Supplementary Materials for

**Metal/metalloid levels and variation in lifetime cancer risks among tissues**

Xiang Wanga†, Zhuozhi Lianga†, Jiayu Guoa, Meixia Wangb, Ruimei Zhuc, Yuelin Lia, Jiayi Zhanga, Yixin Zhanga, Luying Tangd\*and Zefang Rena\*

1. *School of Public Health, Sun Yat-sen University, Guangzhou, China*
2. *Xiamen Branch, Zhongshan Hospital, Fudan University, Xiamen, China*
3. *The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China*
4. *The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China*

\*Correspondence to:

Ze-Fang Ren

Email: [renzef@mail.sysu.edu.cn](mailto:renzef@mail.sysu.edu.cn) (Zefang Ren)

Lu-Ying Tang

Email: [tangly@mail.sysu.edu.cn](mailto:tangly@mail.sysu.edu.cn) (Luying Tang)

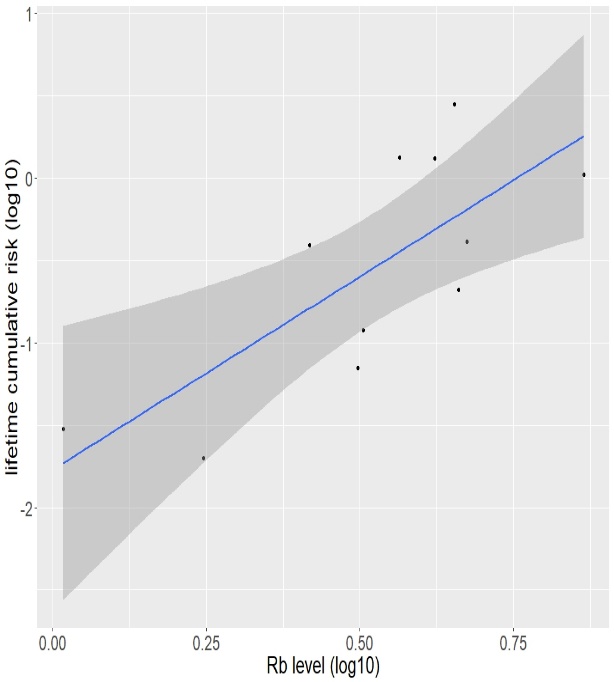
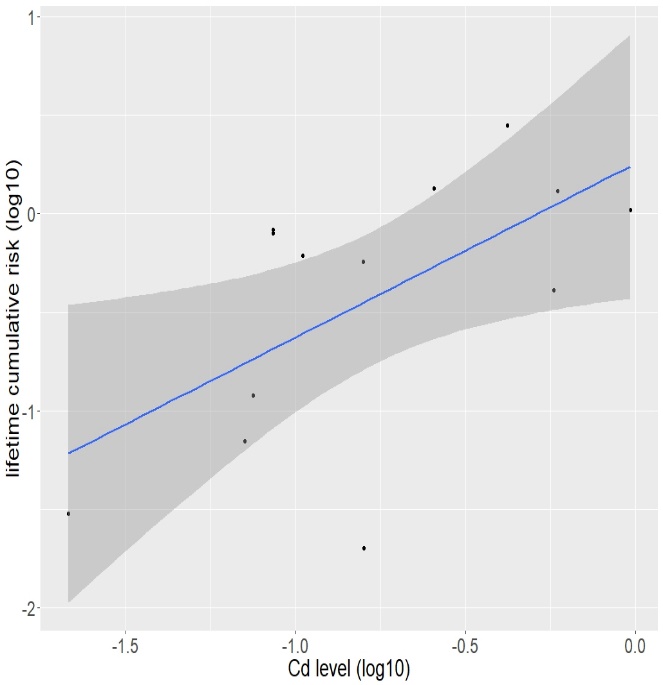
|  |  |  |  |
| --- | --- | --- | --- |
| **Table S1.** Analytical techniques for the 23 metals/metalloids in all tissues.\* | | | |
| Metal/metalloid | Technique | Metal/metalloid | Technique |
| U | ICP-MS | Cu | ICP-MS |
| Th | ICP-MS | Fe | ICP-AES |
| Rb | ICP-MS | Mo | ICP-AES |
| Ba | ICP-AES | Se | ICP-MS |
| Ce | ICP-MS | Zn | ICP-AES |
| Co | ICP-MS | Al | ICP-MS |
| Cs | ICP-MS | As | ICP-MS |
| I | ICP-MS | Cd | ICP-MS |
| La | ICP-MS | Hg | ICP-MS |
| Sr | ICP-MS | Pb | ICP-MS |
| Zr | ICP-MS | Sn | ICP-MS |
| Cr | GF-AAS |  |  |
| ICP-MS inductively coupled plasma mass spectrometry; ICP-AES inductively coupled plasma atomic emission spectrometry; GF-AAS graphite furnace atomic absorption spectrometry | | | |
| \*Source from (IRMCAMS, 2014) | | | |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table S2.** The references ofmetal/metalloid concentrations among tissues for Chinese (mg/kg). †\* | | | | | | | | | | | | | | | | | |
| Metal | Thyroid | Liver | Colon | Rectum | Lung | Kidney | Stomach | Testis | Pancreas | Blood | Ovary | Brain | Bone | Skin | Small intestine | | Adrenal gland |
| U | 1.06 | 0.44 | 6.00 | 6.00 | 1.54 | 1.10 | 1.33 | 0.66 | 1.62 | 0.10 | NA | NA | 1.58 | 1.00 | 2.01 | 1.58 | |
| Th | 1.32 | 0.30 | 0.32 | 0.32 | 8.44 | 0.27 | 0.65 | 0.24 | 0.33 | 0.15 | NA | NA | 1.82 | 0.62 | 0.98 | 0.73 | |
| Rb | 4.19 | 7.31 | 0.64 | 0.64 | 4.51 | 4.58 | 3.67 | 3.86 | 4.72 | 2.62 | NA | NA | 3.20 | 1.04 | 3.14 | 1.76 | |
| Ba | 0.10 | 0.09 | 0.19 | 0.19 | 0.73 | 0.05 | 0.19 | 0.10 | 0.09 | 0.07 | NA | NA | 3.20 | 0.13 | 0.56 | 0.18 | |
| Ce | 55.00 | 91.40 | 2.47 | 2.47 | 113.00 | 2.16 | 3.20 | 1.99 | 6.12 | 0.57 | NA | NA | 36.60 | 9.28 | 3.24 | 4.27 | |
| Co | 35.00 | 40.40 | 3.96 | 3.96 | 24.20 | 13.20 | 6.21 | 3.25 | 6.88 | 0.66 | 15.00 | 27.00 | 33.60 | 2.52 | 28.50 | 8.32 | |
| Cs | 11.60 | 12.20 | 2.52 | 2.52 | 16.40 | 14.70 | 10.30 | 9.07 | 10.00 | 3.06 | NA | NA | 8.86 | 3.82 | 9.82 | 3.46 | |
| I | 662.00 | 0.27 | 0.15 | 0.15 | 0.15 | 0.25 | 0.18 | 0.14 | 0.28 | 0.06 | 0.14 | NA | 0.23 | 0.14 | 0.21 | 0.17 | |
| La | 13.00 | 34.50 | 4.81 | 4.81 | 62.30 | 2.58 | 15.10 | 1.14 | 1.95 | 1.22 | NA | NA | 27.00 | 4.36 | 14.30 | 4.13 | |
| Sr | 0.38 | 0.10 | 0.84 | 0.84 | 0.19 | 0.13 | 0.34 | 0.12 | 0.15 | 0.04 | 0.17 | 0.09 | 42.30 | 0.15 | 0.43 | 0.16 | |
| Zr | 47.00 | 71.00 | 8.04 | 8.04 | 28.00 | 9.80 | 8.00 | 7.57 | 16.20 | 5.11 | NA | NA | 56.70 | 19.20 | 25.50 | 16.10 | |
| Cr | 0.09 | 0.11 | 0.04 | 0.04 | 0.13 | 0.06 | 0.08 | 0.01 | 0.06 | 0.01 | 1.16 | 0.16 | 0.13 | 0.04 | 0.14 | 0.08 | |
| Cu | 2.05 | 8.90 | 0.91 | 0.91 | 1.32 | 2.80 | 1.94 | 0.64 | 1.08 | 0.74 | 0.89 | 4.40 | 0.70 | 0.52 | 2.74 | 1.38 | |
| Fe | 52.30 | 282.00 | 18.50 | 18.50 | 169.00 | 90.20 | 36.50 | 16.80 | 42.20 | 506.00 | 44.60 | 61.70 | 81.20 | 11.20 | 31.90 | 67.30 | |
| Mo | 0.18 | 0.81 | 0.02 | 0.02 | 0.01 | 0.25 | 0.11 | 0.03 | 0.06 | 0.00 | 0.29 | 0.04 | 0.02 | 0.02 | 0.03 | 0.09 | |
| Se | 0.70 | 0.37 | 0.14 | 0.14 | 0.18 | 0.86 | 0.19 | 0.43 | 0.29 | 0.11 | NA | 1.56 | 0.12 | 0.11 | 0.18 | 0.31 | |
| Zn | 28.80 | 53.90 | 12.80 | 12.80 | 12.10 | 34.30 | 16.40 | 11.40 | 31.70 | 7.22 | 10.80 | 13.90 | 50.00 | 5.66 | 16.00 | 13.10 | |
| Al | 12.80 | 1.58 | 2.62 | 2.62 | 20.00 | 0.78 | 0.97 | 0.90 | 0.86 | 0.41 | NA | NA | 7.69 | 0.70 | 11.20 | 1.72 | |
| As | 53.10 | 40.60 | 29.40 | 29.40 | 26.30 | 29.00 | 30.80 | 35.50 | 34.20 | 25.40 | NA | NA | 102.00 | 38.20 | 19.00 | 27.80 | |
| Cd | 0.59 | 0.97 | 0.09 | 0.09 | 0.42 | 5.88 | 0.26 | 0.09 | 0.58 | 0.00 | 0.16 | 0.11 | 0.08 | 0.02 | 0.07 | 0.16 | |
| Hg | 6.02 | 16.50 | 2.02 | 2.02 | 6.60 | 31.00 | 5.44 | 5.73 | 9.46 | 6.30 | NA | NA | 10.00 | 3.49 | 1.40 | 3.18 | |
| Pb | 0.07 | 0.38 | 0.05 | 0.05 | 0.17 | 0.16 | 0.06 | 0.03 | 0.11 | 0.10 | 0.07 | 0.15 | 1.12 | 0.05 | 0.07 | 0.15 | |
| Sn | 5.88 | 22.00 | 5.13 | 5.13 | 31.10 | 12.10 | 6.90 | 7.57 | 5.68 | 6.87 | NA | NA | 12.80 | 7.36 | 9.16 | 7.85 | |
| †The concentration of metal/metalloid was described in median. | | | | | | | | | | | | | | | | | |
| \*Source from (IRMCAMS, 2014) | | | | | | | | | | | | | | | | | |

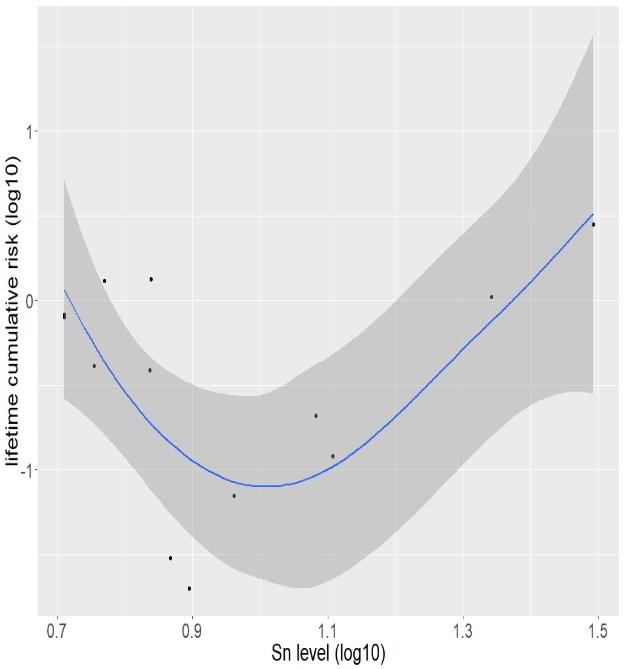
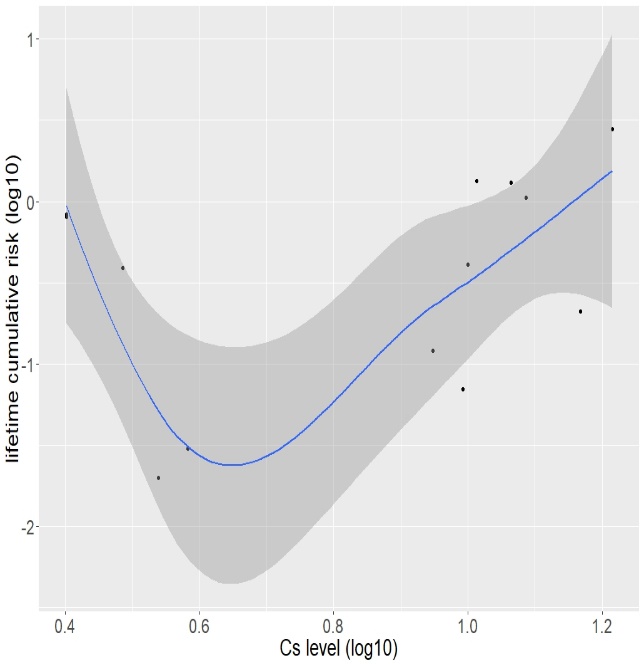
|  |  |  |  |
| --- | --- | --- | --- |
| **Table S3.** Lifetime cumulative cancer risks of the tissues for Chinese (%).\* | | | |
| Tissue | Lifetime cumulative risk  (male) | Lifetime cumulative risk  (female) | Lifetime cumulative risk  (both sexes) |
| Thyroid | 0.43 | 1.31 | 0.86 |
| Liver | 3.15 | 1.05 | 2.10 |
| Colon | 1.13 | 0.83 | 0.98 |
| Rectum | 1.27 | 0.80 | 1.04 |
| Lung | 6.20 | 2.80 | 4.48 |
| Kidney | 0.39 | 0.21 | 0.30 |
| Stomach | 3.58 | 1.34 | 2.45 |
| Testis | 0.03 | NA | 0.03 |
| Pancreas | 0.59 | 0.41 | 0.50 |
| Blood | 0.52 | 0.39 | 0.46 |
| Ovary | NA | 0.57 | 0.57 |
| Brain | 0.54 | 0.61 | 0.58 |
| Bone | 0.16 | 0.12 | 0.14 |
| Skin | 0.04 | 0.03 | 0.04 |
| Small intestine | 0.10 | 0.07 | 0.09 |
| Adrenal gland | 0.02 | 0.02 | 0.02 |
| \*Source from (He and Chen 2017) | | | |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table S4.** Pearson correlations between each two log10-transformed concentrations of metals/metalloids. | | | | | | | | | | | | | | | | | | | | | | | |
| Metal | U | Th | Rb | Ba | Ce | Co | Cs | I | La | Sr | Zr | Cr | Cu | Fe | Mo | Se | Zn | Al | As | Cd | Hg | Pb | Sn |
| U | 1 | 0.27 | -0.53 | 0.36 | 0.06 | 0.25 | -0.17 | 0.02 | 0.22 | 0.52 | 0.01 | 0.36 | -0.10 | -0.66 | 0.15 | -0.12 | 0.07 | 0.43 | -0.03 | 0.27 | -0.47 | -0.18 | -0.23 |
| Th | 0.27 | 1 | 0.19 | 0.71 | 0.70 | 0.61 | 0.43 | 0.26 | 0.77 | 0.39 | 0.57 | 0.69 | 0.02 | 0.07 | -0.05 | -0.13 | 0.08 | 0.82 | 0.21 | 0.18 | -0.09 | 0.33 | 0.54 |
| Rb | -0.53 | 0.19 | 1 | -0.05 | 0.42 | 0.52 | 0.89 | 0.24 | 0.28 | -0.21 | 0.44 | 0.30 | 0.56 | 0.56 | 0.41 | 0.55 | 0.58 | 0.09 | 0.16 | 0.50 | **0.70** | 0.42 | 0.57 |
| Ba | 0.36 | 0.71 | -0.05 | 1 | 0.40 | 0.45 | 0.12 | -0.14 | 0.63 | 0.80 | 0.44 | 0.52 | -0.19 | -0.02 | -0.28 | -0.51 | 0.15 | 0.68 | 0.38 | -0.17 | -0.25 | 0.49 | 0.36 |
| Ce | 0.06 | 0.70 | 0.42 | 0.40 | 1 | 0.77 | 0.54 | 0.44 | 0.81 | 0.27 | 0.89 | 0.68 | 0.37 | 0.24 | 0.39 | 0.15 | 0.49 | 0.63 | 0.51 | 0.42 | 0.30 | 0.54 | 0.65 |
| Co | 0.25 | 0.61 | 0.52 | 0.45 | 0.77 | 1 | 0.70 | 0.44 | 0.77 | 0.32 | 0.85 | 0.72 | 0.64 | 0.17 | 0.59 | 0.46 | 0.67 | 0.73 | 0.35 | 0.62 | 0.27 | 0.53 | 0.57 |
| Cs | -0.17 | 0.43 | 0.89 | 0.12 | 0.54 | **0.70** | 1 | 0.31 | 0.46 | -0.02 | 0.50 | 0.51 | 0.54 | 0.28 | 0.48 | 0.56 | 0.60 | 0.34 | 0.18 | 0.68 | **0.61** | 0.33 | 0.61 |
| I | 0.02 | 0.26 | 0.24 | -0.14 | 0.44 | 0.44 | 0.31 | 1 | 0.21 | 0.10 | 0.45 | 0.14 | 0.26 | -0.02 | 0.35 | 0.54 | 0.35 | 0.44 | 0.36 | 0.34 | 0.09 | -0.05 | -0.16 |
| La | 0.22 | 0.77 | 0.28 | 0.63 | 0.81 | 0.77 | 0.46 | 0.21 | 1 | 0.41 | 0.74 | 0.82 | 0.47 | 0.24 | 0.28 | -0.12 | 0.40 | 0.74 | 0.27 | 0.30 | 0.04 | 0.50 | 0.66 |
| Sr | 0.52 | 0.39 | -0.21 | 0.80 | 0.27 | 0.32 | -0.02 | 0.10 | 0.41 | 1 | 0.36 | 0.18 | -0.26 | -0.23 | -0.07 | -0.37 | 0.41 | 0.50 | 0.67 | -0.02 | -0.13 | 0.42 | -0.01 |
| Zr | 0.01 | 0.57 | 0.44 | 0.44 | 0.89 | 0.85 | 0.50 | 0.45 | 0.74 | 0.36 | 1 | 0.74 | 0.46 | 0.24 | 0.45 | 0.16 | 0.62 | 0.61 | 0.55 | 0.34 | 0.24 | 0.64 | 0.55 |
| Cr | 0.36 | 0.69 | 0.30 | 0.52 | 0.68 | 0.72 | 0.51 | 0.14 | 0.82 | 0.18 | 0.74 | 1 | 0.34 | 0.07 | 0.53 | 0.25 | 0.25 | 0.65 | 0.21 | 0.36 | 0.11 | 0.34 | 0.48 |
| Cu | -0.10 | 0.02 | 0.56 | -0.19 | 0.37 | 0.64 | 0.54 | 0.26 | 0.47 | -0.26 | 0.46 | 0.34 | 1 | 0.40 | 0.60 | 0.62 | 0.54 | 0.18 | -0.16 | 0.56 | 0.36 | 0.31 | 0.45 |
| Fe | -0.66 | 0.07 | 0.56 | -0.02 | 0.24 | 0.17 | 0.28 | -0.02 | 0.24 | -0.23 | 0.24 | 0.07 | 0.40 | 1 | -0.04 | 0.10 | 0.30 | 0.01 | 0.01 | 0.06 | 0.55 | 0.62 | 0.57 |
| Mo | 0.15 | -0.05 | 0.41 | -0.28 | 0.39 | 0.59 | 0.48 | 0.35 | 0.28 | -0.07 | 0.45 | 0.53 | 0.60 | -0.04 | 1 | 0.58 | 0.58 | 0.02 | 0.20 | 0.78 | 0.43 | 0.15 | 0.18 |
| Se | -0.12 | -0.13 | 0.55 | -0.51 | 0.15 | 0.46 | 0.56 | 0.54 | -0.12 | -0.37 | 0.16 | 0.25 | 0.62 | 0.10 | 0.58 | 1 | 0.34 | -0.02 | 0.03 | 0.58 | 0.54 | 0.04 | 0.10 |
| Zn | 0.07 | 0.08 | 0.58 | 0.15 | 0.49 | 0.67 | 0.60 | 0.35 | 0.40 | 0.41 | 0.62 | 0.25 | 0.54 | 0.30 | 0.58 | 0.34 | 1 | 0.25 | 0.53 | 0.68 | 0.61 | 0.65 | 0.33 |
| Al | 0.43 | 0.82 | 0.09 | 0.68 | 0.63 | 0.73 | 0.34 | 0.44 | 0.74 | 0.50 | 0.61 | 0.65 | 0.18 | 0.01 | 0.02 | -0.02 | 0.25 | 1 | 0.18 | 0.19 | -0.26 | 0.23 | 0.37 |
| As | -0.03 | 0.21 | 0.16 | 0.38 | 0.51 | 0.35 | 0.18 | 0.36 | 0.27 | 0.67 | 0.55 | 0.21 | -0.16 | 0.01 | 0.20 | 0.03 | 0.53 | 0.18 | 1 | 0.08 | 0.38 | 0.57 | 0.09 |
| Cd | 0.27 | 0.18 | 0.50 | -0.17 | 0.42 | **0.62** | 0.68 | 0.34 | 0.30 | -0.02 | 0.34 | 0.36 | 0.56 | 0.06 | **0.78** | 0.58 | **0.68** | 0.19 | 0.08 | 1 | 0.57 | 0.23 | 0.36 |
| Hg | -0.47 | -0.09 | 0.70 | -0.25 | 0.30 | 0.27 | 0.61 | 0.09 | 0.04 | -0.13 | 0.24 | 0.11 | 0.36 | 0.55 | 0.43 | 0.54 | 0.61 | -0.26 | 0.38 | 0.57 | 1 | 0.56 | 0.48 |
| Pb | -0.18 | 0.33 | 0.42 | 0.49 | 0.54 | 0.53 | 0.33 | -0.05 | 0.50 | 0.42 | 0.64 | 0.34 | 0.31 | 0.62 | 0.15 | 0.04 | 0.65 | 0.23 | 0.57 | 0.23 | 0.56 | 1 | 0.62 |
| Sn | -0.23 | 0.54 | 0.57 | 0.36 | **0.65** | 0.57 | 0.61 | -0.16 | **0.66** | -0.01 | 0.55 | 0.48 | 0.45 | 0.57 | 0.18 | 0.10 | 0.33 | 0.37 | 0.09 | 0.36 | 0.48 | **0.62** | 1 |
| The bold indicated that this metal/metalloid was highly correlated with Cd/Rb/Cs/Sn, with a Pearson coefficient larger than 0.6. | | | | | | | | | | | | | | | | | | | | | | | |

1. b.

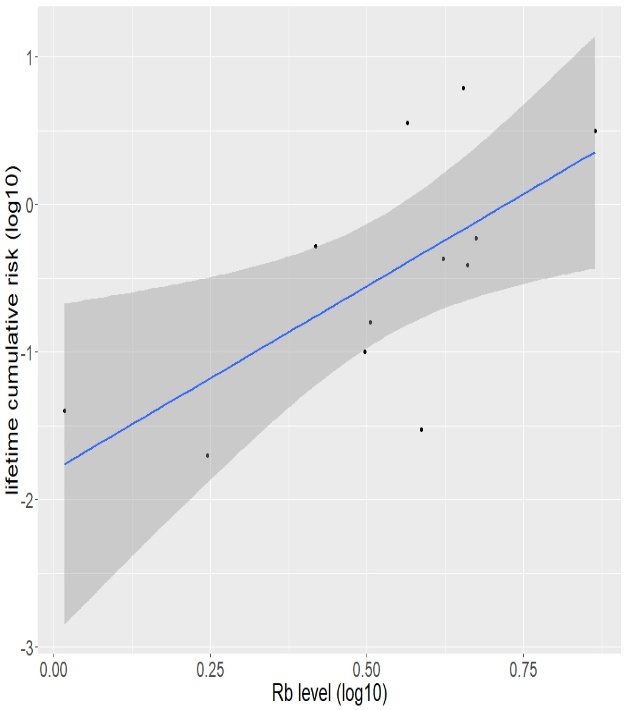
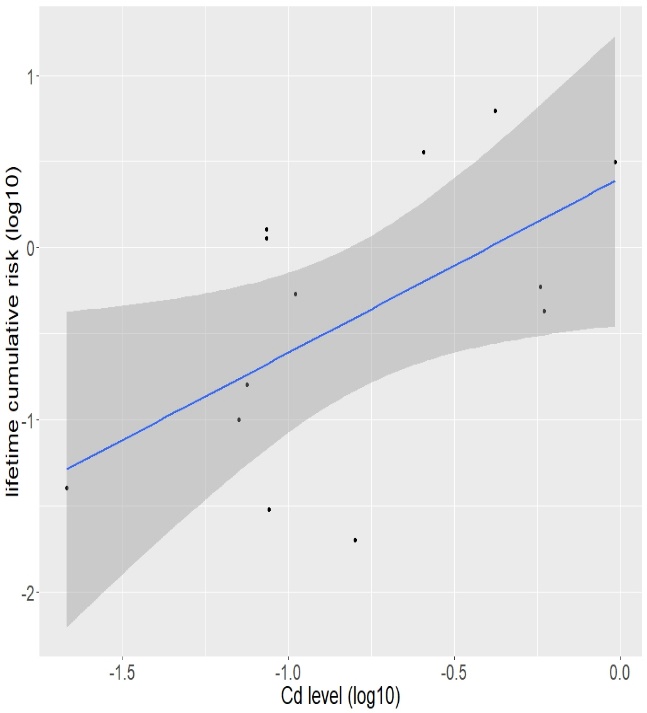


c. d.

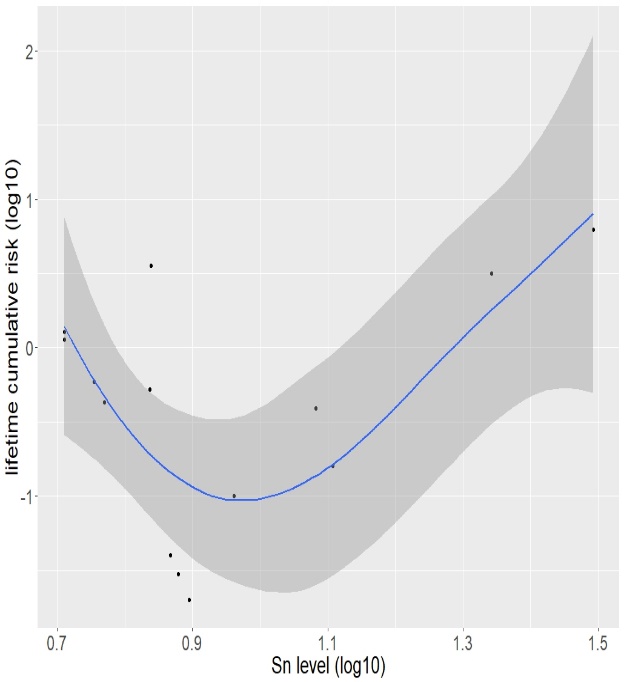


**Figure S1.** Linear/nonlinear correlation curves and 95% confidence bands for each element with the lifetime cancer risks of the tissues among females. (a) linear correlation curve for Cd; (b) linear correlation curve for Rb; (c) nonlinear correlation curve for Cs; (d) nonlinear correlation curve for Sn.

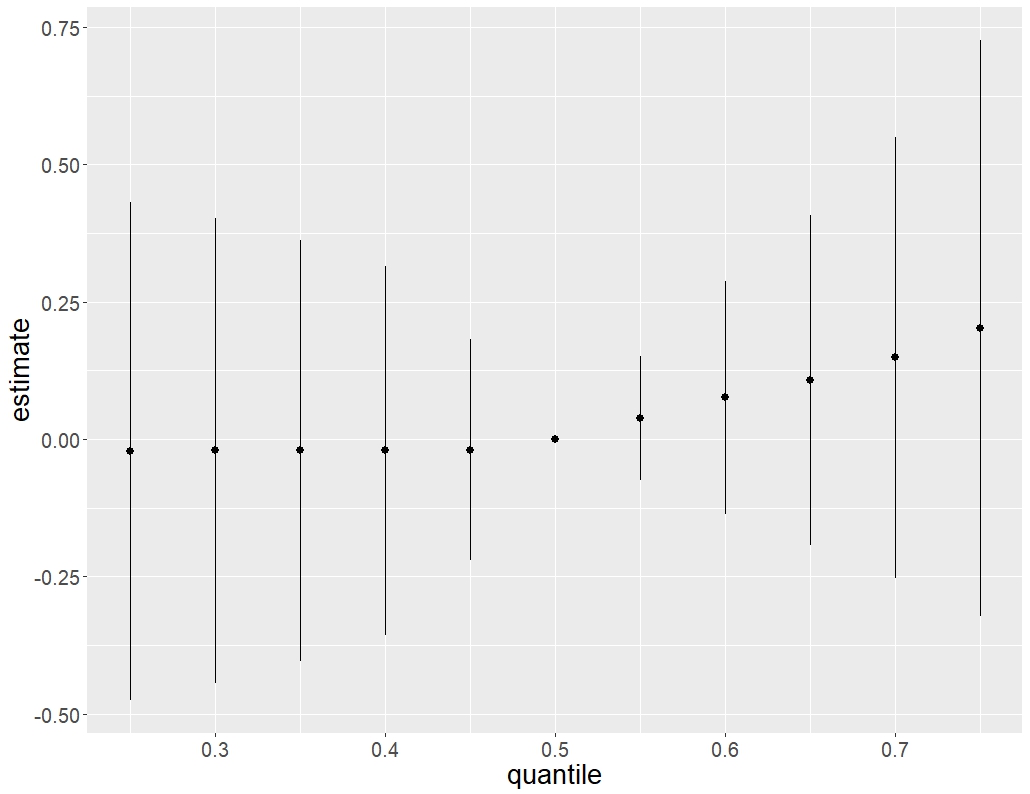
1. b.



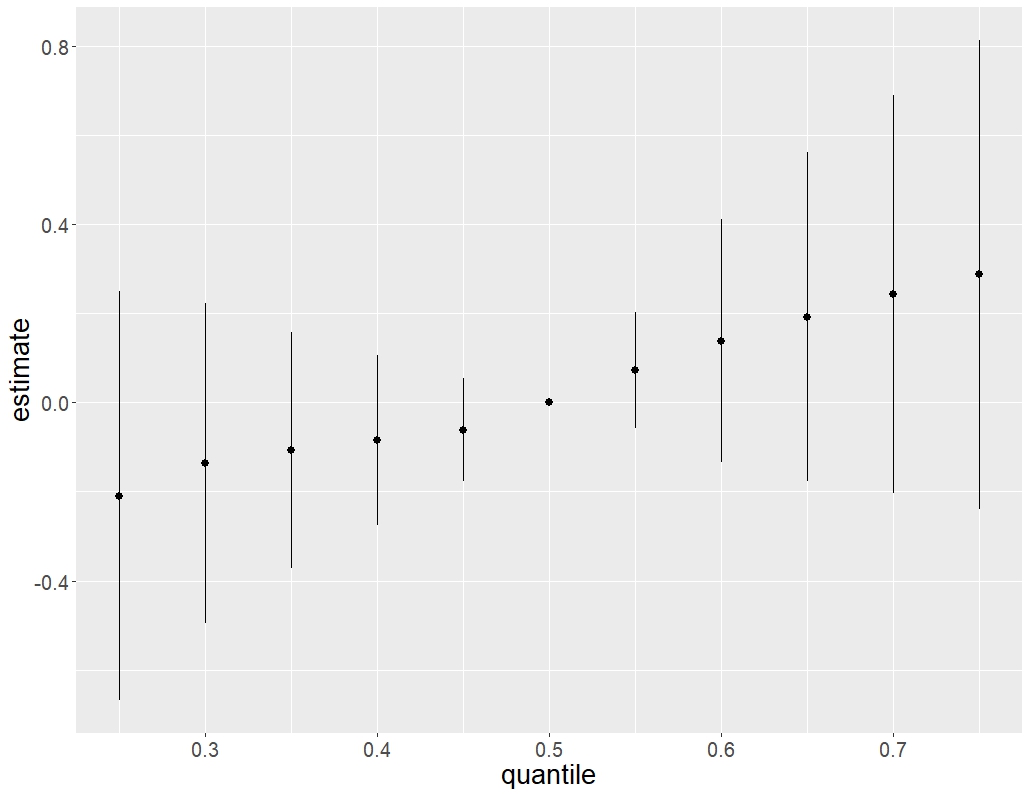
c. d.



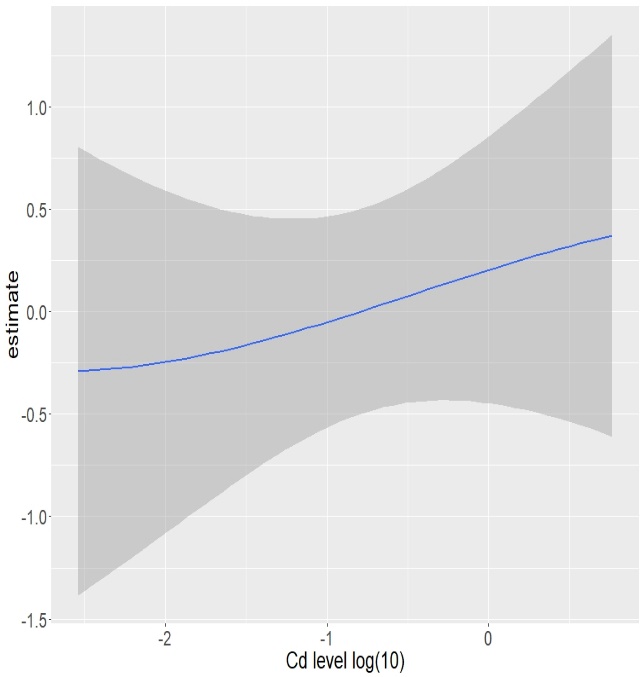
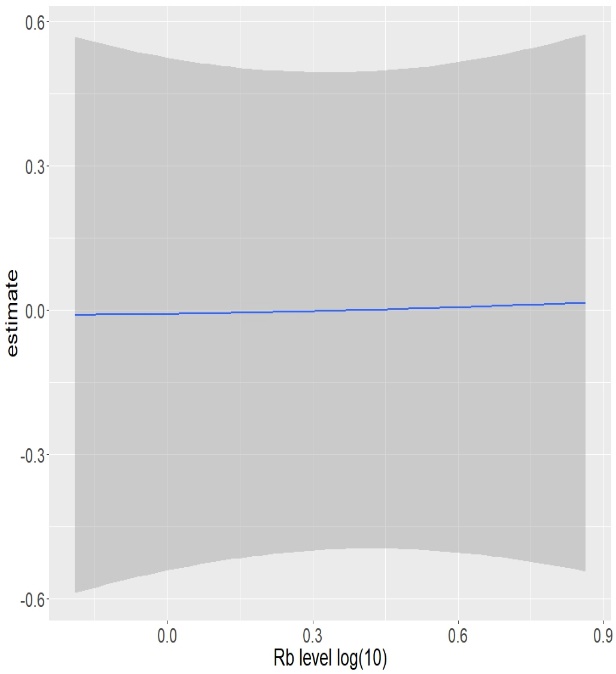
**Figure S2.** Linear/nonlinear correlation curves and 95% confidence bands for each element with the lifetime cancer risks of the tissues among males. (a) linear correlation curve for Cd; (b) linear correlation curve for Rb; (c) nonlinear correlation curve for Cs; (d) nonlinear correlation curve for Sn.



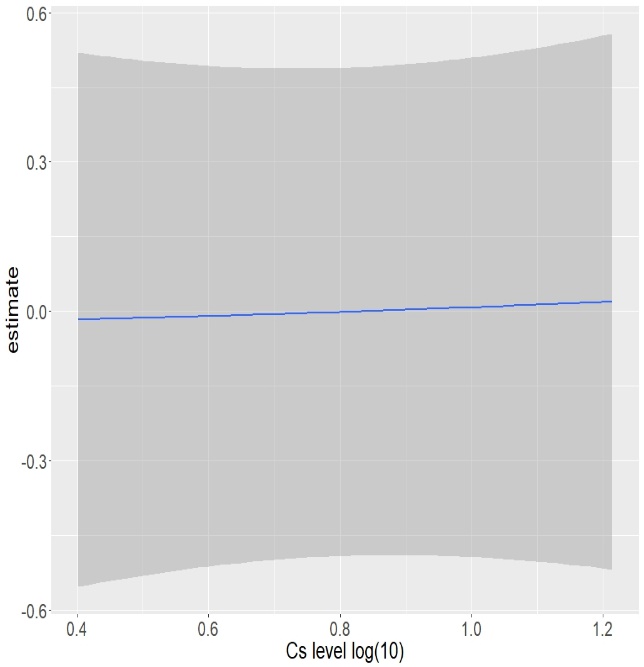
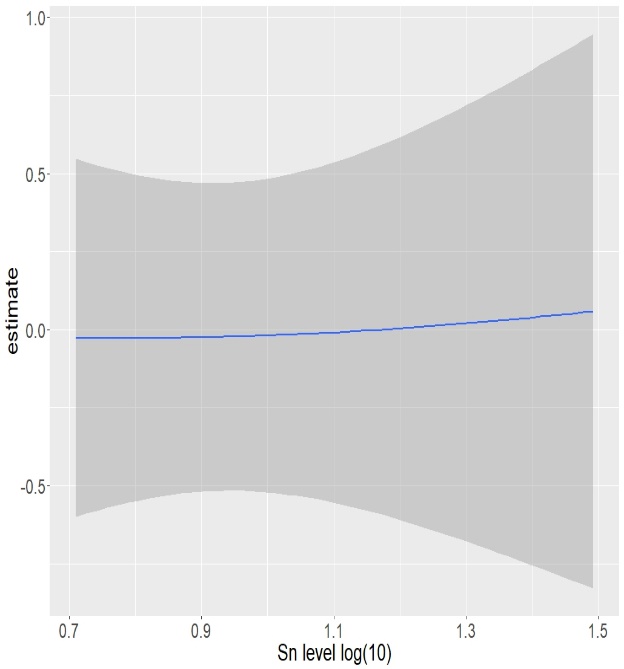
**Figure S3.** Overall correlation of the mixture (estimates and 95% credible intervals) with the lifetime cancer risks of the tissues among females. The plot compared the lifetime cumulative risk when all the exposures are at a particular percentile to when all are at 50th percentile. X-axis (quantile) referred to the percentile of the metal and metalloid mixture, which was between the 25th and 75th in 5% increments; Y-axis (estimate) referred to estimated overall correlation of the mixture with the lifetime cumulative cancer risk.

**Figure S4.** Overall correlation of the mixture (estimates and 95% credible intervals) with the lifetime cancer risks of the tissues among males. The plot compared the lifetime cumulative risk when all the exposures are at a particular percentile to when all are at 50th percentile. X-axis (quantile) referred to the percentile of the metal and metalloid mixture, which was between the 25th and 75th in 5% increments; Y-axis (estimate) referred to estimated overall correlation of the mixture with the lifetime cumulative cancer risk.

1. b.

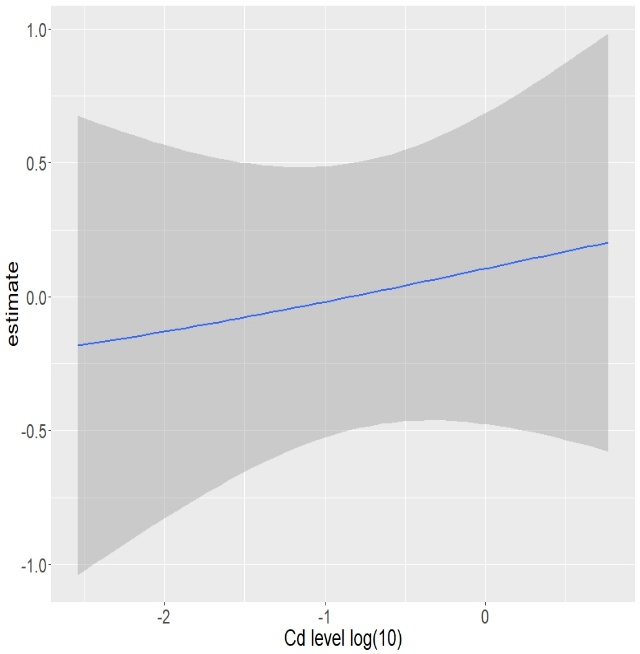
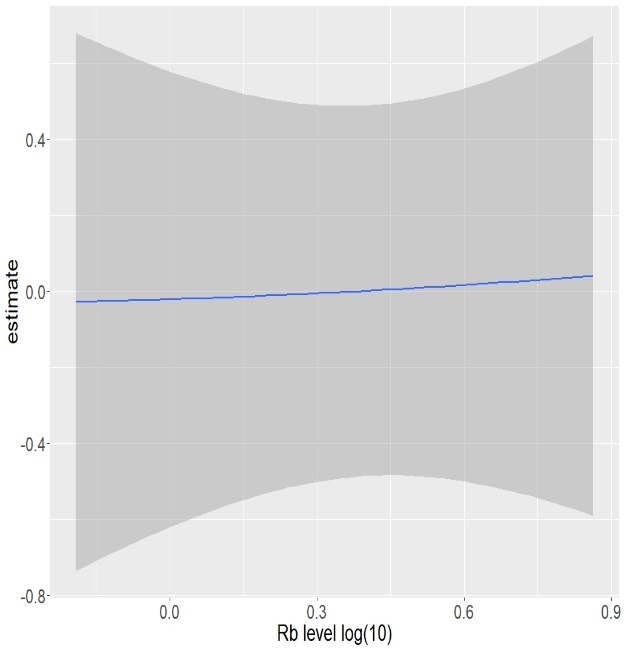
 

c. d.

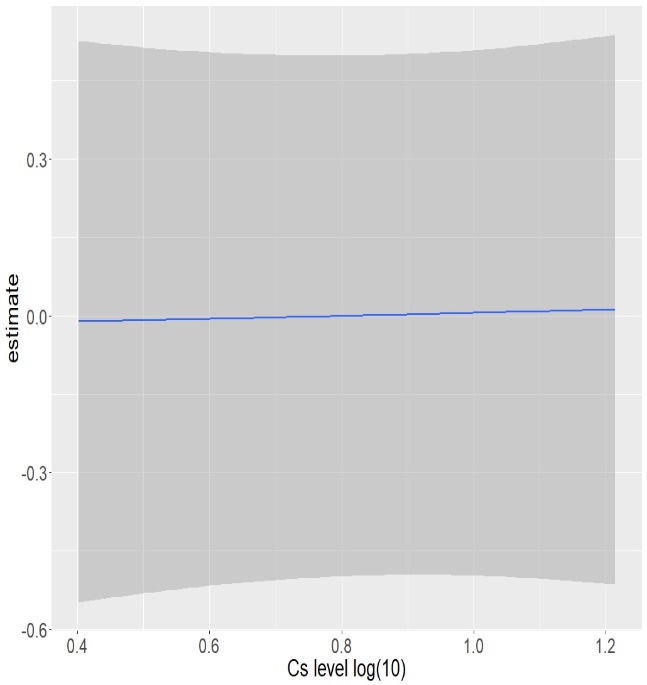
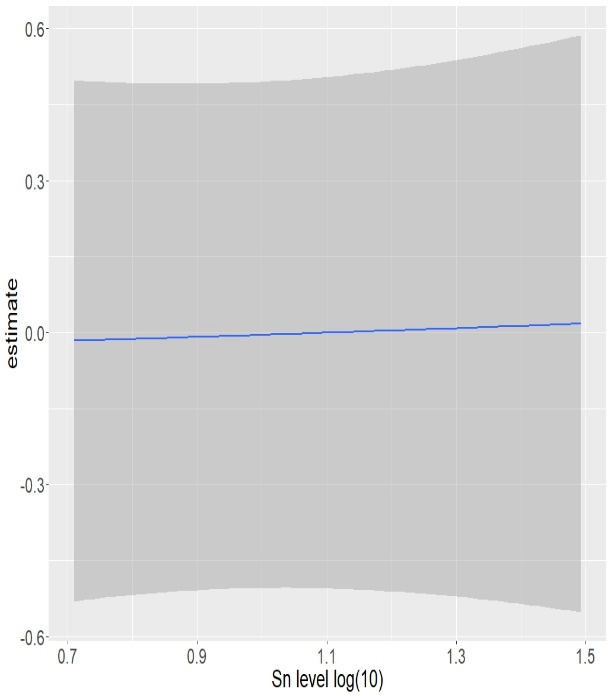
 

**Figure S5.** Univariate exposure-response curves and 95% confidence bands for each element with the other elements fixed at the median among females. X-axis referred to the log10-transformed concentration of a certain element. Y-axis (estimate) referred to estimated univarite correlation of a certain element with the lifetime cumulative cancer risk. (a) univariate exposure-response curve for Cd; (b) univariate exposure-response curve for Rb; (c) univariate exposure-response curve for Cs; (d) univariate exposure-response curve for Sn.

1. b.

c. d.

**Figure S6.** Univariate exposure-response curves and 95% confidence bands for each element with the other elements fixed at the median among males. X-axis referred to the log10-transformed concentration of a certain element. Y-axis (estimate) referred to estimated univarite correlation of a certain element with the lifetime cumulative cancer risk. (a) univariate exposure-response curve for Cd; (b) univariate exposure-response curve for Rb; (c) univariate exposure-response curve for Cs; (d) univariate exposure-response curve for Sn.