Current Epidemiology Reports (2019) 6:34–49
https://doi.org/10.1007/s40471-019-0182-3

ENVIRONMENTAL EPIDEMIOLOGY (F LADEN AND J HART, SECTION EDITORS)

A Review of Metal Exposure Studies Conducted in the Rural Southwestern and Mountain West Region of the United States

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Published online: 12 February 2019

Abstract

Purpose of Review This review summarizes recent literature examining exposure to environmental metals in rural areas of the southwestern/mountain west region of the U.S. focusing on the range of exposures and exposure pathways unique to this region.

Recent Findings Recent studies (2013–2018) indicated that exposures to arsenic (As), uranium (U), and cadmium (Cd) were the most commonly quantified metals in the study area. One or more of these three metals was analyzed in each study reviewed.

Summary The current review draws attention to the variety of exposure assessment methods, analytical tools, and unique non-occupational exposure pathways in this region. The reviewed studies identified potential sources of metal exposure including regulated and unregulated drinking water, particulate matter, and food items, and provided information about the levels of exposures experienced by populations through a variety of exposure assessment methods including spatial analysis methodologies. The findings suggest that exposure assessment methods could be further integrated with population studies to assess health effects of environmental metal exposure through pathways unique to southwestern and mountain west U.S.

Keywords Environmental metals · Environmental exposure · Rural population · Minority population · Western United States · Southwestern United States

Introduction

The risk of exposure to metals found in the environment is a health concern for the rural communities in the southwest/mountain west region of the United States (U.S.) due to abundant mineral deposits and a land-use ethic that intimately connects many communities to the environment [1]. The potential for daily activities, and traditional cultural practices, to result in community-level non-occupational exposure to metal mixtures is a new and recently identified public health concern in the region. A recent review of the epidemiological literature demonstrated consistent adverse health outcomes associated with arsenic (As) and cadmium (Cd) exposures among rural, minority populations living in this region [2]. This review also determined that the exposure range and assessment methods varied widely across the epidemiology studies. Additionally, exposure assessment studies have been conducted for other metals common to the region, but are not

This article is part of the Topical Collection on *Environmental Epidemiology*

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s40471-019-0182-3) contains supplementary material, which is available to authorized users.

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represented in the epidemiological literature alone. Thus, a review of these exposure-specific results was needed to support future epidemiologic health studies of metals and metal mixture exposure. Our objective is to conduct a systemized review of environmental metal exposure studies conducted in rural areas of the southwestern/mountain west region of the U.S. published between June 2013 and June 2018.

Methods

Database Search and Eligibility Criteria

The authors met to discuss inclusion/exclusion criteria and scope of the search prior to database searching. Searches were performed in PubMed, Web of Science, and Google Scholar in May 2018 using controlled and keyword terms for environmental exposure, rural, minority, and various monitoring terms such as blood, urine, water, soil, and biomonitoring. Searches in each database were limited to those studies published in the 5-year period between June 2013 and June 2018 in English. The full search strategy is available in supplemental information.

Studies were eligible for inclusion if they included an environmental exposure assessment; conducted in the Southwest and Mountain West geographical locations of the U.S., an area including the states of Arizona (AZ), Colorado (CO), Nevada (NV), New Mexico (NM), Texas (TX), and Utah (UT), and reported metal contaminant exposures. These states were selected because of the prevalence of mining-related exposure sources, substantial representation of isolated, rural, and minority populations with distinct exposure risks not represented in other geographic areas of the U.S., and environmental health research in this area is underrepresented in the published literature [2]. Studies that were conducted in urban locations were excluded. Three investigators independently screened titles and abstracts against the exclusion criteria. The same investigators then screened full-text articles against the inclusion criteria and met in person to discuss and resolve any discrepancies. The review process was managed with the systematic review application Rayyan [3].

Data Abstraction, Evaluation, and Synthesis

Data were abstracted from the records to capture the metal, study location, population impacted, type of exposure, exposure metric, exposure assessment methods, exposure estimates, and any human health outcomes that were examined. The main results during the article evaluation and selection phase were defined as the measures of exposure. Records were also classified by exposure type and the data were organized into tables.

Results

The systematized review of environmental exposure studies yielded information about (1) the study area and populations investigated; (2) the analytical methods used to quantify exposure; and (3) exposure estimates in biological and environmental media. The results included studies from eight states that most commonly measured arsenic (As), uranium (U), or cadmium (Cd) in environmental or biological media using spectroscopy methods.

Search Results

Our search identified 165 studies via database searching and hand-searching relevant publications, which included scanning reference lists; keyword searching in Google, Google Scholar, and PubMed; and citation searching in Web of Science and Google Scholar. After removing duplicates, 139 records remained to be screened by review of the title and abstract, of which, 81 were excluded. After screening the remaining studies by reading the full text ($N = 58$), we further excluded 31 that did not fully fit the above inclusion criteria, as they were not a rural population ($N = 3$), were an incorrect study design ($N = 7$), were outside of the geographical region of interest ($N = 1$), or did not evaluate exposure to a metal ($N = 20$). Twenty-seven studies were included in our final narrative synthesis. Figure 1 is a flowchart of the search, screening, and inclusion/exclusion process. Tables 1, 2 and 3 describes the data organized by exposure category: air, water/soil, and biomarker.

Study Locations and Populations

The results included studies from eight states (AZ, CO, NM, TX, Oklahoma (OK), North Dakota (ND), South Dakota (SD), and UT). Five of these states were included among our original six target states and OK, ND, and SD were included as these populations were aggregated with a large rural Native American cohort from AZ; it was not possible to disaggregate the results by geographic location.

Twelve of the 27 reviewed articles investigated metal exposure and health outcome using an epidemiological study design. Of these, ten studies were from the Strong Heart Study cohort of Native Americans living in non-urban locations included in the geographic area of this review [4–11, 12•, 13]. Additionally, two studies were included from the Facing Rural Obstacles Now Through Intervention, Education, and Research (FRONTIER) study, based in rural western TX and focused on Hispanics [14, 15]. Fourteen of the reviewed studies quantified metal exposure based on concentrations in environmental media (water, air, soil), vegetation, or livestock meat and organs that may be consumed by local communities, but did not associate exposure levels with health outcomes.

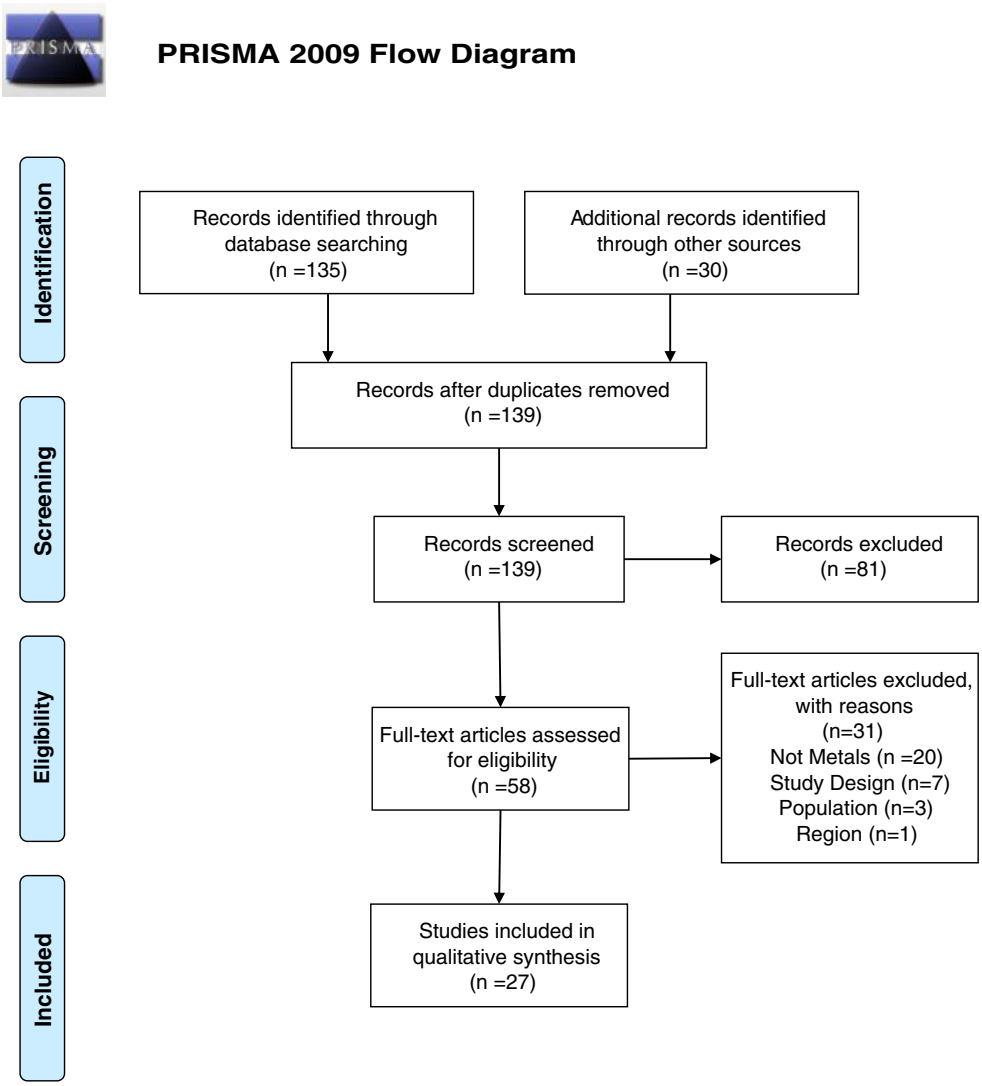

Fig. 1 Flowchart of the search, screening, and inclusion/exclusion process. For more information, visit www.prisma-statement.org

These studies were included in our review because they assessed environmental metal exposure potential for a rural population in the study region. Two of these studies reported associations between environmental metals in water and markers of potential health effect [16, 17••], and two other studies reported associations between As in water with levels in blood or nail clippings [18, 19••].

Analytical Methods Used to Quantify Exposure

Results indicate that inductively coupled plasma (ICP)-optical emissions spectroscopy and ICP-mass spectroscopy were most commonly employed to measure metal concentrations in environmental and biological media. Use of more specialized analytical methods, such as X-ray fluorescence, X-ray diffraction, scanning electron microscopy, X-ray photoelectron spectroscopy, and X-ray absorption spectroscopy were used in environmental studies.

Methods Used to Measure Metals in Environmental Media

Concentrations of As, U, Cd, and other metals were reported for public water sources and unregulated water sources (e.g., private groundwater wells). Sampling methods were conducted in a prospective fashion including one-time grab samples and repeat sample collection to observe seasonal variability. Chemical concentrations were measured using inductively coupled plasma (ICP)-optical emissions spectroscopy [16, 17••, 20, 21••, 22], ICP-atomic emissions spectroscopy [16, 17••, 20, 21••], ICP-mass spectroscopy [14, 16, 17••, 18, 20, 21••, 22–25], or graphite furnace atomic absorption spectroscopy [19••]. Additionally, concentrations of As, U, chromium (Cr), lead (Pb), iron (Fe), and vanadium (V) were measured in mine waste, soil, sediment, and other solid material using X-ray fluorescence [22, 23], X-ray diffraction, scanning electron microscopy, X-ray photoelectron spectroscopy, and X-ray absorption spectroscopy [22].

Table 1 Water/Soil/Sediment. Summary of environmental exposure studies among rural, minority populations in the southwest/mountain west region of the United States published between 2013 and 2018 by media used to assess exposure

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
Blake et al. (2017)	Uranium	Laguna Pueblo, New Mexico, USA	A community located downstream from an abandoned uranium mine	Measured	Water and sediment concentrations of uranium	Uranium sediment concentrations measured using X-Ray fluorescence; water uranium measured using ICP-MS	Sediment uranium concentrations 320–9200 mg/kg; surface water uranium concentrations ranged 6–110 ug/L 4.5 km downstream from the mine site to 35–770 ug/L adjecent to the mine site	None
Blake et al. (2015)	Arsenic, Uranium, Vanadium	Navajo Nation (Arizona)	A community located near an abandoned uranium mine site	Measured	Water and soil concentrations of arsenic, uranium, and vanadium	Concentrations in water and acid digested mine waste measured using ICP-OES and, ICP-MS; bulk elemental content of mine waste measured using X-ray fluorescence	Uranium concentrations in water ranged between 67−169 μg/L; Uranium (6,614 mg kg^{-1}), vanadium (15,814 mg kg^{-1}), and arsenic (40 mg kg^{-1}) concentrations in mine waste solids.	None
Calderon et al. (2013)	Arsenic	Churchill County, Nevada, USA	904 men and women, older than 45 years	Measured	Limited to county residents using private wells and public water containing arsenic	Water total arsenic measured using ICP-MS or GF-AAS; Urine arsenic species measured by ion-pair chromatographic separation with hydride generation-atomic fluorescence detection; urine total arsenic measured by ICP-MS; toenail total arsenic measured by instrumental neutron activation analysis	Untreated well water arsenic concentrations range -<3–1200 ug/L; median urine total arsenic 39.0 ug/L; median urine speciated arsenic 31.0 ug/L; median toenail arsenic 0.609 ug/g. When stratified by smoking status a difference was observed (p=0.03)	None; reference also included in biomarker list
Corlin et al. (2016)	Arsenic, uranium	Navajo Nation (Arizona and Utah, USA)	Rural residents drinking unregulated water	Measured	Arsenic and uranium concentrations in untreated groundwater	Measured arsenic and uranium in 144 unregulated water sources using ICP-MS	Median (range) uranium 2.3 (<1.0–170) ug/L; arsenic median (range) 2.7 (<1.0–120) ug/L	None
Del Rio et al. (2017)	Arsenic	Two rural communities in western Texas	252 children aged 4 to 12 years	Measured	Home well arsenic water concentrations; blood arsenic concentrations	Water total arsenic determined using ICP-MS; blood arsenic measured using ICP-MS	Community 1 mean (range) 7.1 (0–16.0) μg/L; Community 2 mean (range) 3.7 (0–10.0) μg/L; Blood arsenic mean (standard deviation) 0.97 (0.47), range 0.09–2.61 μg/dL	Reference also included in biomarker list

Table 1 (continued)

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
Edwards et al. (2014)	Arsenic	Project FRONTIER (Bailey, Cochran, Hockley, Parmer Counties West Texas, USA)	527 Hispanic (42%) and Non-Hispanic White Hispanic,	Modeled	Groundwater arsenic concentrations	Groundwater arsenic concentrations from Texas Water Development Board; Household arsenic groundwater concentrations modeled using inverse-distance weighted (IDW) in a Geographic Information System	Mean (standard deviation) groundwater arsenic 6.42 (2.99) μg/L; range 2.19–15.25 μg/L	Limited to FRONTIER Projet participants with a complete neuropsychological examination; outcomes examined include language, memory, and executive function
Gong et al (2015)	Arsenic, iodine	Project FRONTIER (Bailey, Cochran, Hockley, Parmer Counties West Texas, USA)	723 Hispanic and Non-Hispanic White adults, ages 40–79 years	Measured and modeled	Groundwater concentrations of arsenic and iodine; geospatially modeled groundwater concentrations at unsampled locations	Water arsenic and iodine measured in 198 water samples using ICP-MS; Arsenic and iodine groundwater concentrationsl were modeled using methods descrbied in Edwards et al (2014)	Arsenic mean 5.6 μg/L, median (std) 3.9 (3.0) μg/L; 91.3% of groundwater wells had iodine concentration <1 mg/L	Hypothyroidism
Hargrove et al. (2015	Arsenic	Vinton, TX, USA	Hispanic populations living along US-Mexico border with inadequate water supply and sanitation	Measured	Arsenic concentrations in tap water	Arsenic concentrations measured in 113 tap water samples using ICP-MS	Water arsenic mean (Std) -7.8 (3.0) μg/L Arsenic. range 2.6–15.8 μg/L	Health Impact Assessment
Harmon et al. (2017)	Abandoned uranium mine (AUM) waste	DiNEH Project, Navajo Nation (New Mexico, USA)	145 Native American adults, mean age 56 years	Modeled	Area-weighted AUM proximity; estimated metal intake via drinking water	AUM proximity calculated as square root of the sum of the inverse distance between a participant's home and all AUM features in the study area, weighted by surface area of each AUM; Estimated individual water consumption using survey data; water arsenic and uranium concentrations were measured in 124 water sources and in urine samples using ICP-MS	Median (IQR) residential linear actual distance from AUM 3.54 (1.81, 8.0) km; Median area-weighted proximity median (IQR) 0.207 0.179, 0.224); Median annual arsenic intake 0.49 mg/year (IQR 0–1.09) and median uranium intake 0.46 mg/year (IQR 0–1.13).	Serum inflamatory potential; reference also included in biomarker list

Table 1 (continued)

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
Harmon et al. (2018)	Arsenic, uranium	DiNEH Project, Navajo Nation (New Mexico, USA)	252 Native American adults, mean age 55 years	Measured and modeled	Annual arsenic and uranium intake modeled from self-reported volume of water consumed and metal concentration for each water source used; urine arsenic and uranium concentrations	Estimated individual water consumption using survey data; water arsenic and uranium concentrations were measured in 124 water sources and in urine samples using ICP-MS	Median annual arsenic intake 0.49 mg/year (IQR 0–1.09) and median uranium intake 0.46 mg/year (IQR 0–1.13). Median urine arsenic 4.21 (IQR 2.25–6.78) μg/L and median urine uranium not reported.	oxidized low-density lipoprotein (LDL) cholesterol, C-reactive protein; reference also included in biomarker list
Hoover et al. (2017)	Arsenic, uranium	DiNEH Project, Navajo Nation (Arizona, Utah, New Mexico, USA)	Rural residents drinking unregulated water	Measured	Arsenic and uranium concentrations in untreated groundwater	Measured arsenic and uranium in 467 unregulated water sources using ICP-AES or ICP-MS.	Median groundwater As 3.0 μg/L and 3.8 μg/L for uranium	None
Hoover et al. (2018)	Arsenic, uranium, lead, manganese	Navajo Nation (Arizona, Utah, New Mexico, USA)	Rural residents drinking unregulated water	Measured	Groundwater concentrations of arsenic, uranium, lead, manganese; bayesian profile clustering of water sources	Measured water contaminants in 467 unregulated water sources using ICP-AES or ICP-MS.	Median (IQR): Arsenic -1.95 (0.42–5.7) μg/L; Manganese 4.8 (1.2–23.2)μg/L; Uranium 3.76 (0.51–13) μg/L	None
Samuel-Nakamura et al. (2017)	Arsenic, cadmium, lead, molybdenum, selenium, uranium	Navajo Nation (New Mexico)	Sheep, grass, soil, and water proximal to abandoned uranium mine waste in New Mexico	Measured	Heavy metal concentations in sheep tissue, soil, and water; metal bio-accumulation factors for vegetation	Tissue samples from 3 sheep collected in the field immediately after slaughter (muscle, bone, intestine, lung, liver, kidney); 24 composited topsoil (0–15 cm) samples; 24 samples of local forage/grasses; 14 drinking water samples (n = 14); All samples analyzed using ICP-MS	U ranged from 3.77–8.24 μg/L; Cd ranged from 0.03 to 0.65 μg/L; As ranged from 0.77–1.25 μg/L; Lead ranged from 7.49–7.98 μg/L; Molybdenum and selenium ranged from 1.94–4.42 and 4.78–6.29 μg/L respectively	Reference also included in biomarker list

Table 2 Biological. Summary of environmental exposure studies among rural, minority populations in the southwest/mountain west region of the United States published between 2013 and 2018 by media used to assess exposure

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
Adams et al. (2015)	Arsenic, cadmium, lead, uranium	Doña Ana County, Southern New Mexico	188 Hispanic adults ages 40–85 years	Measured	Urinary metal to-creatinine ratio	Spot urine samples collected; Urine metal concentrations using magnetic-sector (high-resolution) ICP-MS; urine creatinine measured using Roche Cobas Mira Plus Chemistry Analyzer	Mean (IQR) arsenic -14.02 (8.2, 20.3) ug/L; cadmium –0.30 (0.12, 0.60); lead –0.60 (0.32, 0.99); uranium -0.0131 (0.006, 0.029)	None
Calderon et al. (2013)	Arsenic	Churchill County, Nevada, USA	904 men and women, older than 45 years	Measured	Limited to county residents using private wells and public water containing arsenic	Water total arsenic measured using ICP-MS or GF-AAS; Urine arsenic species measured by ion-pair chromatographic separation with hydride generation-atomic fluorescence detection; urine total arsenic measured by ICP-MS; toenail total arsenic measured by instrumental neutron activation analysis	Untreated well water arsenic concentrations range -<3 –1200 ug/L; median urine total arsenic 39.0 ug/L; median urine speciated arsenic 31.0 ug/L; median toenail arsenic 0.609 ug/g. When stratified by smoking status a difference was observed (p = 0.03)	None; reference also included in biomarker list
Del Rio et al. (2017)	Arsenic	Two rural communities in western Texas	252 children aged 4 to 12 years	Measured	Home well arsenic water concentrations; blood arsenic concentrations	Water total arsenic determined using ICP-MS; blood arsenic measured using ICP-MS	Community 1 mean (range) 7.1 (0–16.0) μg/L; Community 2 mean (range) 3.7 (0–10.0) μg/L; Blood arsenic mean (standard deviation) 0.97 (0.47), range 0.09–2.61 μg/dL	None; reference also included in biomarker list
Franceschini et al. (2017)	Cadmium	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	3714 Native American adults, ages 45–74 years in 1989–1991	Measured	Urinary Cd (creatinine corrected)	(Analytical methods and associated QC criteria for arsenic analysis described in detail by Tellez-Plaze et al (2013)	Geometric mean = 0.94 μg g/L; higher average among ever-smokers and current-smokers than neversmokers	Blood pressure traits of systolic and diastolic blood pressures
Garcia-Esquinas et al. (2014)	Cadmium	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	3792 Native American adults, ages 45–74 years in 1989–1991	Measured	Urinary Cd (creatinine corrected)	(Analytical methods and associated QC criteria for arsenic analysis described in detail by Tellez-Plaze et al (2013)	Median cadmium (IQR): 0.93 (0.61–1.46) ug/g creatinine; Differences were observed when stratified by smoking status (p-value <0.001)	Cancer mortality

Table 2 (continued)

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
Gribble et al. (2013)	Arsenic	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	3663 Native American adults, ages 45–74 years in 1989–1991	Measured	percent inorganic Arsenic (%iAs); percent monometheyle… (%MMA), and percent dimethly…(%DMA) as the relative contribution of iAs, MMA, or DMA to their sum	Spot urine samples collected in the morning; Urine total arsenic concentrations measured by ICP-MS; arsenic species measured with HPLC coupled to ICP-MS; urine creatinine measured by alkaline picrate methodology	Median (IQR) %iAs -7.9 (5.6, 11.0)%; %MMA -13.9 (10.8, 17.5)%; %DMA -77.8 (72.0, 82.7)%	Body mass index, % body fat, fat free mass and waist circumference
Harmon et al. (2018)	Arsenic, uranium	DiNEH Project, Navajo Nation (New Mexico, USA)	252 Native American adults, mean age 55 years	Measured and modeled	Annual arsenic and uranium intake modeled from self-reported volume of water consumed and metal concentration for each water source used; urine arsenic and uranium concentrations	Estimated individual water consumption using survey data; water arsenic and uranium concentrations were measured in 124 water sources and in urine samples using ICP-MS	Median annual arsenic intake 0.49 mg/year (IQR 0–1.09) and median uranium intake 0.46 mg/year (IQR 0–1.13). Median urine arsenic 4.21 (IQR 2.25–6.78) μg/L and median urine uranium not reported.	oxidized low-density lipoprotein (LDL) cholesterol, C-reactive protein; also in biomonitoring list
Kuo et al. (2015)	Arsenic	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	1986 Native American adults, ages 45–74 years in 1989–1991	Measured	%iAs, %MMA, and %DMA as the relative contribution of iAs, MMA, or DMA to their sum	(Analytical methods and associated QC criteria for arsenic analysis described in Gribble et al (2013)	Median (IQR) urine inorganic+methylated arsenic species10.2 (IQR, 6.1–17.7) ug/L; iAs% -8.3% (5.7– 11.3%); MMA% -15.2% (11.7–18.8%);DMA%--76.4% (70.3–81.4%)	Diabetes; limited to individuals without diabetes at baseline examination
Moon et al. (2013)	Arsenic	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	3575 Native American adults, ages 45–74 years in 1989–1991	Measured	Ratio of sum of urine inorganic arsenic (arsenite and arsenate) and methylated arsenic species (DMA and MMA) (creatinine corrected)	(Analytical methods and associated QC criteria for arsenic analysis described in Gribble et al (2013)	Median (IQR) total arsenic -9.7 (5.8,15.7) ug/g creatinine; Differences observed when stratified by smoking status	Fatal and nonfatal cardiovascular disease
Newman et al. (2016)	Arsenic	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	2875 Native American adults who were aged 45–74 years in 1989–1991	Measured	sum of urinary inorganic arsenic (arsenite and arsenate) and the methylated species (DMA and MMA) (creatinine corrected)	(Analytical methods and associated QC criteria for arsenic analysis described in Gribble et al (2013)	Median urine total As 9.9 (IQR, 6.0–15.7) μg/g creatinine)	Peripheral Arterial Disease and Its Association With Arsenic Exposure

Table 2 (continued)

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
Olmedo et al. (2017)	Cadmium	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	1725 Native American adults, ages 45–74 years in 1989–1991	Measured	Urine cadmium (standardized to urine creatinine); food frequency questionnaire data grouped in 24 categories, including processed meat.	(Analytical methods and associated QC criteria for arsenic analysis described in detail by Tellez-Plaze et al (2013)	Median (IQR) urinary cadmium 0.44 (0.20–0.85) ug/g creatinine; adjusted geometric mean ratio (GMR) (95%CI) of urinary cadmium concentrations per IQR increase in each dietary category was 1.16 (1.04–1.29) for processed meat, 1.10 (1.00–1.21) for fries and chips, 0.87 (0.80–0.95) for dairy products, and 0.89 (0.82–0.97) for fruit juices	
Samuel-Nakamura et al (2017)	Arsenic, cadmium, lead, molybdenum, selenium, uranium	Navajo Nation (New Mexico)	Sheep, grass, soil, and water proximal to abandoned uranium mine waste in New Mexico	Measured	Heavy metal concentrations in sheep tissue, soil, and water; metal bio-accumulation factors for vegetation	Tissue samples from 3 sheep collected in the field immediately after slaughter (muscle, bone, intestine, lung,liver, kidney); 24 composited topsoil (0–15 cm) samples; 24 samples of local forage/grasses; 14 drinking water samples (n = 14); All samples analyzed using ICP-MS	Metals concentrated more in the roots of forage compared to the above ground parts. Liver concentrations of: Se 3.28–5.93 mg/kg; Cd 0.06–0.23 mg/kg; Mo 1.20–1.47 mg/kg. Wool concentrations of: Se 1.30–3.85 mg/kg; As 0.04–0.71 mg/kg; Pb 1.07–1.90; U 0.06–0.09 mg/kg	Of the calculated human intake, Se Reference Dietary Intake and Mo Recommended Dietary Allowance were exceeded, but the tolerable upper limits for both were not exceeded.
Tellez-Plaza et al (2013)	Cadmium	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	2864 Native American adults, ages 45–74 years in 1989–1991	Measured	Urinary Cd (creatinine corrected)	Spot urine samples collected in the morning; Urine cadmium measured using ICP-MS; urine creatinine measured using alkaline picrate methodology conducted in a rapid flow analyzer	Geometric mean cadium -0.94 μg/g creatinine (at baseline)	Peripheral Arterial Disease, limited to individuals free of peripheral artery disease at baseline enrollment (1989–1991)
Tellez-Plaza et al., (2013)	Cadmium	Strong Heart Study (Arizona, Oklahoma, and	3348 Native American adults, ages 45–74 years in 1989–1991	Measured	Urinary Cd (creatinine corrected)	(Analytical methods and associated QC criteria for arsenic analysis described in detail by	Geometric mean cadmium 0.94 μg/g (95% CI = 0.92–0.93)	Cardiovascular events including deaths, coronary heart disease mortality,

Table 2 (continued)

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
		North and South Dakota USA)				Tellez-Plaze et al (2013)		incident cardiovascular disease, coronary heart disease, stroke, and heart failure
Zheng et al (2013)	Arsenic	Strong Heart Study (Arizona, Oklahoma, and North and South Dakota USA)	3821 Native American adults, ages 45–74 years in 1989–1991	Measured	Urine total arsenic, sum of inorganic and methylated species (creatinine corrected)	(Analytical methods and associated QC criteria for arsenic analysis described in Gribble et al (2013)	Median total arsenic -12.7 ug/g; median sum of inorganic and methylated arsenic species -9.7 ug/g; No difference when stratified by smoking status (p-value = 0.3)	Urine albumin-creatinine ratio and albuminuria status

ICP-MS was also used to measure As, U, Cd, selenium (Se), Pb, and molybdenum (Mo) in soil and in grasses consumed by sheep [26•].

Methods Used to Measure Metals in Particulate Matter Metal concentrations in particulate matter (PM) were reported for two studies. Gonzales-Maddux et al. (2014) used a filter-based chemical speciation monitor to collect $PM_{2.5}$ samples [27]. Subsequently, concentrations of 64 trace elements were measured using a double-focusing magnetic sector ICP-MS. Beamer et al. (2014) used ICP-MS to quantify As, Cd, aluminum (Al), beryllium (Be), Cr, Pb, manganese (Mn), and nickel (Ni) in PM collected using dust fall passive samplers and active air samplers [28••].

Methods Used to Measure Metals in Biological Media Spot urine samples were collected and analyzed for total As, U, Cd, and other metals using ICP-mass spectroscopy (ICP-MS). Additionally, As species concentrations were measured with high-performance liquid chromatography coupled with ICP-MS [4, 5, 9, 13] or ion-pair chromatographic separation with hydride generation-atomic fluorescence detection [19••]. Blood As, Cd, and Pb were also measured using ICP-MS [18] and toenail total As was measured by instrumental neutron activation analysis [19••]. Samuel-Nakamura et al. (2017) quantified accumulated As, U, Cd, Se, Pb, and Mo in sheep muscle, bone, intestine, lung, liver, kidney, and wool using ICP-MS [26•].

Exposure Estimates for Metals and Metal Mixtures

Results indicated that As, U, and Cd were the most commonly quantified metal exposures in the geographic study area. One or more of these metals were analyzed in each study reviewed. Reviewed articles also reported metal concentrations of Al, Be, Cr, copper (Cu), Cr, Fe, Pb, Mn, Mo, Ni, Se, and V.

Public Water Supply Arsenic was the only metal evaluated in regulated, public water sources (Table 4). The median As concentrations reported from two studies of public water supplies in west Texas ranged from 3.8–7.8 μg/L [18, 25] (Table 5). Calderon et al. (2014) also measured As concentrations in public water supply sources in Nevada but did not report ambient concentrations [19••].

Unregulated Water Sources In unregulated water sources (UWSs), primarily groundwater wells in AZ and NM, median total As and U concentrations ranged from 1.95–6.4 and 2.3–3.8 μg/L respectively. Minimal seasonal/temporal variability was reported for As and U measured in UWSs in the Arizona portion of Navajo Nation [24] and UWSs across the Navajo Nation [20]. Blake et al. (2017) observed As concentrations less than 10 μg/L in replicate surface water sources located

Table 3 Air. Summary of environmental exposure studies among rural, minority populations in the southwest/mountain west region of the United States published between 2013 and 2018 by media used to assess exposure

Author (date)	Contaminant	Study Location	Population Impacted	Type of Exposure (category)	Exposure Metric	Exposure Method(s) (detail)	Exposure estimates	Health Outcome examined/Notes
Beamer et al. (2014)	Arsenic, aluminum, beryllium, cadmium, chromium, lead, manganese, and nickel in particulate matter	Rural Arizona, two neighborhoods outside of Tucson and 1 close to Superfund smelter site	41 homes in rural Arizona	Measured	Metal concentrations	Passive filters used concurrently with indoor active air filters; samples collected in 2009 (10 homes) and 2012–2013 (31 homes)	Passive samplers: Mean (Std) Arsenic 0.28 (0.35) ng/m3; Be 0.009 (0.01) ng/m3; Mn 13.8 (20.2) ng/m3; Ni 7.5 (9.9) ng/m3; Cd 0.05 (0.04) ng/m3; Pb 1.8 (1.7) ng/m3; Al 184 (614) ng/m3; Active samples: Median Arsenic 0.18 ng/m3; Be Not Detected; Mn 5.3 ng/m3; Ni 0.6 ng/m3; Cd 0.3 ng/m3; Pb 0.9 ng/m3; Al 192 ng/m3	None
Gonzales-Maddux et al. (2014)	PM2.5, elemental analysis of PM	Shiprock, NM	11 homes in a community living proximal to abandoned mine waste and in the vicinity of coal power plants	Measured	PM2.5 concentration (μg/m3), elemental concentrations (ng/m3) and principle components	A filter–based chemical speciation monitor was housed 3.5 m above the ground. A sharp cut cyclone impactor was used to remove particles >2.5 μm in diameter. Monitor had a dedicated flow–controlled pump. PM2.5 samples were collected on pre–weighed Teflon filters (47 mm). 64 trace elements were determined using a double–focusing magnetic sector ICP-MS. Principle components determined using Varimax rotated PCA.	The average PM2.5 concentration was 7.0 μg/m3 (range = 3.8–11.6 μg/m3). Identified 4 principle components that represented soil, coal combustion industrial/anthropogenic sources, and sea salt	None

Table 4 Metals in environmental and biological media

Exposure media	Sample source	Metals			
		Arsenic	Uranium	Cadmium	Other metals
Water	Public water source	Del Rio et al. (2017), Hargove et al. (2015), Calderon et al. (2013), Harmon et al. (2018)*, Harmon et al. (2017)*	Harmon et al. (2018)*, Harmon et al. (2017)*		
	Unregulated water source	Calderon et al. (2013), Edwards et al. (2014)*, Gong et al. (2015)*, Corlin et al. (2016), Hoover et al. (2017), Hoover et al. (2018), Blake et al. (2015), Harmon et al. (2018)*, Harmon et al. (2017)*; Samuel-Nakamura (2017)	Corlin et al. (2016), Hoover et al. (2017), Hoover et al. (2018), Blake et al. (2015), Blake et al. (2017), Harmon et al. (2018)*, Harmon et al. (2017)*; Samuel-Nakamura (2017)	Hoover et al. (2018); Samuel-Nakamura (2017)	Hoover et al. (2018), Blake et al. (2015), Gong et al. (2015)*
Solids	Soil or sediment	Blake et al. 2015; Blake et al. 2017; Samuel-Nakamura et al. 2017	Blake et al. 2015; Blake et al. 2017; Samuel-Nakamura et al. 2017	Samuel-Nakamura et al. 2017	Blake et al. 2015; Blake et al. 2017; Samuel-Nakamura et al. 2017
	Mine Waste	Blake et al. 2015; Blake et al. 2017	Blake et al. 2015; Blake et al. 2017	Blake et al. 2015; Blake et al. 2017	Blake et al. 2015; Blake et al. 2017
Urine	Spot sample (creatanine corrected)	Gribble et al. (2013), Zheng et al. (2013), Moon et al. (2013), Kuo et al. (2015), Adams et al. (2015), Newman et al. (2016)	Adams et al. (2015)	Adams et al. (2015), Tellez-Plaza et al. (2013a), Tellez-Plaza et al. (2013b), Franceshini et al. (2017), Garcia-Esquinas et al. (2014), Olmedo et al. (2017)	Adams et al. (2015)
	Spot sample (uncorrected)	Calderon et al. (2013), Harmon et al. (2018)*	Harmon et al. (2018)*		Harmon et al. (2018)*
Air	PM (not fractionated)	Beamer et al. (2014)		Beamer et al. (2014)	Beamer et al. (2014)
	PM2.5	Gonzales-Maddux et al. (2014)	Gonzales-Maddux et al. (2014)		Gonzales-Maddux et al. (2014)
Other	Vegetation and livestock tissue	Samuel-Nakamura (2017)	Samuel-Nakamura (2017)	Samuel-Nakamura (2017)	Samuel-Nakamura (2017)
	Blood	Del Rio et al. (2017)		Del Rio et al. (2017)	Del Rio et al. (2017)
	Nail clippings	Calderon et al. (2013)			

*Include both direct measurements and modeled estimates of exposures

Table 5 Median concentrations of directly measured arsenic, uranium, and cadmium in water, soil/sediment, urine, or particulate matter in exposure studies conducted in the rural, southwestern/mountain west region of the U.S.

	Exposure media	Arsenic Median reported exposure	Uranium Median reported exposure	Cadmium Median reported exposure
Water	Public water source	3.7–7.8 μg/L		
	Unregulated water source	1.95–6.4 μg/L	2.3–3.8 μg/L	<1 μg/L
Solids	Soil or sediment	1.20–4.53 mg/kg	0.36–1400 mg/kg	0.05–0.17 mg/kg
	Mine waste	< 40 mg/kg	6614–9300 mg/kg	Not detected
Urine	spot sample (creatanine corrected)	9.7–14 μg/g	0.013 μg/g	0.3–0.94 μg/g
	spot sample (creatanine un-corrected)	4.2–39 μg/L		
Air	PM2.5	0.18 ng/m3	0.01 ng/m3	
	Total PM	0.28 ng/m3		0.05 ng/m3
Other	Blood	0.97 μg/dL^		0.07 μg/dL^
	Nail clippings	0.609 ppm*		

*Parts per million (ppm)

^Denotes a mean concentration

downstream of a U mine in New Mexico [23]. In the same samples, however, U concentrations ranged between < LOD and > 700 μg/L and exhibited a strong season effect. Two additional studies measured As and U concentrations in both public supply and UWSs in the Navajo Nation [16, 17••]. These measurements were used to estimate annual oral intake of As and U for modeling and were not reported as ambient measurements.

The reviewed studies indicated that Cd water concentrations were generally low in the study area. Hoover et al. (2018) reported Cd concentrations were less than the limit of detection (1 μg/L) for more than 70% of unregulated water sources on the Navajo Nation tested between 1998 and 2010 [21••]. Samuel-Nakamura et al. (2017) reported Cd concentrations ranging from 0.03 to 0.65 μg/L for eight water sources used by sheep in a Navajo community in New Mexico [26•]. Four studies reported concentrations of other metals in UWSs (Table 4) including iodine in groundwater in west TX [15, 29]; V [22], Al, Fe, Mn, Pb, Se, Mo, and other metals [21••, 22, 23, 26•].

Soil, Sediment, and Mine Waste Three studies were conducted in or near abandoned U mining sites. Blake et al. (2017) reported 9300 mg/kg of U in unremediated mine waste materials mixed with soil and 320–1400 mg/kg in sediment samples. Concentrations of other metals were at or below the limit of detection in soil and sediment samples. At an abandoned uranium mine site in AZ, Blake et al. (2015) reported U, V, and As concentrations of 6614, 15,814, and 40 mg/kg respectively. Samuel-Nakamura et al. (2017) also reported soil concentrations of U, As, Cd, and Pb to range from 0.36–1.15, 1.20–4.53, 0.05–0.17, and 3.91–9.07 mg/kg respectively.

Ambient and Indoor Particulate Matter Metals concentrations in particulate matter (PM) were quantified in two studies. Beamer et al. (2014) reported concentrations of eight metals in particulate matter samples collected by active and dust fall samplers in a mining community located in southern AZ. Reported mean concentrations were 972 $\mu g/m^3$ for Al, 1.39 $\mu g/m^3$ for As, 0.385 $\mu g/m^3$ for Cd, and 0.028 $\mu g/m^3$ for Be. Gonzales-Maddux et al. (2014) used active sampling methods to collect PM2.5 inside of homes in the Navajo Nation in northern NM and reported analytical results for 64 elements. The average $PM_{2.5}$ concentrations across all indoor samples were 7.0 $\mu g/m^3$; the geometric means of As and U were 0.18 and 0.01 $\mu g/m^3$ respectively. Principle components analysis indicated that indoor PM likely originated from local soil, coal combustion, industrial activity, and sea salt.

Urine Median total As concentrations (creatinine adjusted results) ranged from 9.7 μg/g in Strong Heart Study participants (AZ, OK, ND, and SD) to 14 μg/g among Hispanics non-White men and women living in southern NM [5, 10, 13, 30], and 4.5 μg/L on the Navajo Nation and 39.0 μg/L in Nevada among non-adjusted results [16, 19••]. Urine As results were also reported as the sum of inorganic and methylated species [9] and as the percentages of inorganic, methylarsonate, and dimethylarsinate to their sum [4], among Native American participants of the Strong Heart Study.

Adams et al. (2015) reported a median creatinine-corrected U concentration of 0.013 μg/g for Hispanic non-White men and women in southern NM. For Navajo Nation residents living in New Mexico, Harmon et al. (2018) reported that 14.6% of study participants had urine U concentrations exceeding the NHANES 95th percentile (0.031 μg/L) for the 2003–2004 cycle.

Median-adjusted urinary Cd concentrations ranged from 0.30–0.94 μg/g creatinine. Four studies measured urinary Cd in samples from 2864 to 3792 Native American adult participants of the Strong Heart Study, and all reported a median adjusted Cd concentration of 0.94 μg/g in their epidemiological analyses [6–8, 11]. An additional study examining 1725 Strong Heart Study participants reported a lower median creatinine-corrected urinary concentration of 0.44 μg/g among the subset of participants in their analyses [12•]. Adams et al. (2015) reported a median adjusted urine Cd concentration of 0.30 μg/g for Hispanic residents of southern NM. The same study also reported adjusted urinary concentrations of lead. Harmon et al. (2018) reported urinary Cu, Ni, and V results for participants in a Navajo cohort.

Vegetation, Livestock Tissue, and Organs Samuel-Nakamura et al. (2017) reported that the kidney cortex had greater uptake of U, Se, Mo, and As compared to the kidney medulla. The liver uptake of Se and Mo was observed, as well as Pb accumulation, in wool. The authors noted that the mean concentrations of these metals did not exceed National Research Council maximum tolerable concentrations in the shoots or roots of the collected plants [31]. It was also observed that roots generally had higher metal concentrations of U and As than the above-ground shoots. Cd, Se, and Mo were both observed to accumulate at higher concentrations in shoots compared to roots.

Conclusions

Results indicated that exposure to As, U, Cd, either alone or in combination, were quantified in each study reviewed. Exposure was also assessed for other metals including Al, Be, Cu, Fe, Pb, Mo, Ni, Se, and V. Although small, the current body of literature suggests that rural populations in the southwest, mountain west, and adjacent regions of the U.S. experience exposures to mixtures of environmental metals. Rural populations in this region experience exposure to metals through unique pathways and sources, which differ from those in urban areas. Sources include active and abandoned mining and smelter operations, locally grown foodstuffs (plants and free-range livestock), and contaminated natural materials, such as the wool from locally raised sheep for weaving.

Most of the reviewed studies applied direct measurements to assess metal exposures. Cumulative, body burden of exposure was assessed through measurement of metals accumulated in biological samples (e.g., urine, blood, and nail clippings from humans) and in livestock tissues and organs used for food. Exposure to metals was also directly measured in environmental media such as public water supplies, unregulated water sources (e.g., private wells), soil, indoor and outdoor particulate matter, local vegetation used for food, and in wool collected and used by local weavers. Indirect exposure assessment methods incorporated directly measured concentrations of metals to model representative exposures based on geographic proximity to sources or to more precisely estimate individual-level exposures by applying survey-reported intake of the potentially contaminated media.

Six studies illustrated how individual survey results and spatial analysis methods can model exposure estimates using direct measurements. In the FRONTIER study in west TX, direct measurements were used in geospatial models to estimate groundwater concentrations at unsampled locations [14, 15]. Hoover et al. (2017) used geospatial spatial analysis methods to assess the influence of distance from an abandoned U mining (AUM) site on levels of As and U measured in UWSs on the Navajo Nation [20]. Additionally, Hoover et al. (2018) identified metal mixtures found in UWSs on the Navajo Nation and evaluated the geographic distribution of these metal mixture clusters using spatial analysis methods [21••]. Also on the Navajo Nation, Harmon et al. (2017) used residential proximity to AUMs sites, weighted by surface area of each AUM, to assess exposure in a cohort study [17••]. Harmon et al. (2017, 2018) also estimated annual As and U intake modeled from self-reported volume of water consumed and the measured metal concentrations for each water source used [16].

A previous review of the epidemiological literature in this study area reported consistent adverse health outcomes associated with environmental exposure to particulate matter, As and Cd, for rural, minority populations [2]. The health effects associated with metal exposure in this region are comparable in magnitude to those reported in urban settings, often at lower exposure levels. This observation highlights a gap in the current understanding of the role of exposure duration in rural communities given their prolonged, close contact with the natural environment. Our current review emphasizes the unique exposure pathways and the significant risk of exposure to environmental metals, especially U, Cd, and As, in this region. The studies reviewed attempted to identify potential sources of metal exposure and provide information about the levels of exposures experienced by these populations through a variety of methods including spatial analytical methodologies.

It is important to emphasize that gaps remain in our understanding of the associations between environmental metal exposures and health effects, especially effects from long-term exposures, as the current body of environmental epidemiologic studies in this region is sparse. There remains an opportunity to expand the use of existing exposure assessment methods into population studies in the region. In addition, population-representative exposure assessments may require novel refinements to modeling methods used in more urban and densely populated settings to account for the different

resource- and land-use patterns among rural minority populations in the southwestern/western region of the U.S.

Funding This work was supported by National Institutes of Health grants 1P50ES026102, 1P42ES025589, and 1U54MD00481106, and Assistance Agreement No. 83615701 awarded by the U.S. Environmental Protection Agency to the University of New Mexico Health Sciences Center. This work has not been formally reviewed by EPA. The views expressed are solely those of the authors and do not necessarily reflect those of the Agency.

Compliance with Ethical Standards

Conflict of Interest Melissa Gonzales reports grants 1P50ES026102, 1P42ES025589, and 1U54MD00481106 from National Institutes of Health, Assistance Agreement no. 83615701 from the U.S. Environmental Protection Agency to the University of New Mexico Health Sciences Center, and an honorarium for scientific review to Southwest Tribal IRB, outside the submitted work. Joseph Hoover reports grants from NIH and grants from USEPA during the conduct of the study. This work has not been formally reviewed by EPA. The views expressed are solely those of the authors and do not necessarily reflect those of the Agency. Jacob Nash and Esther Erdei each declare no potential conflicts of interest.

Human and Animal Rights This article does not contain any studies with human or animal subjects performed by any of the authors.

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