
Supplementary Materials: Exposure to Metal Mixtures in Association with Cardiovascular Risk Factors and Outcomes: A Scoping Review

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Table S1. Search strategy

(a) Database: MEDLINE (PubMed)

Publication timeline range: 1998 to October 1, 2021

| # | Searches | Results |
|---|--|-----------|
| 1 | "metals"[tiab] OR "Actinium"[tiab] OR "Aluminum"[tiab] OR "Americium"[tiab] OR "Antimony"[tiab] OR "Arsenic"[tiab] OR "Barium"[tiab] OR "Berkelium"[tiab] OR "Beryllium"[tiab] OR "Bismuth"[tiab] OR "Boron"[tiab] OR "Cadmium"[tiab] OR "Calcium"[tiab] OR "Californium"[tiab] OR "Cesium"[tiab] OR "Chromium"[tiab] OR "Cobalt"[tiab] OR "Copper"[tiab] OR "Curium"[tiab] OR "Einsteinium"[tiab] OR "Fermium"[tiab] OR "Francium"[tiab] OR "Gallium"[tiab] OR "Germanium"[tiab] OR "Gold"[tiab] OR "Hafnium"[tiab] OR "Indium"[tiab] OR "Iridium"[tiab] OR "Iron"[tiab] OR "Lawrencium"[tiab] OR "Lead"[tiab] OR "Lithium"[tiab] OR "Lutetium"[tiab] OR "Magnesium"[tiab] OR "Manganese"[tiab] OR "Mendelevium"[tiab] OR "Mercury"[tiab] OR "Molybdenum"[tiab] OR "Neptunium"[tiab] OR "Nickel"[tiab] OR "Niobium"[tiab] OR "Nobelium"[tiab] OR "Osmium"[tiab] OR "Palladium"[tiab] OR "Platinum"[tiab] OR "Plutonium"[tiab] OR "Polonium"[tiab] OR "Potassium"[tiab] OR "Protactinium"[tiab] OR "Radium"[tiab] OR "Rhenium"[tiab] OR "Rhodium"[tiab] OR "Rubidium"[tiab] OR "Ruthenium"[tiab] OR "Scandium"[tiab] OR "Silicon"[tiab] OR "Silver"[tiab] OR "Sodium"[tiab] OR "Strontium"[tiab] OR "Tantalum"[tiab] OR "Technetium"[tiab] OR "Tellurium"[tiab] OR "Thallium"[tiab] OR "Thorium"[tiab] OR "Tin"[tiab] OR "Titanium"[tiab] OR "Tungsten"[tiab] OR "Uranium"[tiab] OR "Vanadium"[tiab] OR "Yttrium"[tiab] OR "Zinc"[tiab] OR "Zirconium"[tiab] OR "Trace Elements"[Mesh] Filters: from 1998 - 2022 | 1,988,795 |
| 2 | "Cardiometabolic Risk Factors"[Mesh] OR "Heart Diseases"[Mesh] OR "Vascular Diseases"[Mesh] OR "Blood Pressure"[Mesh] OR "Lipoproteins, HDL"[Mesh] OR "Lipoproteins, LDL"[Mesh] OR "Pregnancy Complications, Cardiovascular"[Mesh] OR "Hypertension, Pregnancy-Induced"[Mesh] OR "Cardiovascular disease*"[tiab] OR "myocardial infarction*"[tiab] OR "myocardial ischemia*"[tiab] OR "coronary artery*"[tiab] OR "coronary heart"[tiab] OR "cerebrovascular dis*"[tiab] OR "stroke*"[tiab] OR "atherosclerosis*"[tiab] OR "carotid artery"[tiab] OR "peripheral arterial dis*"[tiab] OR "hypercholesterolemia*"[tiab] OR "hyperlipidemia*"[tiab] OR "dyslipidemia*"[tiab] OR "serum lipid"[tiab] OR "preeclampsia"[tiab] OR "preeclampsia"[tiab] OR "pregnancy hypertens*"[tiab] OR "HELLP"[tiab] Filters: from 1998 - 2022 | 1,903,479 |
| 3 | "mixture*"[tiab] OR "multi-pollutant*"[tiab] OR "multiple metals"[tiab] OR "multi-metal*"[tiab] OR "joint effect*"[tiab] OR "joint association*"[tiab] OR "joint exposure*"[tiab] OR "overall effect*"[tiab] OR "overall association*"[tiab] OR "overall exposure*"[tiab] OR "joint and individual"[tiab] OR "co-pollutant*"[tiab] OR "co-exposure*"[tiab] OR "combined metal*"[tiab] OR "mixed metal*"[tiab] OR "principal component analysis"[tiab] OR "exploratory factor analysis"[tiab] OR "Bayesian Kernel Machine Regression"[tiab] OR "Least Absolute Shrinkage and Selection Operator"[tiab] OR "penalized regression*"[tiab] OR "Weighted Quantile Sum"[tiab] OR "quantile-based g-computation"[tiab] OR "quantile g-computation"[tiab] OR "cluster analysis"[tiab] OR "Bayesian"[tiab] OR "classification and regression tree*"[tiab] OR "random forest*"[tiab] OR "shrinkage-based"[tiab] OR | 410,767 |

| | | |
|---|--|------|
| | "shrinkage method*" [tiab] OR "variable selection regression*" [tiab] OR "structural equation model*" [tiab] OR "multivariate adaptive regression spline*" [tiab] OR "machine learning" [tiab] Filters: from 1998 - 2022 | |
| 4 | #1 AND #2 AND #3 | 1673 |

(b) Database: Scopus

Publication timeline range: 1998 to October 1, 2021

| # | Searches | Results |
|---|---|-----------|
| 1 | TITLE-ABS ("metals" OR "Actinium" OR "Aluminum" OR "Americium" OR "Antimony" OR "Arsenic" OR "Barium" OR "Berkelium" OR "Beryllium" OR "Bismuth" OR "Boron" OR "Cadmium" OR "Calcium" OR "Californium" OR "Cesium" OR "Chromium" OR "Cobalt" OR "Copper" OR "Curium" OR "Einsteinium" OR "Fermium" OR "Francium" OR "Gallium" OR "Germanium" OR "Gold" OR "Hafnium" OR "Indium" OR "Iridium" OR "Iron" OR "Lawrencium" OR "Lead" OR "Lithium" OR "Lutetium" OR "Magnesium" OR "Manganese" OR "Mendelevium" OR "Mercury" OR "Molybdenum" OR "Neptunium" OR "Nickel" OR "Niobium" OR "Nobelium" OR "Osmium" OR "Palladium" OR "Platinum" OR "Plutonium" OR "Polonium" OR "Potassium" OR "Protactinium" OR "Radium" OR "Rhenium" OR "Rhodium" OR "Rubidium" OR "Ruthenium" OR "Scandium" OR "Silicon" OR "Silver" OR "Sodium" OR "Strontium" OR "Tantalum" OR "Technetium" OR "Tellurium" OR "Thallium" OR "Thorium" OR "Tin" OR "Titanium" OR "Tungsten" OR "Uranium" OR "Vanadium" OR "Yttrium" OR "Zinc" OR "Zirconium") AND (LIMIT-TO (PUBYEAR , 2023) OR LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUBYEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000) OR LIMIT-TO (PUBYEAR , 1999) OR LIMIT-TO (PUBYEAR , 1998)) | 7,143,923 |
| 2 | TITLE-ABS-KEY ("Trace Elements") AND (LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUBYEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000) OR LIMIT-TO (PUBYEAR , 1999) OR LIMIT-TO (PUBYEAR , 1998)) | 93,976 |

| | | |
|---|--|-----------|
| | (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUBYEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000) OR LIMIT-TO (PUBYEAR , 1999) OR LIMIT-TO (PUBYEAR , 1998)) | |
| 3 | TITLE-ABS-KEY ("Cardiometabolic Risk Factors" OR "Heart Diseases" OR "Vascular Diseases" OR "Blood Pressure" "High Density Lipoprotein*" OR "Low Density Lipoprotein*" OR "Cardiovascular Pregnancy Complication*" OR "Pregnancy Induced Hypertension" OR "Gestational Hypertension" OR "Pregnancy Transient Hypertension") AND (LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUBYEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000) OR LIMIT-TO (PUBYEAR , 1999) OR LIMIT-TO (PUBYEAR , 1998)) | 64,327 |
| 4 | TITLE-ABS ("Cardiovascular disease*" OR "myocardial infarction*" OR "myocardial ischemia*" OR "coronary artery*" OR "coronary heart" OR "cerebrovascular dis*" OR "stroke*" OR "atherosclerosis*" OR "carotid artery" OR "peripheral arterial dis*" OR "hypercholesterolemia*" OR "hyperlipidemia*" OR "dyslipidemia*" OR "serum lipid" OR "pre-eclampsia" OR "preeclampsia" OR "pregnancy hypertens*" OR "HELLP") AND (LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUBYEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000) OR LIMIT-TO (PUBYEAR , 1999) OR LIMIT-TO (PUBYEAR , 1998)) | 974,815 |
| 5 | TITLE-ABS ("mixture*" OR "multi-pollutant*" OR "multiple metals" OR "multi-metal*" OR "joint effect*" OR "joint association*" OR "joint exposure*" OR "overall effect*" OR "overall association*" OR "overall exposure*" OR "joint and individual" OR "co-pollutant*" OR "co-exposure*" OR "combined metal*" OR "mixed metal*" OR "principal component analysis" OR "exploratory | 1,485,981 |

| | | |
|---|--|-----------|
| | factor analysis" OR "Bayesian Kernel Machine Regression" OR "Least Absolute Shrinkage and Selection Operator" OR "penalized regression*" OR "Weighted Quantile Sum" OR "quantile-based g-computation" OR "quantile g-computation" OR "cluster analysis" OR "Bayesian" OR "classification and regression tree*" OR "random forest*" OR "shrinkage-based" OR "shrinkage method*" OR "variable selection regression*" OR "structural equation model*" OR "multivariate adaptive regression spline*" OR "exposure surface smoothing" OR "novel approach and least-angle regression" OR "machine learning") AND (LIMIT-TO (PUBYEAR , 2023) OR LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUBYEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000) OR LIMIT-TO (PUBYEAR , 1999) OR LIMIT-TO (PUBYEAR , 1998)) | |
| 6 | #1 OR #2 | 7,188,444 |
| 7 | #3 OR #4 | 1,002,568 |
| 8 | #5 AND #6 AND #7 | 1743 |

(c) Database: Web of Science

Publication timeline range: 1998 to October 1, 2021

| # | Searches | Results |
|---|---|-----------|
| 1 | "metals" OR "Actinium" OR "Aluminum" OR "Americium" OR "Antimony" OR "Arsenic" OR "Barium" OR "Berkelium" OR "Beryllium" OR "Bismuth" OR "Boron" OR "Cadmium" OR "Calcium" OR "Californium" OR "Cesium" OR "Chromium" OR "Cobalt" OR "Copper" OR "Curium" OR "Einsteinium" OR "Fermium" OR "Francium" OR "Gallium" OR "Germanium" OR "Gold" OR "Hafnium" OR "Indium" OR "Iridium" OR "Iron" OR "Lawrencium" OR "Lead" OR "Lithium" OR "Lutetium" OR "Magnesium" OR "Manganese" OR "Mendelevium" OR "Mercury" OR "Molybdenum" OR "Neptunium" OR "Nickel" OR "Niobium" OR "Nobelium" OR "Osmium" OR "Palladium" OR "Platinum" OR "Plutonium" OR "Polonium" OR "Potassium" OR "Protactinium" OR "Radium" OR "Rhenium" OR "Rhodium" OR "Rubidium" OR "Ruthenium" OR "Scandium" OR "Silicon" OR "Silver" OR "Sodium" OR "Strontium" OR "Tantalum" OR "Technetium" OR "Tellurium" OR "Thallium" OR "Thorium" OR "Tin" OR "Titanium" OR "Tungsten" OR "Uranium" OR "Vanadium" OR "Yttrium" OR "Zinc" OR "Zirconium" (Title) or "metals" OR "Actinium" OR "Aluminum" OR "Americium" OR "Antimony" OR "Arsenic" OR "Barium" OR "Berkelium" OR "Beryllium" OR "Bismuth" OR "Boron" OR | 4,845,259 |

| | | |
|---|---|-----------|
| | "Cadmium" OR "Calcium" OR "Californium" OR "Cesium" OR "Chromium" OR "Cobalt" OR "Copper" OR "Curium" OR "Einsteinium" OR "Fermium" OR "Francium" OR "Gallium" OR "Germanium" OR "Gold" OR "Hafnium" OR "Indium" OR "Iridium" OR "Iron" OR "Lawrencium" OR "Lead" OR "Lithium" OR "Lutetium" OR "Magnesium" OR "Manganese" OR "Mendelevium" OR "Mercury" OR "Molybdenum" OR "Neptunium" OR "Nickel" OR "Niobium" OR "Nobelium" OR "Osmium" OR "Palladium" OR "Platinum" OR "Plutonium" OR "Polonium" OR "Potassium" OR "Protactinium" OR "Radium" OR "Rhenium" OR "Rhodium" OR "Rubidium" OR "Ruthenium" OR "Scandium" OR "Silicon" OR "Silver" OR "Sodium" OR "Strontium" OR "Tantalum" OR "Technetium" OR "Tellurium" OR "Thallium" OR "Thorium" OR "Tin" OR "Titanium" OR "Tungsten" OR "Uranium" OR "Vanadium" OR "Yttrium" OR "Zinc" OR "Zirconium" (Abstract) Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | |
| 2 | "Trace Elements" (Title) or "Trace Elements" (Abstract) or "Trace Elements" (Author Keywords) Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | 36,948 |
| 3 | "Cardiometabolic Risk Factors" OR "Heart Diseases" OR "Vascular Diseases" OR "Blood Pressure" OR "High Density Lipoprotein*" OR "Low Density Lipoprotein*" OR "Cardiovascular Pregnancy Complication*" OR "Pregnancy Induced Hypertension" OR "Gestational Hypertension" OR "Pregnancy Transient Hypertension" (Title) or "Cardiometabolic Risk Factors" OR "Heart Diseases" OR "Vascular Diseases" OR "Blood Pressure" OR "High Density Lipoprotein*" OR "Low Density Lipoprotein*" OR "Cardiovascular Pregnancy Complication*" OR "Pregnancy Induced Hypertension" OR "Gestational Hypertension" OR "Pregnancy Transient Hypertension" (Abstract) or "Cardiometabolic Risk Factors" OR "Heart Diseases" OR "Vascular Diseases" OR "Blood Pressure" OR "High Density Lipoprotein*" OR "Low Density Lipoprotein*" OR "Cardiovascular Pregnancy Complication*" OR "Pregnancy Induced Hypertension" OR "Gestational Hypertension" OR "Pregnancy Transient Hypertension" (Author Keywords) Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | 331,988 |
| 4 | "Cardiovascular disease*" OR "myocardial infarction*" OR "myocardial ischemia*" OR "coronary artery*" OR "coronary heart" OR "cerebrovascular dis*" OR "stroke*" OR "atherosclerosis*" OR "carotid artery" OR "peripheral arterial dis*" OR "hypercholesterolemia*" OR "hyperlipidemia*" OR "dyslipidemia*" OR "serum lipid" OR "pre-eclampsia" OR "preeclampsia" OR "pregnancy hypertens*" OR "HELLP" (Title) or "Cardiovascular disease*" OR "myocardial infarction*" OR "myocardial ischemia*" OR "coronary artery*" OR "coronary heart" OR "cerebrovascular dis*" OR "stroke*" OR "atherosclerosis*" OR "carotid artery" OR "peripheral arterial dis*" OR "hypercholesterolemia*" OR "hyperlipidemia*" OR "dyslipidemia*" OR "serum lipid" OR "pre-eclampsia" OR "preeclampsia" OR "pregnancy hypertens*" OR "HELLP" (Abstract) Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | 907,580 |
| 5 | "mixture*" OR "multi-pollutant*" OR "multiple metals" OR "multi-metal*" OR "joint effect*" OR "joint association*" OR "joint exposure*" OR "overall effect*" OR "overall association*" OR "overall exposure*" OR "joint and individual" OR "co-pollutant*" OR "co-exposure*" OR "combined metal*" OR "mixed metal*" OR "principal component analysis" OR "exploratory factor analysis" OR "Bayesian Kernel Machine Regression" OR "Least Absolute Shrinkage and Selection Operator" OR "penalized regression*" OR "Weighted Quantile Sum" OR "quantile-based g-computation" OR | 1,204,124 |

| | | |
|---|--|-----------|
| | "quantile g-computation" OR "cluster analysis" OR "Bayesian" OR "classification and regression tree*" OR "random forest*" OR "shrinkage-based" OR "shrinkage method*" OR "variable selection regression*" OR "structural equation model*" OR "multivariate adaptive regression spline*" OR "exposure surface smoothing" OR "novel approach and least-angle regression" OR "machine learning" (Title) or "mixture*" OR "multi-pollutant*" OR "multiple metals" OR "multi-metal*" OR "joint effect*" OR "joint association*" OR "joint exposure*" OR "overall effect*" OR "overall association*" OR "overall exposure*" OR "joint and individual" OR "co-pollutant*" OR "co-exposure*" OR "combined metal*" OR "mixed metal*" OR "principal component analysis" OR "exploratory factor analysis" OR "Bayesian Kernel Machine Regression" OR "Least Absolute Shrinkage and Selection Operator" OR "penalized regression*" OR "Weighted Quantile Sum" OR "quantile-based g-computation" OR "quantile g-computation" OR "cluster analysis" OR "Bayesian" OR "classification and regression tree*" OR "random forest*" OR "shrinkage-based" OR "shrinkage method*" OR "variable selection regression*" OR "structural equation model*" OR "multivariate adaptive regression spline*" OR "exposure surface smoothing" OR "novel approach and least-angle regression" OR "machine learning" (Abstract) Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | |
| 6 | #1 OR #2 Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | 4,863,674 |
| 7 | #3 OR #4 Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | 1,136,396 |
| 8 | #5 AND #6 AND #7 Timespan: 1998-01-01 to 2021-10-01 (Publication Date) | 1433 |

Table S2. Metal concentrations from the studies included in this review

| Source | Exposure matrix | Metal concentrations | | |
|---------------------------------|--|----------------------|-----------|-------------------------------------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Blood pressure and hypertension | | | | |
| Park et al. 2017 | Blood and urine (µg/dL) | | | Sb: 0.06 (2.21) |
| | | | | Total As: 8.88 (3.17) |
| | | | | Arsenous acid: 0.65 (1.91) |
| | | | | Arsenic acid: 0.68 (1.21) |
| | | | | Arsenobetaine: 1.99 (5.19) |
| | | | | Arsenocholine: 0.30 (1.91) |
| | | | | Dimethylarsonic acid: 3.85 (2.27) |
| | | | | Monomethylarsonic acid: 0.73 (1.85) |
| | | | | Ba: 1.20 (2.72) |
| | | | | Cd: 0.24 (2.77) |
| | | | | Co: 0.34 (2.26) |
| | | | | Cs: 4.22 (2.00) |
| | | | | Pb: 0.51 (2.47) |
| | | | | Mo: 38.64 (2.42) |
| | | | | Tl: 0.14 (2.09) |
| | | | | W: 0.07 (2.77) |
| | | | | U: 0.01 (2.65) |
| | | | | In blood |
| | | | | Cd: 0.37 (2.22) |
| | | | | Pb: 1.32 (2.00) |
| | | | | Total Hg: 0.93 (2.68) |
| Wang et al. 2018 | Blood and urine (µg/L for all but serum Pb (µg/dL)) | | | In urine |
| | | | | Sb: 0.06 (2.21) |
| | | | | Total As: 8.85 (3.16) |
| | | | | Arsenobetaine: 1.98 (5.17) |
| | | | | monomethylarsonic acid: 0.73 (1.85) |
| | | | | dimethylarsinic acid: 3.84 (2.26) |
| | | | | Ba: 1.20 (2.72) |
| | | | | Cd: 0.24 (2.77) |
| | | | | Co: 0.34 (2.25) |
| | | | | Cs: 4.21 (2.01) |

| Source | Exposure matrix | Metal concentrations | | |
|---------------------------|-----------------------------------|----------------------|-----------|------------------------------------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Kupsco et al. 2019 | Blood (µg/dL) | | | Pb: 0.50 (2.47) |
| | | | | Hg: 0.39 (2.93) |
| | | | | Mo: 38.59 (2.42) |
| | | | | Tl: 0.14 (2.09) |
| | | | | W: 0.07 (2.77) |
| | | | | U: 0.01 (2.64) |
| | | | | |
| | | | | As: 0.085 (0.058) |
| | | | | Cd: 0.029 (0.019) |
| | | | | Co: 0.022 (0.024) |
| | | | | Cr: 0.080 (0.128) |
| | | | | Cs: 0.310 (0.135) |
| | | | | Cu: 158 (32) |
| | | | | Mn: 1.5 (0.50) |
| | | | | Pb: 3.7 (2.7) |
| Warembourg et al. 2019 | Blood (µg/L) | | | Sb: 0.38 (0.10) |
| | | | | Se: 25 (4.5) |
| | | | | Zn: 613 (130) |
| | | | | |
| | | | | As: 1.2 (0.3, 2.3) |
| | | | | Cd: 0.2 (0.1, 0.3) |
| | | | | Co: 0.2 (0.1, 0.3) |
| | | | | Cs: 1.6 (1.2, 2.1) |
| | | | | Cu: 1420 (1270, 1610) |
| | | | | Hg: 1.9 (1.0, 3.4) |
| | | | | Mn: 11.1 (8.5, 14.3) |
| | | | | Mo: 0.6 (0.5, 0.8) |
| | | | | Pb: 9.7 (7.1, 13.2) |
| | | | | Tl: 2.0 (2.0, 2.0) |
| | | | | |
| Castiello et al. 2020 | Urine (µg/g, creatinine adjusted) | | | As: 12.1 (5.02, 25.7) ^a |
| | | | | Cd: 0.04 (0.03, 0.06) ^a |
| | | | | Hg: 0.30 (0.17, 0.57) ^a |
| | | | | Ni: - (<0.55, 3.03) ^a |
| | | | | Pb: 0.24 (0.16, 0.34) ^a |
| | | | | Cr: - (<0.44, 1.22) ^a |
| | | | | Mn: - (<0.02, 0.82) ^a |

| Source | Exposure matrix | Metal concentrations | | |
|------------------------|---|--|-----------|---|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Desai et al. 2021 | Blood and urine (µg/dL for Pb; µg/L for Hg; and µg/g creati- nine for As and Cd) | In blood Pb: 0.57 (0.26, 1.60) ^b Hg: 0.37 (0.19, 2.12) ^b | | |
| | | In urine As: 5.61 (1.37, 33.2) ^b Cd: 0.06 (0.03, 0.23) ^b | | |
| | | In blood Pb: 1.5 (1, 2.2) ^c | | |
| Everson et al. 2021 | Blood and urine (µg/g for Ba, Cd, Co, Cs, Mo, Sb, Tl, and W; µg/dL for Pb) | In urine Ba: 1.33 (0.75, 2.31) ^c Cd: 0.23 (0.13, 0.40) ^c Co: 0.28 (0.19, 0.42) ^c Cs: 4.24 (3.23, 5.67) ^c Mo: 37.3 (25.4, 52.4) ^c Sb: 0.10 (0.06, 0.15) ^c Tl: 0.15 (0.11, 0.20) ^c W: 0.06 (0.03, 0.11) ^c Mg: 71.3 (50.5, 100.9) ^d | | |
| | | Co: 0.46 (0.28, 1.01) ^d Se: 21.8 (17.3, 27.0) ^d Mo: 64.9 (50.5, 86.7) ^d As: 12.2 (5.2, 34.5) ^d Cd: 0.47 (0.30, 0.69) ^d Sb: 0.05 (0.04, 0.07) ^d Pb: 1.00 (0.69, 1.48) ^d | | Mg: 66.9 (61.3, 72.9) ^d Co: 0.54 (0.48, 0.61) ^d Se: 21.72 (20.72, 22.77) ^d Mo: 65.26 (61.13, 69.66) ^d As: 15.21 (12.50, 18.49) ^d Cd: 0.45 (0.41, 0.50) ^d Sb: 0.05 (0.05, 0.06) ^d Pb: 0.92 (0.82, 1.04) ^d |
| | | | | Pb (µg/dL): 1.89 (1.88, 1.91) ^a Hg (µg/L): 3.35 (3.31, 3.39) ^a Cd (µg/L): 0.94 (0.93, 0.95) ^a |
| Kim and Park. 2021 | Blood (µg/dL for Pb, and µg/L for Hg and Cd) | | | |
| Shih et al. 2021 | Toenail (µg/g) | Al: 401.89 (342.89) V: 0.99 (0.85) Cr: 1.21 (1.11) Mn: 14.71 (14.63) | | |

| Source | Exposure matrix | Metal concentrations | | |
|-------------------|-------------------------|--------------------------|-------------------------|----------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Xu et al. 2021 | Blood (ng/mL) | Fe: 753.62 (638.22) | | |
| | | Co: 0.35 (0.31) | | |
| | | Ni: 2.76 (2.29) | | |
| | | Cu: 4.91 (1.98) | | |
| | | Zn: 134.12 (41.80) | | |
| | | As: 1.69 (2.04) | | |
| | | Se: 0.69 (0.19) | | |
| | | Mo: 0.04 (0.03) | | |
| | | Cd: 0.11 (0.13) | | |
| | | Sn: 0.23 (0.22) | | |
| | | Hg: 0.19 (0.17) | | |
| | | Pb: 1.90 (1.66) | | |
| | | U: 0.07 (0.02) | | |
| | | Cd: 0.4 (0.2, 0.8) | | |
| | | Pb: 1.2 (0.8, 1.9) | | |
| | | Hg: 0.9 (0.5, 1.9) | | |
| | | Mn: 8.4 (6.9, 10.6) | | |
| | | Se: 198.0 (184.2, 215.6) | | |
| Yao et al. 2021 | Blood and urine (µg/dL) | | In blood | |
| | | | Pb: 1.71 (1.66) | |
| | | | Cd: 0.52 (0.58) | |
| | | | Total Hg: 1.59 (2.45) | |
| | | | In urine | |
| Zhang et al. 2021 | Blood (µg/dL) | | Total As: 20.49 (55.39) | |
| | | | Cd: 0.4 (0.47) | |
| | | | Pb: 0.78 (1.33) | |
| | | | Pb: 3.29 (3.03) | |
| | | | Hg: 3.15 (3.60) | |
| Zhong et al. 2021 | Urine (µg/g creatinine) | | Cd: 0.86 (0.68) | |
| | | | Se: 289.50 (60.49) | |
| | | | Mn: 39.57 (15.28) | |
| | | | | |
| | | | | |

| Source | Exposure matrix | Metal concentrations | | |
|---------------------------------------|--|------------------------------------|------------------|----------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Zuk et al. 2021 | Blood (µmol/L for Pb and Se; nmol/L for the others) | Ba: 5.37 (2.12, 11.10) | | |
| | | Bi: 16.92 (1.39, 45.61) | | |
| | | Cd: 2.35 (1.15, 5.22) | | |
| | | Co: 2.46 (0.22, 6.20) | | |
| | | Cr: 18.74 (6.66, 34.01) | | |
| | | Cu: 14.19 (9.07, 21.64) | | |
| | | Fe: 14.27 (4.76, 37.40) | | |
| | | Li: 13.55 (8.08, 20.84) | | |
| | | Mg: 32.49 (21.49, 49.64) | | |
| | | Mn: 0.39 (0.13, 1.43) | | |
| | | Mo: 73.71 (38.21, 133.05) | | |
| | | Rb: 308.52 (127.10, 555.63) | | |
| | | Se: 33.95 (7.95, 68.31) | | |
| | | Sr: 115.73 (69.33, 187.31) | | |
| | | Zn: 462.98 (281.81, 801.68) | | |
| | | | Female | |
| | | | Cd: 8.18 (2.82) | |
| | | | Hg: 15.79 (3.88) | |
| | | | Pb: 0.12 (2.93) | |
| | | | Se: 2.13 (1.16) | |
| | | | Male | |
| | | | Cd: 7.79 (3.11) | |
| | | | Hg: 21.40 (3.95) | |
| | | | Pb: 0.19 (2.53) | |
| | | | Se: 2.24 (1.14) | |
| Preeclampsia | | | | |
| Bommarito et al. 2019 ^e | 3 rd trimester urine (µg/L) | As: 17.9 (9.59, 32.6) ^d | | |
| | | Ba: 1.93 (0.98, 3.34) ^d | | |
| | | Cd: 0.08 (0.04, 0.14) ^d | | |
| | | Cu: 8.96 (6.73, 12.1) ^d | | |
| | | Hg: 0.51 (0.27, 0.97) ^d | | |
| | | Mn: 0.73 (0.51, 1.13) ^d | | |
| | | Mo: 51.3 (37.1, 68.8) ^d | | |

| Source | Exposure matrix | Metal concentrations | | |
|-------------------------------------|---|--|-----------|--|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Wang et al. 2020 | Blood (µg/L for Cr, Co, Ni, As, Cd, Sb, and Hg, and µg/dL for Pb) | Ni: 2.84 (1.88, 3.97) ^d | | |
| | | Pb: 0.35 (0.15, 0.62) ^d | | |
| | | Se: 37.0 (29.6, 45.6) ^d | | |
| | | Sn: 0.63 (0.35, 1.22) ^d | | |
| | | Tl: 0.13 (0.08, 0.18) ^d | | |
| | | Zn: 242 (146, 364) ^d | | |
| | | Be, Cr, U, and W: Metals with >70% of sam- ples below the LOD | | |
| | | Cr: 8.52 (2.68, 33.52) | | |
| | | Co: 0.37 (0.05, 1.83) | | |
| | | Ni: 7.46 (1.50, 14.76) | | |
| | | As: 15.55 (8.39, 23.00) | | |
| | | Cd: 1.11 (0.61, 4.26) | | |
| | | Sb: 1.67 (0.55, 10.59) | | |
| | | Hg: 1.50 (0.96, 2.22) | | |
| | | Pb: 2.96 (2.25,3.84) | | |
| | | Ba: 1.09 (0.80, 1.57) | | |
| | | Co: 0.26 (0.23, 0.31) | | |
| | | Cs: 0.39 (0.30, 0.49) | | |
| Liu et al. 2021 | Blood (µg/L) | Cu: 1873.77 (1632.56, 2106.86) | | |
| | | Mo: 1.94 (1.36, 2.68) | | |
| | | Sb: 3.03 (2.51, 3.60) | | |
| | | Se: 122.88 (113.58, 133.02) | | |
| | | Zn: 803.34 (712.82, 898.97) | | |
| Dyslipidemia and serum lipid levels | | | | |
| Park et al. 2014 | Blood and urine | NA | NA | NA |
| Kupsco et al. 2019 | | Please see above | | |
| Zhu et al. 2020 | Blood (µg/L) | | | Sr: 23.15 (18.27, 29.03) ^f |
| | | | | Cd: 1.06 (0.66, 1.58) ^f |
| | | | | Pb: 28.07 (20.35, 36.15) ^f |
| | | | | V: 0.73 (0.46, 1.02) ^f |
| | | | | Al: 67.94 (42.58, 115.85) ^f |

| Source | Exposure matrix | Metal concentrations | | |
|-----------------------------|---------------------------|-------------------------------|-----------|--|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Jiang et al. 2021 | Blood (µg/L) | | | Co: 0.14 (0.10, 0.19) ^f |
| | | | | Mn: 27.05 (24.15, 29.49) ^f |
| | | Al: 47.20 (29.14, 92.27) | | Al: 57.29 (29.14, 92.27) ^a |
| | | Sb: 0.12 (0.07, 0.20) | | Sb: 0.11 (0.07, 0.20) ^a |
| | | As: 1.86 (1.21, 3.42) | | As: 2.05 (1.21, 3.42) ^a |
| | | Ba: 32.82 (21.94, 60.39) | | Ba: 37.33 (21.94, 60.39) ^a |
| | | Co: 0.16 (0.12, 0.20) | | Co: 0.16 (0.12, 0.20) ^a |
| | | Cu: 951.51 (841.44, 1068.77) | | Cu: 943.35 (841.44, 1068.77) ^a |
| | | Pb: 12.73 (8.74, 20.09) | | Pb: 15.14 (8.74, 20.09) ^a |
| | | Mn: 3.71 (2.70, 5.23) | | Mn: 3.75 (2.70, 5.23) ^a |
| | | Mo: 1.32 (1.05, 1.70) | | Mo: 1.33 (1.05, 1.70) ^a |
| | | Ni: 2.72 (2.01, 4.02) | | Ni: 3.08 (2.01, 4.02) ^a |
| | | Rb: 348.71 (311.66, 391.10) | | Rb: 349.65 (311.66, 391.10) ^a |
| | | Se: 64.88 (56.03, 75.06) | | Se: 65.26 (56.03, 75.06) ^a |
| | | Sr: 34.94 (29.61, 41.30) | | Sr: 35.22 (29.61, 41.30) ^a |
| | | Tl: 0.13 (0.10, 0.17) | | Tl: 0.13 (0.10, 0.17) ^a |
| | | Ti: 32.40 (25.54, 41.08) | | Ti: 32.55 (25.54, 41.08) ^a |
| | | V: 0.75 (0.56, 1.25) | | V: 0.87 (0.56, 1.25) ^a |
| | | Zn: 1157.38 (978.94, 2459.94) | | Zn: 1752.26 (978.94, 2459.94) ^a |
| | | In blood, Shimen area | | |
| | | Fe: 1014.72(733.75,1293.04) | | |
| | | Cu: 851.85(716.45,1019.25) | | |
| | | Zn: 907.25(802.21,1036.03) | | |
| | | Se: 111.28(93.80,136.68) | | |
| Li et al. 2021 ^g | Blood and urine (µg/L) | In urine, Shimen area | | |
| | | Al: 7.92(4.79,11.98) | | |
| | | Ti: 170.23(113.23,257.18) | | |
| | | V: 1.31(1.02,1.62) | | |
| | | Cr: 1.82(1.15,3.52) | | |
| | | Mn: 0.32(0.19,0.51) | | |
| | | Co: 0.32(0.21,0.51) | | |
| | | Ni: 2.70(1.59,4.82) | | |
| | | As: 57.67(41.22,83.51) | | |

| Source | Exposure matrix | Metal concentrations | | |
|--------|-----------------|------------------------------|-----------|----------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| | | Rb: 2324.83(1545.34,3209.57) | | |
| | | Sr: 149.35(95.07,229.90) | | |
| | | Mo: 88.47(58.98,138.67) | | |
| | | Cd: 2.70(1.48,4.79) | | |
| | | Sn: 0.26(0.18,0.41) | | |
| | | Sb: 0.08(0.06,0.13) | | |
| | | Ba: 1.89(1.04,3.43) | | |
| | | W: 0.07(0.04,0.12) | | |
| | | Tl: 0.81(0.53,1.19) | | |
| | | U: 0.01(0.01,0.02) | | |
| | | In blood, Huayuan area | | |
| | | Fe: 845.60(608.30,1129.81) | | |
| | | Cu: 801.60(680.36,1030.70) | | |
| | | Zn: 825.79(715.38,938.90) | | |
| | | Se: 65.78(55.81,76.36) | | |
| | | In urine, Huayuan area | | |
| | | Al: 8.73(5.21,14.70) | | |
| | | Ti: 77.01(48.27,124.82) | | |
| | | V: 0.72(0.53,0.94) | | |
| | | Cr: 1.12(0.67,1.62) | | |
| | | Mn: 0.35(0.18,1.04) | | |
| | | Co: 0.32(0.21,0.53) | | |
| | | Ni: 1.81(1.05,3.02) | | |
| | | As: 40.08(24.16,59.46) | | |
| | | Rb: 2365.91(1500.01,3434.93) | | |
| | | Sr: 93.72(51.43,157.02) | | |
| | | Mo: 111.02(66.38,185.67) | | |
| | | Cd: 2.15(1.20,3.54) | | |
| | | Sn: 0.26(0.16,0.44) | | |
| | | Sb: 0.09(0.06,0.13) | | |
| | | Ba: 1.41(0.68,2.71) | | |
| | | W: 0.07(0.04,0.12) | | |

| Source | Exposure matrix | Metal concentrations | | |
|-----------------------|-----------------|--------------------------------|-------------------------|----------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| | | Tl: 0.52(0.31,0.83) | | |
| | | U: 0.01(0.01,0.02) | | |
| <i>CVD outcomes</i> | | | | |
| | | Co: 0.23 (0.13, 0.48) | | |
| | | Cu: 6.06 (3.78, 9.74) | | |
| | | Mo: 25.37 (13.41, 50.32) | | |
| | | Zn: 183.16 (95.85, 341.73) | | |
| | | Sb: 0.08 (0.03, 0.16) | | |
| | | Ba: 58.44 (31.71, 103.61) | | |
| | | Cd: 0.38 (0.23, 0.64) | | |
| | | Cr: 3.58 (2.27, 5.88) | | |
| | | V: 2.12 (1.32, 3.47) | | |
| Kupsco et al. 2019 | | | <i>Please see above</i> | |
| | | | As: 0.07 (0.08) | |
| | | | Cd: 14.18 (14.22) | |
| | | | Co: 4.28 (10.05) | |
| | | | Cu: 15.27 (2.42) | |
| | | | Pb: 0.23 (0.25) | |
| | | | Hg: 34.15 (62.25) | |
| | | | Mo: 6.15 (3.12) | |
| | | | Ni: 21.84 (10.03) | |
| | | | Se: 2.19 (0.32) | |
| | | | Zn: 96.99 (12.24) | |
| | | Al: 25.98 (17.76, 41.78) | | |
| | | As: 1.18 (0.66, 2.39) | | |
| | | Cd: 0.05 (0.03, 0.08) | | |
| | | Co: 0.24 (0.19, 0.30) | | |
| | | Cu: 890.43 (751.50, 1029.45) | | |
| | | Fe: 1759.33 (1366.16, 2280.28) | | |
| | | Mn: 9.61 (7.61, 11.85) | | |
| | | Mo: 1.12 (0.90, 1.44) | | |
| | | Se: 97.42 (84.66, 113.42) | | |
| | | Tl: 0.11 (0.09, 0.15) | | |

| Source | Exposure matrix | Metal concentrations | | |
|----------------------------------|------------------|--|-----------|----------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Xiao et al. 2019 ^e | Blood (µg/dL) | Zn: 1033.04 (857.54, 1228.16) | | |
| | | Controls matched to ischemic stroke cases | | |
| | | Al: 56.78 (36.96, 103.64) | | |
| | | As: 1.86 (1.09, 3.77) | | |
| | | Ba: 38.33 (23.04, 67.81) | | |
| | | Co: 0.17 (0.14, 0.21) | | |
| | | Cu: 953.14 (850.30, 1071.60) | | |
| | | Pb: 13.30 (8.75, 23.75) | | |
| | | Mn: 2.79 (2.12, 3.90) | | |
| | | Hg: 0.55 (0.36, 0.84) | | |
| | | Mo: 1.27 (1.00, 1.66) | | |
| | | Ni: 2.44 (1.83, 3.55) | | |
| | | Rb: 348.50 (309.66, 394.25) | | |
| | | Se: 66.36 (57.50, 78.59) | | |
| | | Sr: 33.92 (28.56, 41.63) | | |
| | | Tl: 0.10 (0.08, 0.13) | | |
| | | Ti: 49.09 (41.49, 56.95) | | |
| | | W: 0.05 (0.03, 0.07) | | |
| | | V: 1.41 (1.13, 1.95) | | |
| | | Zn: 1383.21 (1046.25, 2775.78) | | |
| | | Controls matched to hemorrhagic stroke cases | | |
| | | Al: 60.23 (38.98, 131.83) | | |
| | | As: 1.91 (1.04, 4.38) | | |
| | | Ba: 41.37 (23.12, 69.01) | | |
| | | Co: 0.16 (0.13, 0.21) | | |
| | | Cu: 999.38 (884.52, 1120.40) | | |
| | | Pb: 13.18 (8.79, 23.70) | | |
| | | Mn: 2.97 (2.06, 4.05) | | |
| | | Hg: 0.55 (0.33, 0.86) | | |
| | | Mo: 1.34 (1.02, 1.71) | | |
| | | Ni: 2.36 (1.77, 3.36) | | |
| | | Rb: 357.90 (318.82, 396.32) | | |

| Source | Exposure matrix | Metal concentrations | | |
|--------------------|--|--------------------------------|-----------|----------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| Cabral et al. 2021 | Blood (µg/L for Mn, Fe, Cu, Zn, I, and Se; mg/L for SELENOP; and nM for free-Zn) | Se: 68.86 (57.14, 78.66) | | |
| | | Sr: 34.59 (28.30, 40.55) | | |
| | | Tl: 0.10 (0.08, 0.14) | | |
| | | Ti: 44.13 (35.50, 55.49) | | |
| | | W: 0.05 (0.03, 0.07) | | |
| | | V: 1.42 (1.14, 2.01) | | |
| | | Zn: 1461.55 (1072.69, 2830.71) | | |
| | | Mn: 1.04 (1.14) | | |
| | | Fe: 928 (433) | | |
| | | Cu: 1021 (333) | | |
| | | Zn: 728 (185) | | |
| | | I: 56.7 (15.9) | | |
| | | Se: 80.0 (19.1) | | |
| | | SELENOP: 5.3 (1.8) | | |
| | | Free-Zn: 0.59 (0.31) | | |
| | | Cr: 1.352 (0.886, 1.902) | | |
| | | Mn: 12.219 (9.005, 15.767) | | |
| Liu et al. 2021 | Blood (µg/L) | Co: 0.336 (0.268, 0.395) | | |
| | | Ni: 0.729 (0.311, 1.163) | | |
| | | Cu: 508.271 (401.244, 672.552) | | |
| | | Mo: 0.485 (0.256, 0.757) | | |
| | | Cs: 1.047 (0.779, 1.314) | | |
| | | Ba: 3.191 (1.994, 4.529) | | |
| | | Tl: 0.027 (0.019, 0.038) | | |
| | | Pb: 0.625 (0.269, 1.127) | | |
| | | Al: 0.64 (0.34, 1.45) | | |
| | | Ti: 9.94 (6.82, 14.48) | | |
| Yang et al. 2021 | Urine (µg/mmol creatinine) | V: 0.06 (0.04, 0.09) | | |
| | | Cr: 0.04 (0.03, 0.06) | | |
| | | Mn: 0.03 (0.01, 0.06) | | |
| | | Fe: 0.78 (0.50, 1.48) | | |
| | | Co: 0.03 (0.02, 0.05) | | |
| | | Ni: 0.37 (0.25, 0.63) | | |
| | | Cu: 0.91 (0.71, 1.22) | | |

| Source | Exposure matrix | Metal concentrations | | |
|--------|-----------------|-----------------------------|-----------|----------|
| | | Median (IQR) | Mean (SD) | GM (GSD) |
| | | Zn: 35.23 (20.58, 52.00) | | |
| | | As: 3.05 (2.05, 4.65) | | |
| | | Se: 1.63 (1.25, 2.12) | | |
| | | Rb: 152.76 (108.30, 207.83) | | |
| | | Sr: 13.17 (9.11, 23.48) | | |
| | | Mo: 5.51 (3.92, 8.37) | | |
| | | Cd: 0.08 (0.05, 0.18) | | |
| | | Sn: 0.04 (0.02, 0.05) | | |
| | | Sb: 0.01 (0.01, 0.02) | | |
| | | Ba: 0.18 (0.09, 0.37) | | |
| | | Tl: 0.03 (0.02, 0.04) | | |
| | | Pb: 0.11 (0.07, 0.16) | | |
| | | U: 0.002 (0.000, 0.003) | | |

Al, Aluminum; As, Arsenic; B, Boron; Ba, Barium; Be, Beryllium; Bi, Bismuth; Cd, Cadmium; Co, Cobalt; Cr, Chromium; Cs, Cesium; Cu, Copper; Fe, Iron; GM, geometric mean; GSD, geometric standard deviation; Hg, Mercury; I, Iodine; IQR, interquartile range; Li, Lithium; Mg, Magnesium; Mn, Manganese; Mo, Molybdenum; Ni, Nickel; Pb, Lead; Rb, Rubidium; Sb, Antimony; SD, standard deviation; Se, Selenium; Selenop, selenoprotein; Sn, Tin; Sr, Strontium; Ti, Titanium; Tl, Thallium; U, Uranium; V, Vanadium; W, Tungsten; Zn, Zinc; ^a GM (IQR); ^b The range between 5th and 95th percentiles; ^c Weighted median; ^d Specific gravity-adjusted median or geometric mean; ^e Among non-cases; ^f GM (95% confidence interval); ^g The range of the summary measure was not specified to be as accurate as possible (e.g., IQR or 5th and 95th percentile range).

Table S3. Comparisons of the mixtures analysis methods most commonly used in this review

| Principal component analysis (PCA) | Bayesian kernel machine regression (BKMR) | Weighted quantile sum regression (WQSR) |
|--|--|---|
| Unsupervised | Supervised | |
| <ul style="list-style-type: none">Can be used to identify exposure patternsRelies on an orthogonal solutionPotentially driven by variables irrelevant to the outcomesNumber of components to retain is determined by the investigator | <ul style="list-style-type: none">Can estimate joint association for the mixture (WQSR can estimate a single coefficient)Can estimate individual chemical associations with the outcome (posterior inclusion probabilities from BKMR and weight from WQSR indicate each component’s relative importance within a mixture)Can be used for variable selectionSemi-parametricNonadditivityNonlinearityFlexible directionalityComputationally expensive- | <ul style="list-style-type: none">ParametricInteractions between the mixture components need to be hard-codedAssumes a linear association between the mixture and outcomeHomogeneous directionality assumed-Uses quantiles of exposure and choice of number of quantiles is subjective |