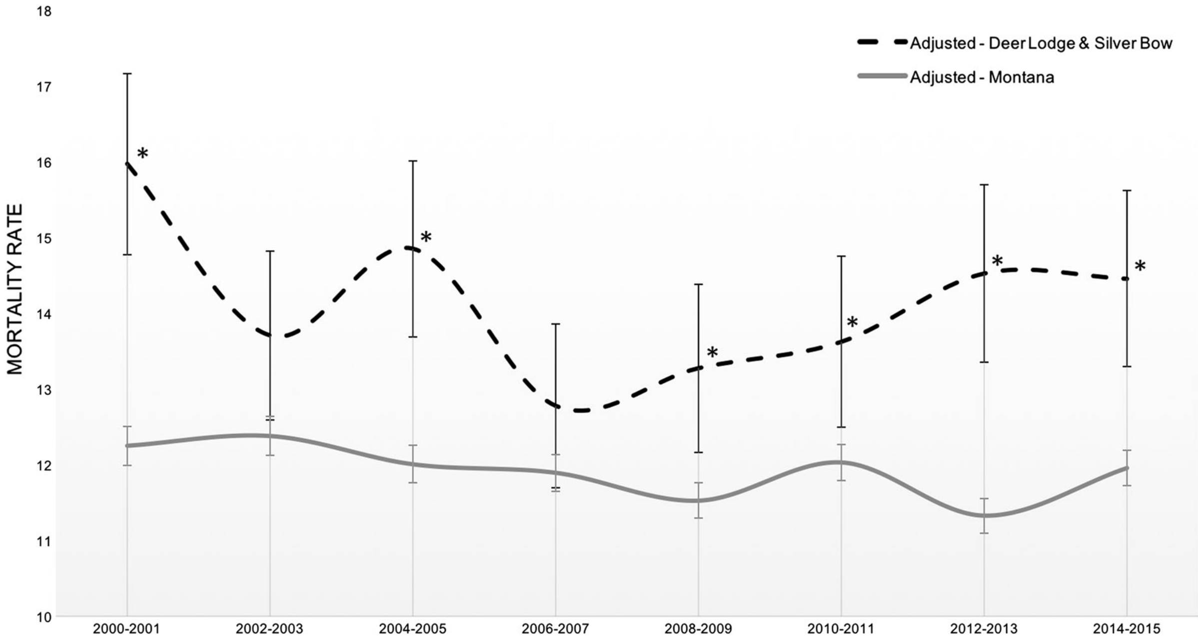

Fig. 1 Cancer related mortality rates for Deer Lodge and Silver Bow compared to all remaining Montana counties, 2000–2015. *Indicates significant differences between case and comparison groups

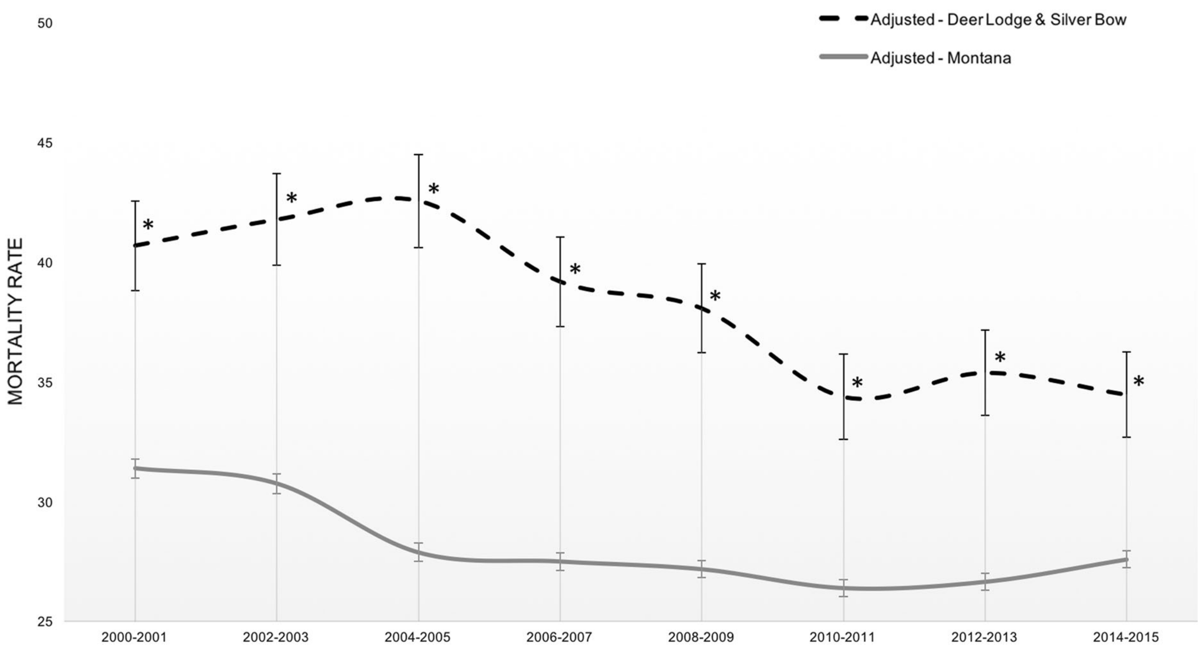

Fig. 2 Cerebro- and cardiovascular disease related mortality rates for Deer Lodge and Silver Bow compared to all remaining Montana counties, 2000–2015. *Indicates significant differences between case and comparison groups

the residents of these two counties as a whole, and further remediation is required to protect human health.

The first hypothesis, which claimed there would be a significant difference between the SMRs for Deer Lodge and Silver Bow counties compared to the rest of

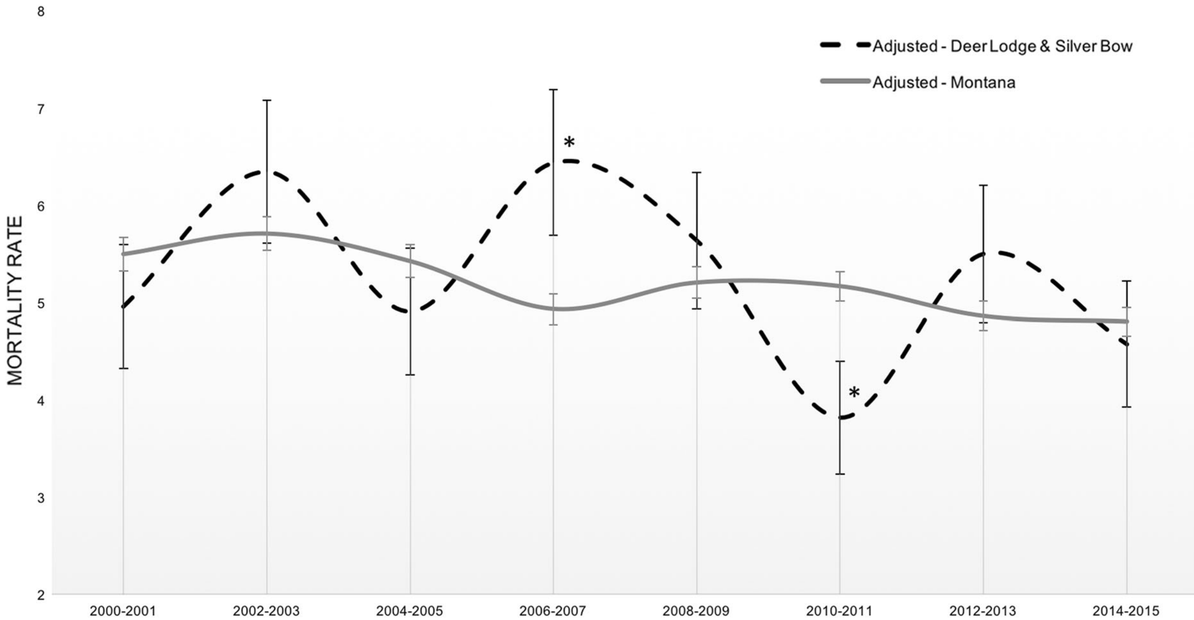

Fig. 3 Neurological disease related mortality rates for Deer Lodge and Silver Bow compared to all remaining Montana counties, 2000–2015. *Indicates significant differences between case and comparison groups

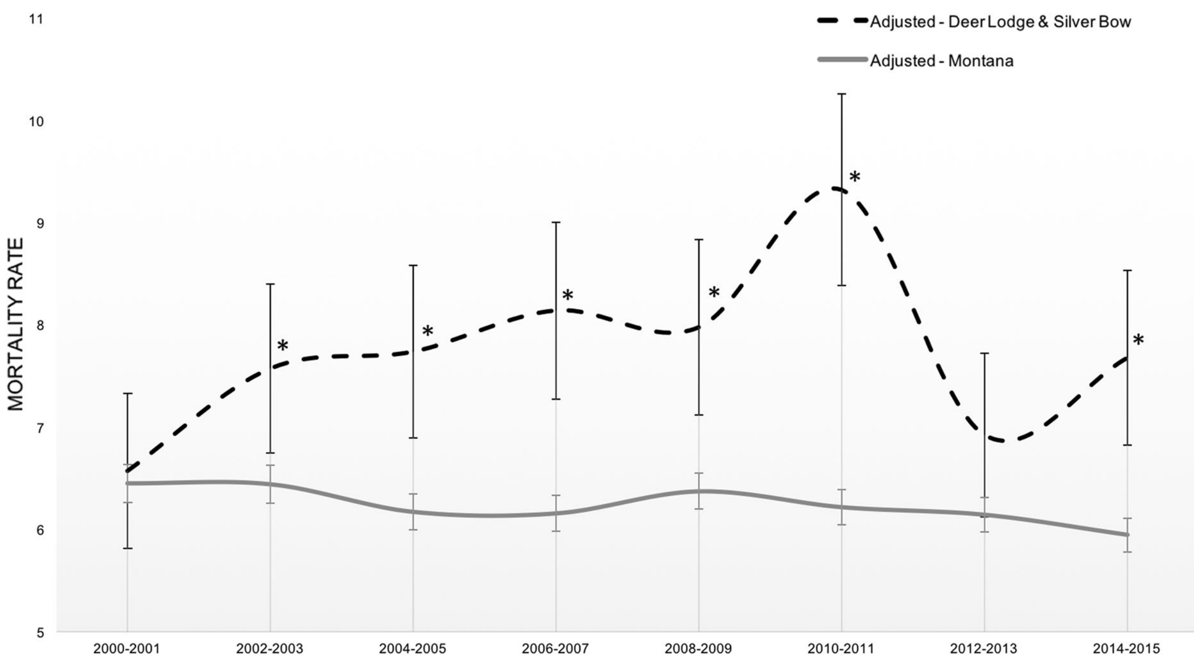

Fig. 4 Organ failure related mortality rates for Deer Lodge and Silver Bow compared to all remaining Montana counties, 2000–2015. *Indicates significant differences between case and comparison groups

Montana, was not supported for neurologic conditions. Conversely, the age and sex-adjusted standardized mortality ratios for cancer and organ failure were significantly elevated for the case counties. Compared to all other Montana counties, residents of Deer Lodge and Silver Bow experienced an estimated 19%

increase in cancer mortality (SMR 1.19; 95% CI 1.10, 1.29) and a 24% increase in organ failure mortality (SMR 1.24; 95% CI 1.10, 1.38) during the study period. Tests performed to assess homogeneity across age and sex groups revealed heterogeneity across age for CCVDs, thus the overall SMR is not meaningful. Age- and sex-specific SMRs revealed significantly elevated CCVD mortality for both sexes for persons over the age of 35. A 2011 cross-sectional analysis of National Health and Nutrition Examination Survey (NHANES) data, reported a significant, positive relationship between serum lead and cadmium levels and CCVD (Agarwal et al. 2011). Both lead and cadmium are listed as COC for both Deer Lodge's and Silver Bow's Superfund sites. There is considerable literature supporting a causal link between exposure to lead and cadmium and adverse cardiovascular effects. Lead and cadmium have been shown to negatively affect vascular endothelium and smooth muscles via their ability to induce inflammatory responses and oxidative stress (Heo et al. 1996; Kaji et al. 1995; Stohs and Bagchi 1995; Vaziri et al. 2001). It is reasonable that we only detected significant SMRs for residents of Deer Lodge and Silver Bow aged 35 and older, as CCVD typically occurs after long term exposures, affecting older populations (Agarwal et al. 2011).

While the overall SMRs for cancers and organ failure are meaningful, supported by their homogeneity in SMRs across age and sex, we reported age- and sex-specific SMRs to better understand in what ways the population is experiencing elevated mortality. Females in the two oldest age groups experienced significantly increased mortality related to cancers, while only males age 55–74 years did so. This is possibly due to the elevated deaths related to breast cancer, accounting for 14% of all cancer deaths in this population. There were 167 deaths reported for females aged 55 and older; the expected number of deaths for that group was approximately 114, using the remaining Montana counties for standardization.

Conversely, only males experienced a significant greater burden of organ failure. The point estimates for all males over 35 years were higher than their female counterparts. Further, only males aged 55–74 experienced significant increases in mortality related to organ failure. Hyder and colleagues investigated the relationship between cadmium exposure and liver disease. They reported increased morbidity and mortality related to hepatic necroinflammation, non-alcoholic fatty liver disease (NAFLD), and non-alcoholic steatohepatitis (NASH) in males with odds ratios (ORs) of 2.21 (95% CI 1.64, 3.00), 1.30 (95% CI 1.01, 1.68), and 1.95 (95% CI 1.11, 3.41), respectively. Females were only significantly affected by hepatic necroinflammation (OR = 1.26; 95% CI 1.01–1.57). Further their study reported an increase in adjusted all-cause mortality related with increased cadmium exposure, which was more pronounced in males (Hyder et al. 2013). However, nothing was offered as a plausible biological explanation for the gap in liver mortality among the sexes.

The second hypothesis predicted a statistically significant decrease in the mortality rates in Deer Lodge and Silver Bow counties during 2000–2015. This was not supported for mortality related to organ failure. Deaths related to cancer, CCVD, and neurological conditions experienced significant reductions in mortality over the time period. Hazard ratios were estimated for changes in mortality for every additional 2 years. Mortality related to cancer, CCVD, and neurological conditions reduced 3, 5 and 3% for each additional 2 years.

Figures 1, 2, 3 and 4 illustrate the mortality rates for each composite cause of death for residents of Deer Lodge and Silver Bow in relation to all remaining Montana residents. Adjusted rates for both case and comparison groups were estimated using US population and mortality data. Cancer mortality (Fig. 1) remained elevated for Deer Lodge and Silver Bow compared to Montana for much of the study period. Only in two instances (2002–2003 and 2006–2007) did the confidence interval overlap for the two groups. Deer Lodge and Silver Bow experienced greater mortality related to CCVDs (Fig. 2) for the entire study period. As shown in Fig. 3 SMRs for neurological conditions were only statistically significantly different compared to the remaining counties in Montana during 2006–2007 when they were elevated, and 2010–2011 when they were lower. Organ failure was the only composite cause of death to not see any significant reduction in mortality over time, as shown in Fig. 4, although Deer Lodge and Silver Bow experiencing higher mortality, for the study period, with the exception of 2012–2013.

A notable limitation of this study is the reliance on death certificates to report cause of death. The standard death certificate instructions to medical certifiers state that the immediate cause of death and "an explanatory chain of diseases or conditions that resulted in death" should be listed. Most death certificates have fields for up to 20 diagnosis codes in the multiple cause of death file (CDC 1999). We calculated SMRs using multiple causes of death (MCOD) data. While underlying cause of death (UCD) data is sufficient for cancer deaths (Fink et al. 2012) this is not typically the case for cardiovascular disease, neurologic conditions, or organ failure.

Most notably, this is an ecologic study so, we do not have information on exposure to heavy metals on an individual level. We are making the assumption that most residents of these two counties are exposed to metals through air, water, soil, and dust in the environment. Montana is a small state with a population of 1.04 million (Census 2017), however, the statistically significant findings should be generalizable to other areas where the same metals are present in the environment.

We believe our approach to using publicly available death certificate data over time, along with an understanding of the potential risks associated with specific metal exposures, can be utilized to monitor population health impacts during continued mining and remediation efforts. When compared to other Montana Counties, the two Superfund counties showed 19% increased standardized risk for cancer death, 36% increase risk for cardiovascular death, and 24% increased risk for organ failure death during the 16-year study period, when remediation was occurring. However, the time trends indicate there is a downward trajectory in the mortality rates for cancer, cerebro-cardiovascular, and neurological conditions. These findings suggest remediation efforts are slowly improving the human health impact of ongoing and historical pollution from mining and smelting. Nonetheless, the elevated rates for cancer, CCVD, and organ failure suggests there is a continuing need to monitor SMRs and time trends in the mortality experience.

References

Agarwal, S., Zaman, T., Tuzcu, E. M., & Kapadia, S. R. (2011). Heavy metals and cardiovascular disease: Results from the National Health and Nutrition Examination Survey (NHANES). *Angiology, 1999–2006, 62*(5), 422–429.

Arita, A., & Costa, M. (2009). Epigenetics in metal carcinogenesis: Nickel, arsenic, chromium and cadmium. *Metallomics, 845,* 222–228.

Bonda, D. J., Wang, X., Perry, G., Nunomura, A., Tabaton, M., Zhu, X., & Smith, M. A. (2010). Oxidative stress in Alzheimer disease: A possibility for prevention. *Neuropharmacology*, *59*(4–5), 290–294. https://doi.org/10.1016/j.neuropharm.2010.04.005.

Borné, Y., Barregard, L., Persson, M., Hedblad, B., Fagerberg, B., & Engström, G. (2015). Cadmium exposure and incidence of heart failure and atrial fibrillation: A population-based prospective cohort study. *British Medical Journal Open, 5*(6), 1–8.

Brown, C. C., & Chu, K. C. (1983). Implications of the multistage theory of carcinogenesis applied to occupational arsenic exposure. *Journal of the National Cancer Institute*, *70*(3), 455–463.

Butte GIS Department. (2006). *Butte Superfund NRIS data layers*. MT: Butte.

Byrne, C. (2013). Metals and breast cancer. *Journal of Mammary Gland Biology and Neoplasia, 18*(1), 63–73.

Caffo, M., Caruso, G., La Fata, G., Barresi, V., Visalli, M., Venza, M., et al. (2014). Heavy metals and epigenetic alterations in brain tumors. *Current Genomics, 5*(6), 457–463.

Campbell, A. (2006). The role of aluminum and copper on neuroinflammation and Alzheimer's disease. *Journal of Alzheimer's Disease, 10*(2–3), 165–172.

Capozzella, A., Sacco, C., Chighine, A., Loreti, B., Scala, B., Casale, T., et al. (2014). Work related etiology of amyotrophic lateral sclerosis (ALS): A meta-analysis. *Annali DiIgiene: Medicina Preventiva E Di Comunita, 26*(5), 456–472.

Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999–2016 on CDC WONDER Online Database, released December 2017. Data are from the Multiple Cause of Death Files, 1999–2016, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.

Currie, J., Greenstone, M., & Moretti, E. (2011). Superfund cleanups and infant health. *American Econimic Review, 101*(3), 435–441.

Etemadifar, M., Mehrabi, B., Kiani-Peykani, R., Abtahi, S. H., Nekouie-Isfahani, K., Ramagopalan, S. V., et al. (2016). Soil heavy metals are associated with the distribution of multiple sclerosis in Isfahan, Iran. *Acta Neurologica Scandinavica, 134*(4), 292–299.

Fagerberg, B., Barregard, L., Sallsten, G., Forsgard, N., Östling, G., Persson, M., et al. (2015). Cadmium exposure and atherosclerotic carotid plaques—Results from the Malmö diet and Cancer study. *Environmental Research, 136,* 67–74.

Fink, A. K., German, R. R., Heron, M., Stewart, S. L., Johnson, C. J., Finch, J. L., et al. (2012). Impact of using multiple causes of death codes to compute site-specific, death certificate-based cancer mortality statistics in the United States. *Cancer Epidemiology, 36*(1), 22–28.

Gammons, C. H., Metesh, J. J., & Duiame, T. E. (2006). Overview of the mining history and geology of Butte, Montana. *Mine Water and the Environment, 25,* 70–75.

Garcia-Esquinas, E., Pollan, M., Umans, J. G., Francesconi, K. A., Goessler, W., Guallar, E., et al. (2013). Arsenic exposure and cancer mortality in a US-based prospective cohort: the strong heart study. *Cancer Epidemiology, Biomarkers and Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology, 22*(11), 1944–1953.

Hailer, M. K., Peck, C. P., Calhoun, M. W., West, R. F., James, K. J., & Siciliano, S. D. (2017). Assessing human metal accumulations in an urban Superfund site. *Environmental Toxicology and Pharmacology, 54,* 112–119.

Heo, Y., Parsons, P. J., & Lawrence, D. A. (1996). Lead differentially modifies cytokine production in vitro and in vivo. *Toxicology and Applied Pharmacology, 138*(1), 149–157.

Hyder, O., Chung, M., Cosgrove, D., Herman, J. M., Li, Z., Gurakar, A., et al. (2013). Cadmium exposure and liver disease among US adults Omar. *Journal of Gastrointestinal Surgery, 17*(7), 1265–1273.

Jaishankar, M., Tseten, T., Anbalagan, N., Mathew, B. B., & Beeregowda, K. N. (2014). Toxicity, mechanism and health effects of some heavy metals. *Interdisciplinary Toxicology, 7*(2), 60–72.

Kaji, T., Suzuki, M., Yamamoto, C., Mishima, A., Sakamoto, M., & Kozuka, H. (1995). Severe damage of cultured vascular endothelial cell monolayer after simultaneous exposure to cadmium and lead. *Archives of Environmental Contamination and Toxicology, 28*(2), 168–172.

Lee, A. M., & Fraumeni, J. F. (1969). Arsenic and respiratory cancer in man: An occupational study. *Journal of the National Cancer Institute, 42,* 1045–1052.

Lee, M.-S., Park, S. K., Hu, H., & Lee, S. (2011). Cadmium exposure and cardiovascular disease in the 2005 Korea national health and nutrition examination survey. *Environmental Research*, *111*(1), 171–176. https://doi.org/10.1016/j.envres.2010.10.006.

Lee-Feldstein, A. (1986). Cumulative exposure to arsenic and its relationship to respiratory cancer among copper smelter employees. *Journal of Occupational Medicine, 28*(4), 296–302.

Liu, K., Hao, J., Zeng, Y., Dai, F., & Gu, P. (2013). Neurotoxicity and biomarkers of lead exposure: A review. *Chinese Medical Sciences Journal, 28*(3), 178–188.

Lubin, J. H., Pottern, L. M., Stone, B. J., & Fraumeni, J. F. (2000). Respiratory cancer in a cohort of copper smelter workers: Results from more than 50 years of follow-up. *American Journal of Epidemiology, 151*(6), 554–565.

Naujokas, M. F., Anderson, B., Ahsan, H., Aposhian, H. V., Graziano, J. H., Thompson, C., et al. (2013). The broad scope of health effects from chronic arsenic exposure: Update on a worldwide public health problem. *Environmental Health Perspectives, 121*(3), 295–302.

Nawrot, T. S., Martens, D. S., Hara, A., & Plusquin, M. (2015). Association of total cancer and lung cancer with environmental exposure to cadmium: The meta-analytical evidence. *Cancer Causes & Control*, *26*(9), 1281–1288. https://doi.org/10.1007/s10552-015-0621-5.

Neuberger, J. S., Hu, S. C., Drake, K. D., & Jim, R. (2009). Potential health impacts of heavy-metal exposure at the Tar Creek Superfund site, Ottawa County, Oklahoma. *Environmental Geochemistry and Health*, *31*(1), 47–59. https://doi.org/10.1007/s10653-008-9154-0.

Oliveira, M. D., & Bevan, G. (2003). Measuring geographic inequities in the Portuguese health care system: an estimation of hospital care needs. *Health Policy (Amsterdam, Netherlands)*, *66*(3), 277–293.

Racette, B. A., Nielsen, S. S., Sheppard, L., Seixas, N., & Warden, M. N. (2017). Dose-dependent progression of parkinsonism in manganese-exposed welders. *Neurology*, *88*, 344–351.

Rana, S. V. S. (2014). Perspectives in endocrine toxicity of heavy metals—A review. *Biological Trace Element Research, 160,* 1–14.

Sabath, E., & Robles-Osorio, M. L. (2012). Renal health and the environment: heavy metal nephrotoxicity. *Nefrologia, 32*(3), 279–286.

Satterly, A. (1995). *An epidemiological study to determine if heavy metals are a factor in the etiology of Amyotrophic Lateral Sclerosis (Master of Science Thesis)*. Butte, MT: Montana Tech of The University of Montana.

Sharma, B., Singh, S., & Siddiiqi, N. J. (2014). Biomedical implications of heavy metals induced imbalances in redox systems. *BioMed Research International, 2014,* 1–26.

Smith, A. H., Marshall, G., Roh, T., Ferreccio, C., Liaw, J., & Steinmaus, C. (2018). Lung, bladder, and kidney cancer mortality 40 years after arsenic exposure reduction. *Journal of National Cancer Institute, 110*(3), 1–9.

Soderland, P., Lovekar, S., Weiner, D. E., Brooks, D. R., & Kaufman, J. S. (2010). Chronic kidney disease associated with environmental toxins and exposures. *Advances in Chronic Kidney Disease, 17*(3), 254–264.

Solenkova, N. V., Newman, J. D., Berger, J. S., & Thurston, G. (2014). Metal pollutants and cardiovascular disease: Mechanisms and consequences of exposure. *American Heart Journal, 168*(6), 812–822.

Song, J., Luo, H., Yin, X., Huang, G., Luo, S., & Lin, D. (2015). Association between cadmium exposure and renal cancer risk: A meta-analysis of observational studies. *Nature Publishing Group*, *5*(17976), 1–8.

Squitti, R. (2012). Metals in Alzheimer's disease: a systemic perspective. *Frontiers in Bioscience (Landmark Edition), 17,* 451–472.

States, J. C., Srivastava, S., Chen, Y., & Barchowsky, A. (2009). Arsenic and cardiovascular disease. *Toxicological Sciences*, *107*(2), 312–323. https://doi.org/10.1093/toxsci/kfn236.

Stohs, S. J., & Bagchi, D. (1995). Oxidative mechanisms in the toxicity of metal ions. *Free Radical Biology and Medicine, 18*(2), 321–336.

Sutedja, N. A., Veldink, J. H., Fischer, K., Kromhout, H., Heederik, D., Huisman, M. H. B., et al. (2009). Exposure to chemicals and metals and risk of amyotrophic lateral sclerosis: a systematic review. *Amyotrophic Lateral Sclerosis: Official Publication of the World Federation of Neurology Research Group on Motor Neuron Diseases, 10*(5–6), 302–309.

Tellez-Plaza, M., Guallar, E., Howard, B. V., Umans, J. G., Francesconi, K. A., Goessler, W., et al. (2013). Cadmium exposure and incident cardiovascular disease. *Epidemiology (Cambridge, Mass.), 24*(3), 421–429.

Tsai, S. P., & Wen, C. P. (1986). A review of methodological issues of the standardized mortality ratio (SMR) in occupational cohort studies. *International Journal of Epidemiology*, *15*(1), 8–21.

US Census Bureau (2017). https://census.gov. Accessed October 13, 2017.

US Environmental Protection Agency, Region 8 (2015). *Fifth five-year review report for Anaconda Smelter Superfund Site Anaconda-Deer Lodge County*, Montana.

US Environmental Protection Agency, Region 8 (2016). *Fourth five-year review report for silver bow Creek/Butte area Superfund Site*, Butte, Silver Bow and Deer Lodge Counties, Montana.

US Environmental Protection Agency (2017). *News Releases from Region 08.* https://www.epa.gov/newsreleases/anaconda-smelter-and-silver-bow-creekbutte-area-among-superfund-sites-targeted Accessed January 11, 2018.

US Environmental Protection Agency (2018). *Superfund.* https://www.epa.gov/superfund. Accessed October 31, 2017.

US National Cancer Institute of Health, (2009). *State Cancer Profiles*. Bethesda, MD. http://statecancerprofiles.cancer.gov. Accessed October 14, 2017.

Vaziri, N. D., Ding, Y., & Ni, Z. (2001). Compensatory up-regulation of nitric oxide synthase isoforms in lead-induced hypertension; reversal by a superoxide dismutase-mimetic drug. *Journal of Pharmacology and Experimental Therapeutics, 298*(2), 679–685.

Vinceti, M., Bottecchi, I., Fan, A., Finkelstein, Y., & Mandrioli, J. (2012). Are environmental exposures to selenium, heavy metals, and pesticides risk factors for amyotrophic lateral sclerosis? *Reviews on Environmental Health, 27*(1), 19–41.

Von Lindern, I., Spalinger, S., Petroysan, V., & Von Braun, M. (2003). Assessing remedial effectiveness through the blood lead: soil/dust lead relationship at the Bunker Hill Superfund Site in the Silver Valley of Idaho. *The Science of the Total Environment, 303,* 139–170.

Welch, K., Higgins, I., Oh, M., & Burchfiel, C. (1982). Arsenic exposure, smoking, and respiratory cancer in copper smelter workers. *Archives of Environmental Health, 37*(6), 325–335.

Wong, O., Whorton, M. D., Foliart, D. E., & Lowengart, R. (1992). An ecologic study of skin cancer and environmental arsenic exposure. *International Archives of Occupational and Environmental Health, 64,* 235–241.

World Health Organization. (2015). *International classification of diseases, 10th revision, Clinical Modification (ICD-10-CM)*. Geneva, Switzerland.

Yuan, W., Yang, N., & Li, X. (2016). Advances in understanding how heavy metal pollution triggers gastric cancer. *BioMed Research International, 2016,* 1–10.