

1 Joint Associations Among Non-essential Heavy Metals Mixtures and Nutritional  
2 Factors on Glucose Metabolism Indexes in the US Adults: Evidence from  
3 NHANES 2011–2016

4 Xiaolang Chen <sup>1,2‡</sup>, Peipei Li <sup>1,2‡</sup>, Yuanhao Huang <sup>1,2‡</sup>, Yingnan Lv <sup>3</sup>, Xia Xu <sup>1,2</sup>, Huiyun Nong <sup>1,2</sup>,  
5 Lulu Zhang <sup>3</sup>, Huabei Wu <sup>4</sup>, Chao Yu <sup>1,2</sup>, Lina Chen <sup>1,2</sup>, Di Liu <sup>1,2</sup>, Lancheng Wei <sup>1,2</sup>, Haiying  
6 Zhang<sup>1,2,3\*</sup>

7 CONTENTS

8	Supplementary Method.....	4
9	Supplementary Tables.....	5
10	Table S1. Descriptive table of urinary metal concentrations.....	5
11	Table S2. Distribution of glucose metabolism indexes. ....	6
12	Table S3. The posterior inclusion probabilities of metals under the Bayesian kernel machine 13 regression model in glucose metabolism indexes. ....	6
14	Table S4. Descriptive table of nutrients grouped by quantile of energy-adjusted DII. (Median 15 [IQR]).....	7
16	Table S5. Coefficients and 95% confidence intervals for the interquartile change of natural log- 17 transformed urinary metals (ln µg/g creatinine) on glucose metabolism indexes and the 18 interaction term between metal and energy-adjusted diet inflammatory index estimated using 19 multivariate linear regression models. The diet inflammatory index was estimated by 28 20 nutrients which represent the total consumption from food intake.....	8
21	Supplementary Figures .....	9
22	Figure S1. Flowchart of the overall design, NHANES from 2011-2016. NHANES, National 23 Health and Nutrition Examination Survey; E-DII, energy-adjusted diet inflammatory index. 9	
24	Figure S2. Directed acyclic graph of select covariates. ....	10
25	Figure S3. Correlations between urinary metal concentrations (ln ug/g creatinine). ....	11
26	Figure S4. Association of single heavy metal (ln ug/g creatinine) and fasting plasma glucose 27 (ln-mg/dL) in multivariable-adjusted restricted cubic splines. Beta indicates change in 28 predicted fasting plasma glucose (ln-mg/dL) for a unit change in metal. Beta =0 means no 29 association between exposures and the outcome; beta >0 means a positive association between 30 exposures and outcomes; beta <0 means a negative association between exposures and 31 outcomes. The solid red lines correspond to the central estimates, and the red-shaded regions 32 indicate the 95% confidence intervals. The model was adjusted for survey cycle of NHANES 33 (2011-2012, 2013-2014, and 2015-2016), age (continuous), sex, body mass index 34 (continuous), race (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic 35 Black, and other race), alcohol consumption (≥ 12 drinks/year and < 12 drinks/year), and 36 hypertension (yes or no). NHANES, National Health and Nutrition Examination Survey; CI, 37 confidence interval.....	11
38	Figure S5. Association of single heavy metal (ln ug/g creatinine) and hemoglobin A1c (%) in 39 multivariable-adjusted restricted cubic splines. Beta indicates change in predicted hemoglobin 40 A1c (%) for a unit change in metal. Beta =0 means no association between exposures and the 41 outcome; beta >0 means a positive association between exposures and outcomes; beta <0 42 means a negative association between exposures and outcomes. The solid red lines correspond	

43 to the central estimates, and the red-shaded regions indicate the 95% confidence intervals. The  
44 model was adjusted for survey cycle of NHANES (2011-2012, 2013-2014, and 2015-2016),  
45 age (continuous), sex, body mass index (continuous), race (Mexican American, other  
46 Hispanic, non-Hispanic White, non-Hispanic Black, and other race), alcohol consumption ( $\geq$   
47 12 drinks/year and  $<$  12 drinks/year), and hypertension (yes or no). NHANES, National Health  
48 and Nutrition Examination Survey; CI, confidence interval. ....12  
49 Figure S6. Association of single heavy metal (ln ug/g creatinine) and homeostatic model  
50 assessment for insulin resistance (ln) in multivariable-adjusted restricted cubic splines. Beta  
51 indicates change in predicted homeostatic model assessment for insulin resistance (ln) for a  
52 unit change in metal. Beta =0 means no association between exposures and the outcome; beta  
53  $>$ 0 means a positive association between exposures and outcomes; beta  $<$ 0 means a negative  
54 association between exposures and outcomes. The solid red lines correspond to the central  
55 estimates, and the red-shaded regions indicate the 95% confidence intervals. The model was  
56 adjusted for survey cycle of NHANES (2011-2012, 2013-2014, and 2015-2016), age  
57 (continuous), sex, body mass index (continuous), race (Mexican American, other Hispanic,  
58 non-Hispanic White, non-Hispanic Black, and other race), alcohol consumption ( $\geq$  12  
59 drinks/year and  $<$  12 drinks/year), and hypertension (yes or no). NHANES, National Health  
60 and Nutrition Examination Survey; CI, confidence interval. ....13  
61 Figure S7. The Cd-hemoglobin A1c (%) relationships in the “E-DII Q4” group and in the  
62 hypothetically “E-DII Q1-3” group. E-DII, energy-adjusted diet inflammatory index. ....14  
63 Figure S8. The W-hemoglobin A1c (%) relationships in the “E-DII Q4” group and in the  
64 hypothetically “E-DII Q1-3” group. E-DII, energy-adjusted diet inflammatory index.....15  
65 Figure S9. The Ba- homeostatic model assessment for insulin resistance (HOMA-IR) (ln)  
66 relationships in the “E-DII Q4” group and in the hypothetically “E-DII Q1-3” group. E-DII,  
67 energy-adjusted diet inflammatory index. ....16  
68 Figure S10. The Tl- homeostatic model assessment for insulin resistance (ln) relationships in  
69 the “E-DII Q4” group and in the hypothetically “E-DII Q1-3” group. E-DII, energy-adjusted  
70 diet inflammatory index. ....17  
71 Figure S11. Impact of E-DII and metal interactions on diabetes. Bivariate exposure–response  
72 functions for each of the exposure presented on the upper coordinate axis when the other  
73 variables presented on the right longitudinal axis holding at different quantiles (10th, 50th, and  
74 90th percentiles) and the other variables were held at the median. Model adjusted for survey  
75 cycle of NHANES (2011-2012, 2013-2014, and 2015-2016), age (continuous), sex, body mass  
76 index (continuous), race (Mexican American, other Hispanic, non-Hispanic White, non-  
77 Hispanic Black, and other race), alcohol consumption ( $\geq$  12 drinks/year and  $<$  12 drinks/year),  
78 and hypertension (yes or no). DII-ad, adjusted energy diet inflammatory index. ....18  
79 Figure S12. Impact of macro-nutritions and metal interactions on diabetes. Bivariate exposure–  
80 response functions for each of the exposure presented on the upper coordinate axis when the  
81 other variables presented on the right longitudinal axis holding at different quantiles (10th,  
82 50th, and 90th percentiles) and the other variables were held at the median. Model adjusted for  
83 survey cycle of NHANES (2011-2012, 2013-2014, and 2015-2016), age (continuous), sex,  
84 body mass index (continuous), race (Mexican American, other Hispanic, non-Hispanic  
85 White, non-Hispanic Black, and other race), alcohol consumption ( $\geq$  12 drinks/year and  $<$  12  
86 drinks/year), and hypertension (yes or no). ....19

87	Figure S13. Impact of minerals and metal interactions on diabetes. Bivariate exposure–	
88	response functions for each of the exposure presented on the upper coordinate axis when the	
89	other variables presented on the right longitudinal axis holding at different quantiles (10th,	
90	50th, and 90th percentiles) and the other variables were held at the median. Model adjusted for	
91	survey cycle of NHANES (2011-2012, 2013-2014, and 2015-2016), age (continuous), sex,	
92	body mass index (continuous), race (Mexican American, other Hispanic, non-Hispanic	
93	White, non-Hispanic Black, and other race), alcohol consumption ( $\geq 12$ drinks/year and $< 12$	
94	drinks/year), and hypertension (yes or no). .....	20
95	Figure S14. Impact of A vitamins and metal interactions on diabetes. Bivariate exposure–	
96	response functions for each of the exposure presented on the upper coordinate axis when the	
97	other variables presented on the right longitudinal axis holding at different quantiles (10th,	
98	50th, and 90th percentiles) and the other variables were held at the median. Model adjusted for	
99	survey cycle of NHANES (2011-2012, 2013-2014, and 2015-2016), age (continuous), sex,	
100	body mass index (continuous), race (Mexican American, other Hispanic, non-Hispanic	
101	White, non-Hispanic Black, and other race), alcohol consumption ( $\geq 12$ drinks/year and $< 12$	
102	drinks/year), and hypertension (yes or no). .....	21

### 103 **Supplementary Method**

104 We defined diabetes according to the following criteria: ① fasting blood glucose (FPG)  $\geq$  126  
105 mg/dL; ② or postprandial 2h plasma glucose  $\geq$  200 mg/dL, ③ or glycated hemoglobin A1c  
106 (HbA1c)  $\geq$  6.5%, ④ or self-reported doctor diagnosis of diabetes, ⑤ or use of insulin, ⑥ or oral  
107 hypoglycemic medication <sup>1</sup>. According to this definition, our study included 395 individuals with  
108 diabetes and 1,343 individuals without diabetes.

109 We use the Bayesian kernel machine regression (BKMR) model to visualization the interaction  
110 between nutritional factors and metals on the outcome of diabetes. When the remaining other variables  
111 were fixed at the median, the dose-response curve between expos1 concentration and outcome changed  
112 in slope as the expos2 concentration from 10th to 90th, indicating a possible interaction.

## 113 Supplementary Tables

114 Table S1. Descriptive table of urinary metal concentrations.

Metal	LOD	LOD	Urinary concentration (ug/L)					Creatinine-adjusted urinary concentration (ug/g creatinine)					Ln-ug/g (creatinine)
	(ug/L) (2011-2012)	(ug/L) (2013-2016)	5th	25th	50th	75th	95th	5th	25th	50th	75th	95th	Mean (SD)
Barium	0.1000	0.060	0.200	0.510	1.000	1.950	4.482	22.881	58.333	102.964	184.386	425.762	4.625 (0.908)
Cadmium	0.056	0.036	0.041	0.131	0.255	0.496	1.241	6.065	13.771	26.165	46.034	111.141	3.242 (0.887)
Lead	0.080	0.030	0.080	0.200	0.35	0.62	1.380	11.292	21.564	35.279	57.913	117.919	3.575 (0.741)
Antimony	0.041	0.022	0.016	0.029	0.044	0.074	0.176	1.870	3.183	4.531	6.905	16.111	1.579 (0.659)
Thallium	0.02	0.018	0.047	0.098	0.159	0.251	0.430	6.203	10.98	15.74	22.385	40.866	2.756 (0.579)
Tungsten	0.026	0.018	0.013	0.026	0.053	0.107	0.280	1.545	3.25	5.429	9.214	23.705	1.732 (0.840)
Uranium	0.003	0.002	0.001	0.003	0.005	0.010	0.029	0.166	0.319	0.523	0.938	3.025	-0.542 (0.901)
Arsenic	1.25	0.260	1.510	3.592	6.840	14.45	56.982	199.033	377.597	644.827	1369.921	6616.069	6.677 (1.056)

116 Table S2. Distribution of glucose metabolism indexes.

Variables	Original distribution					Ln-transformation
	5th	25th	50th	75th	95th	Mean (SD)
FPG (mg/dL)	82.61	93.00	100.00	110.00	165.71	4.65 (0.23)
HbA1c (%)	4.80	5.30	5.60	5.900	7.70	—
HOMA-IR	0.70	1.42	2.34	4.00	10.43	0.90 (0.85)

117

118 Table S3. The posterior inclusion probabilities of metals under the Bayesian kernel machine regression

119 model in glucose metabolism indexes.

Variables	Barium	Cadmium	Lead	Antimony	Thallium	Tungsten	Uranium	Arsenic
FPG	0.004	8E-05	0	0	0.016	0.002	0.002	0
HbA1c	0.005	1	1	0.013	0.021	0.897	0.003	0.004
HOMA-IR	1	0.232	0.269	0.379	0.874	0.207	0.544	0.114

121 Table S4. Descriptive table of nutrients grouped by quantile of energy-adjusted DII. (Median [IQR]).

Nutrients	Overall (n = 1738)	E-DII Q1 (n = 434)	E-DII Q2 (n = 435)	E-DII Q3 (n = 435)	E-DII Q4 (n = 434)
Protein (mg)	78.50 [65.30, 92.11]	87.39 [75.08, 102.91]	82.20 [70.39, 95.13]	77.33 [64.00, 90.11]	68.01 [57.64, 79.37]
Fat (mg)	76.86 [65.70, 87.85]	77.41 [65.30, 88.42]	74.73 [63.23, 86.26]	76.43 [65.99, 85.98]	78.61 [68.32, 89.59]
Carbohydrate (mg)	242.27 [212.97, 273.05]	237.04 [203.34, 267.65]	237.88 [203.79, 269.58]	240.93 [214.36, 268.22]	256.22 [226.56, 289.65]
Fiber (mg)	16.29 [11.89, 20.91]	20.43 [15.79, 25.89]	17.85 [12.94, 21.81]	15.15 [11.47, 19.24]	12.93 [9.87, 16.64]
VitB1 (mg)	1.50 [1.25, 1.79]	1.60 [1.34, 1.91]	1.51 [1.27, 1.83]	1.48 [1.25, 1.79]	1.38 [1.12, 1.65]
VitB2 (mg)	1.89 [1.52, 2.34]	2.15 [1.73, 2.65]	1.97 [1.61, 2.39]	1.85 [1.49, 2.24]	1.63 [1.30, 2.00]
Niacin (mg)	23.69 [19.29, 28.72]	27.24 [22.61, 33.70]	25.61 [20.79, 29.96]	23.15 [19.20, 27.00]	19.76 [16.78, 23.66]
VitB6 (mg)	1.88 [1.49, 2.33]	2.37 [1.96, 2.97]	2.04 [1.71, 2.45]	1.78 [1.49, 2.10]	1.39 [1.09, 1.67]
Folate (µg)	465.21 [366.53, 601.39]	549.43 [406.76, 689.70]	479.66 [387.00, 610.31]	456.08 [362.43, 554.81]	416.47 [313.31, 527.58]
VitB12 (µg)	4.02 [2.78, 5.52]	5.00 [3.26, 7.45]	4.33 [2.95, 5.90]	3.76 [2.57, 5.03]	3.45 [2.43, 4.59]
Calcium (mg)	861.36 [662.48, 1108.72]	953.08 [734.70, 1178.01]	879.26 [684.19, 1107.15]	850.15 [616.57, 1093.05]	801.21 [597.42, 1037.07]
Phosphorus (mg)	1309.74 [1127.10, 1490.40]	1418.60 [1247.29, 1609.61]	1339.05 [1192.37, 1502.98]	1273.99 [1103.69, 1438.05]	1197.24 [1002.27, 1341.12]
Sodium (mg)	3302.07 [2821.10, 3836.44]	3436.56 [2909.12, 3955.52]	3393.01 [2898.41, 3902.03]	3227.25 [2789.78, 3795.48]	3215.48 [2719.35, 3676.03]
Potassium (mg)	2531.89 [2124.93, 2988.90]	3070.07 [2640.53, 3469.88]	2637.30 [2274.20, 3032.93]	2413.73 [2075.62, 2760.26]	2081.79 [1751.14, 2438.53]
Iron (mg)	13.07 [10.98, 16.08]	14.54 [11.93, 17.96]	13.13 [11.18, 16.27]	12.89 [10.99, 15.69]	12.09 [10.10, 14.27]
Zinc (mg)	10.05 [8.40, 12.26]	11.09 [9.09, 14.04]	10.22 [8.76, 12.16]	9.84 [8.23, 12.04]	9.27 [7.84, 11.02]
Selenium (µg)	109.92 [91.12, 130.42]	118.70 [96.59, 138.00]	115.32 [95.84, 134.28]	108.30 [92.13, 129.68]	98.08 [83.13, 114.24]
Magnesium (mg)	283.17 [231.24, 346.04]	357.81 [302.51, 403.29]	299.10 [263.77, 355.19]	269.47 [224.25, 306.30]	223.23 [185.26, 262.45]
Copper (mg)	1.13 [0.92, 1.40]	1.41 [1.19, 1.71]	1.20 [1.00, 1.46]	1.06 [0.90, 1.26]	0.92 [0.74, 1.09]
Cholin (mg)	310.22 [247.48, 383.69]	352.68 [294.12, 425.07]	325.39 [270.66, 394.23]	309.45 [252.67, 368.66]	250.57 [202.60, 313.15]
VitC (mg)	65.07 [32.96, 112.42]	102.71 [62.62, 153.56]	69.63 [37.53, 118.88]	56.85 [29.28, 99.70]	39.74 [15.58, 72.44]
A vitamins (µg)	1271.86 [858.96, 1981.37]	2214.76 [1486.14, 3433.06]	1435.05 [987.99, 1997.38]	1113.42 [778.57, 1572.27]	889.13 [598.51, 1213.81]
Omega 3 (mg)	1.87 [1.46, 2.40]	2.30 [1.77, 2.94]	1.99 [1.56, 2.51]	1.84 [1.45, 2.22]	1.56 [1.25, 1.94]
Omega 6 (mg)	15.56 [12.16, 19.34]	16.85 [13.63, 21.64]	15.84 [12.50, 20.69]	14.91 [11.92, 18.67]	13.91 [11.25, 17.13]

122 Notes: E-DII, energy-adjusted diet inflammatory index.

123 Table S5. Coefficients and 95% confidence intervals for the interquartile change of natural log-  
 124 transformed urinary metals (ln  $\mu\text{g/g}$  creatinine) on glucose metabolism indexes and the interaction term  
 125 between metal and energy-adjusted diet inflammatory index estimated using multivariate linear  
 126 regression models. The diet inflammatory index was estimated by 28 nutrients which represent the total  
 127 consumption from food intake.

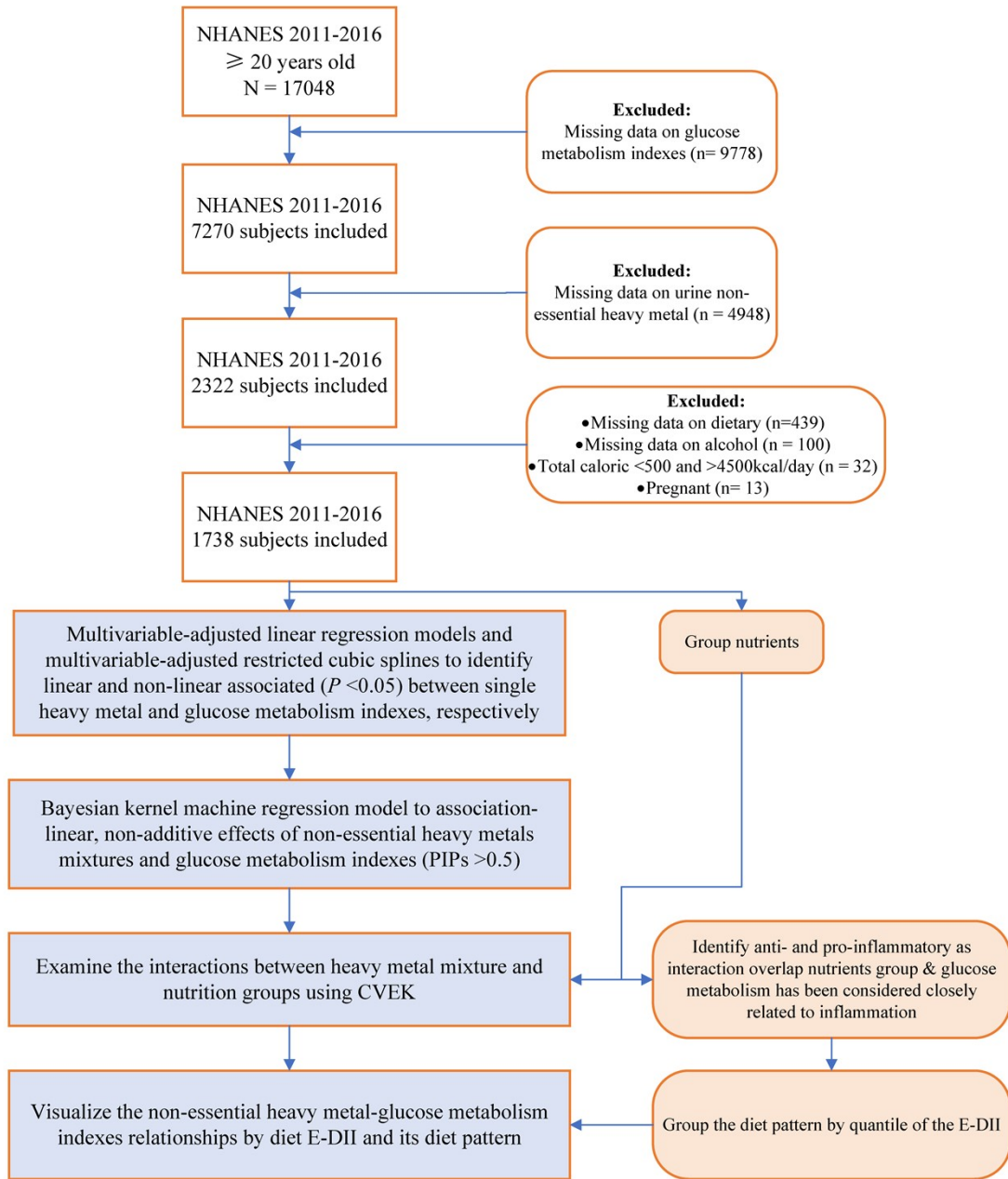
	Barium		Cadmium		Tungsten	
	Coefficient	<i>P</i>	Coefficient	<i>P</i>	Coefficient	<i>P</i>
Metal	-0.070	< 0.001	-0.142	0.030	-0.126	0.001
E-DII	-0.187	0.018	-0.127	0.177	-0.097	0.236
Metal x E-DII	0.050	0.046	-0.166	0.091	-0.063	0.099
Metal	0.167	< 0.001	-0.144	0.030	-0.135	0.001
Dietary range1	0.002	0.134	-0.099	0.143	-0.186	0.168
Metal × Dietary range1	-0.001	0.388	-0.002	0.190	-0.001	0.030
Metal	0.127	0.000	-0.150	0.030	-0.130	0.001
Dietary range2	0.002	0.558	-0.087	0.004	0.139	0.500
Metal × Dietary range2	-0.001	0.620	0.000	0.184	0.002	0.736
Metal	0.183	< 0.001	-0.141	0.030	-0.137	0.001
Dietary range3	2.818e-04	0.669	0.024	0.599	-0.172	0.003
Metal × Dietary range3	-6.611e-05	0.256	0.001	0.608	-0.001	0.045
Metal	0.1710	< 0.001	-0.144	0.030	-0.129	0.001
Dietary range4	0.001	0.000	0.031	0.006	-0.006	0.398
Metal × Dietary range4	-0.001	0.212	0.002	0.478	-0.001	0.263

128 Notes: Barium corresponds to homeostatic model assessment for insulin resistance as the  
 129 outcome; Cadmium and Tungsten correspond to hemoglobinA1c as the outcome. The dietary  
 130 range 1 to 4 for Barium-homeostatic model assessment for insulin resistance were  
 131 carbohydrate, protein, phosphorus, and magnesium; the dietary range 1 to 4 for Cadmium-  
 132 hemoglobin A1c were carbohydrate, phosphorus, potassium, and iron; the dietary range 1 to 4 for  
 133 Tungsten-hemoglobin A1c were carbohydrate, protein, phosphorus, and selenium. All linear  
 134 regression models were adjusted with one metal, one interaction term of metal and nutrient,  
 135 and the same set of covariates. All linear regression models have included the following  
 136 covariates: survey cycle of NHANES (2011-2012, 2013-2014, and 2015-2016), age (continuous),  
 137 sex, BMI (continuous), race (Mexican American, other Hispanic, non-Hispanic White, non-  
 138 Hispanic Black, and other race), alcohol consumption ( $\geq 12$  drinks/year and  $< 12$  drinks/year),  
 139 and hypertension (yes or no).

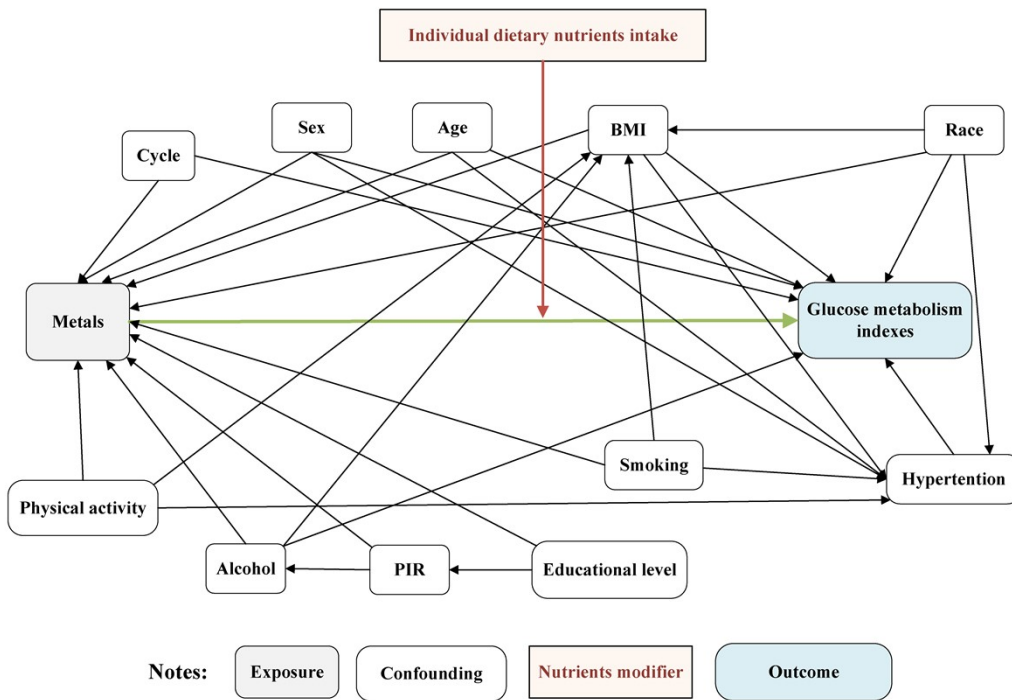


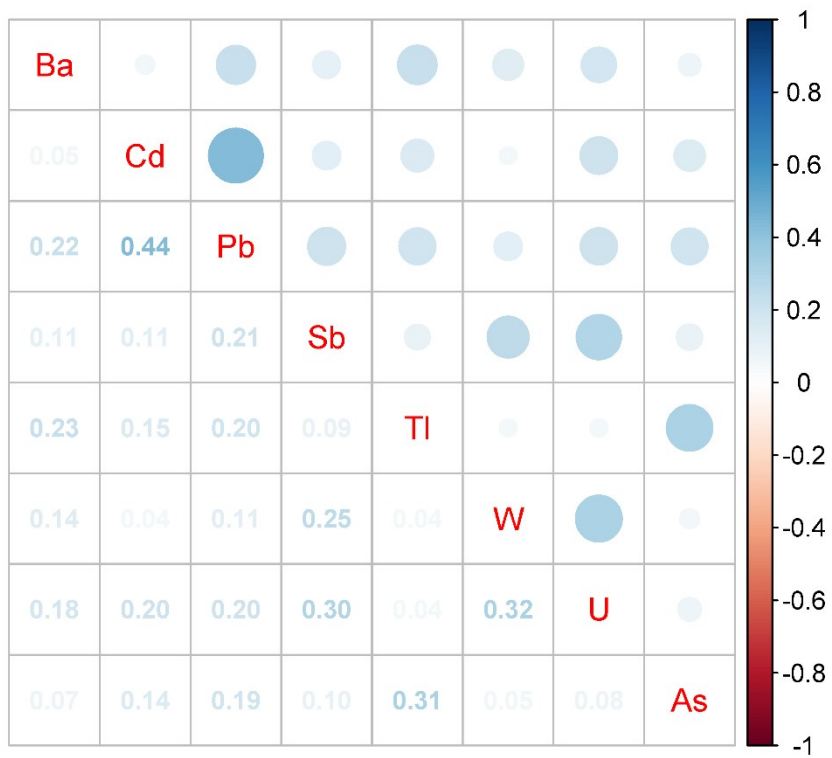
140 **Supplementary Figures**

141 Figure S1. Flowchart of the overall design, NHANES from 2011-2016. NHANES, National Health and  
 142 Nutrition Examination Survey; E-DII, energy-adjusted diet inflammatory index.



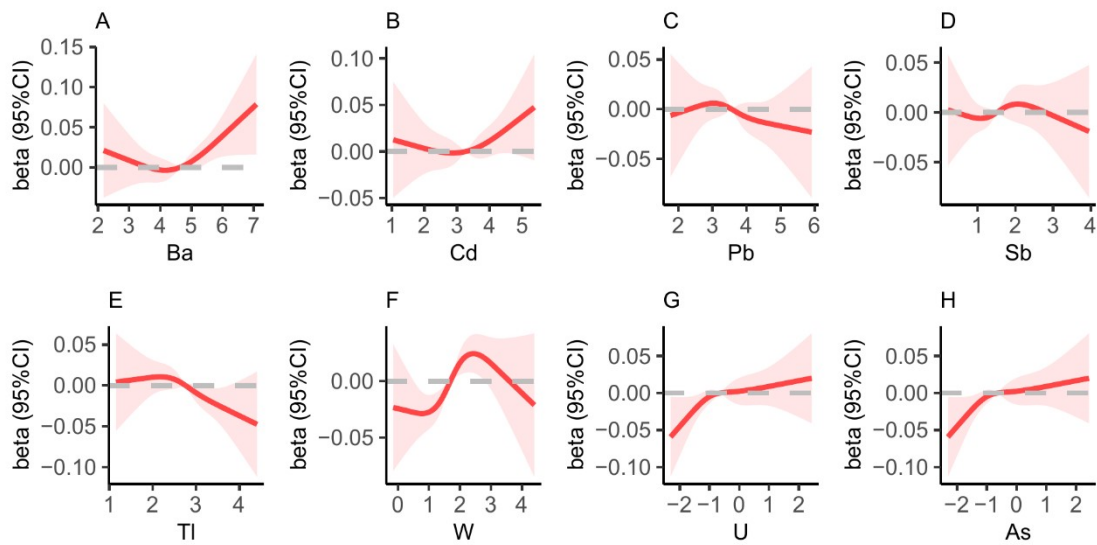
143 Figure S2. Directed acyclic graph of select covariates.



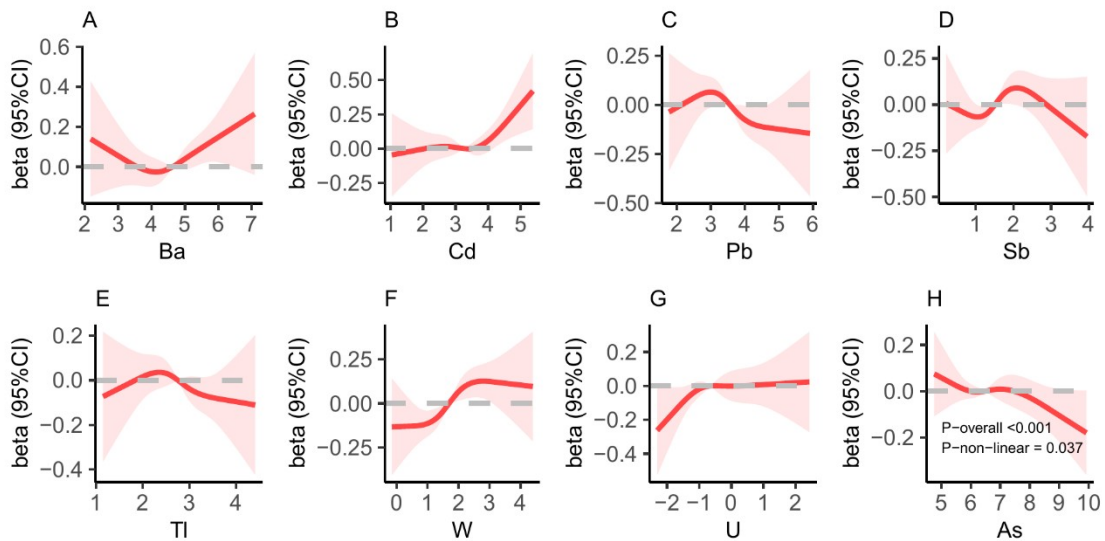


144 Figure S3. Correlations between urinary metal concentrations (ln ug/g creatinine).

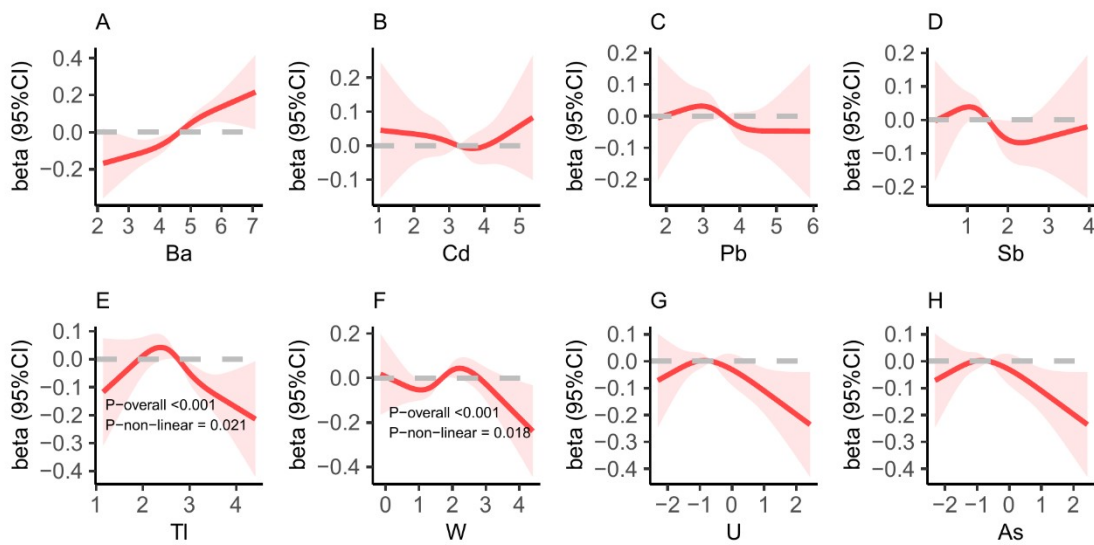
145 Figure S4. Association of single heavy metal (ln ug/g creatinine) and fasting plasma glucose (ln-mg/dL)  
 146 in multivariable-adjusted restricted cubic splines. Beta indicates change in predicted fasting plasma  
 147 glucose (ln-mg/dL) for a unit change in metal. Beta =0 means no association between exposures and the  
 148 outcome; beta >0 means a positive association between exposures and outcomes; beta <0 means a  
 149 negative association between exposures and outcomes. The solid red lines correspond to the central  
 150 estimates, and the red-shaded regions indicate the 95% confidence intervals. The model was adjusted for  
 151 survey cycle of NHANES (2011-2012, 2013-2014, and 2015-2016), age (continuous), sex, body mass  
 152 index (continuous), race (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic  
 153 Black, and other race), alcohol consumption ( $\geq 12$  drinks/year and < 12 drinks/year), and hypertension  
 154 (yes or no). NHANES, National Health and Nutrition Examination Survey; CI, confidence interval.



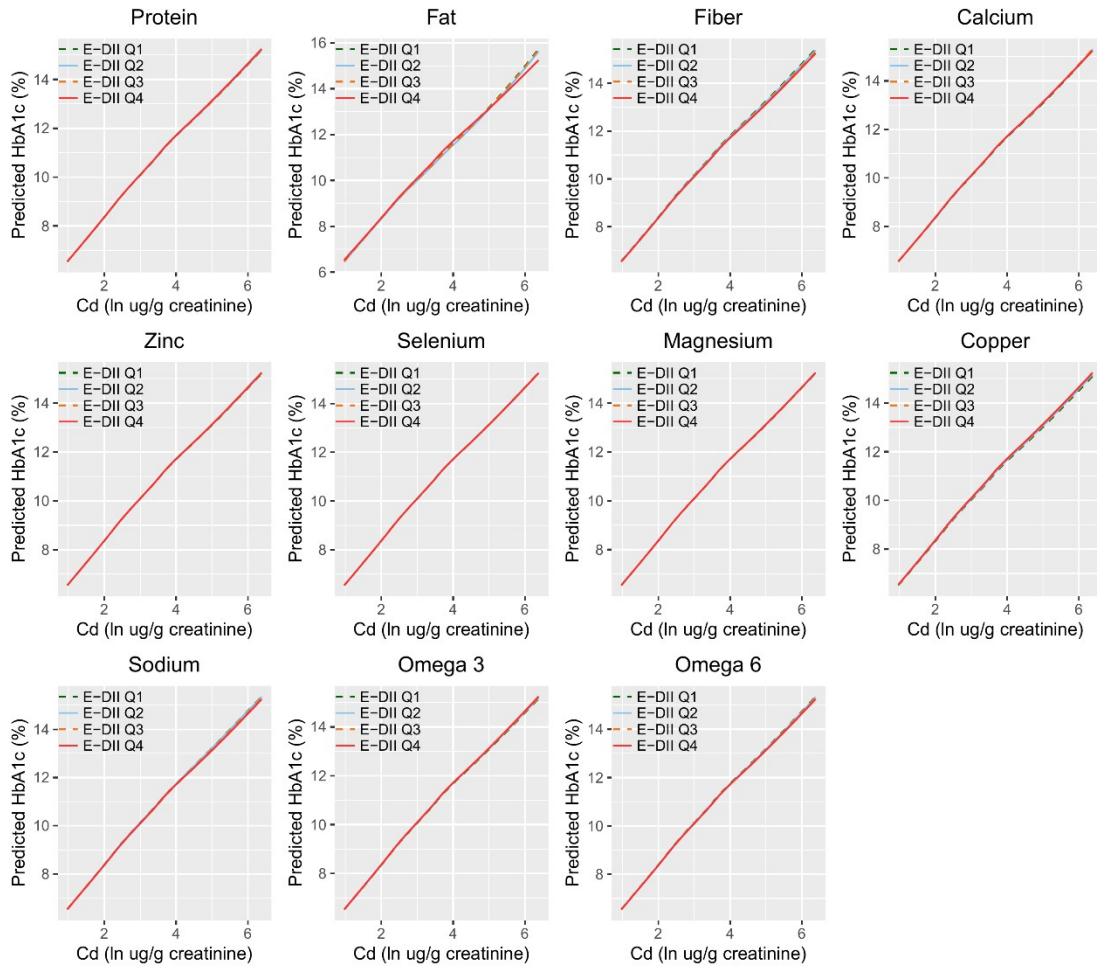
155 Figure S5. Association of single heavy metal (ln ug/g creatinine) and hemoglobin A1c (%) in  
 156 multivariable-adjusted restricted cubic splines. Beta indicates change in predicted hemoglobin A1c (%)  
 157 for a unit change in metal. Beta =0 means no association between exposures and the outcome; beta >0  
 158 means a positive association between exposures and outcomes; beta <0 means a negative association  
 159 between exposures and outcomes. The solid red lines correspond to the central estimates, and the red-  
 160 shaded regions indicate the 95% confidence intervals. The model was adjusted for survey cycle of  
 161 NHANES (2011-2012, 2013-2014, and 2015-2016), age (continuous), sex, body mass index  
 162 (continuous), race (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and  
 163 other race), alcohol consumption ( $\geq 12$  drinks/year and < 12 drinks/year), and hypertension (yes or no).  
 164 NHANES, National Health and Nutrition Examination Survey; CI, confidence interval.



165 Figure S6. Association of single heavy metal (ln ug/g creatinine) and homeostatic model assessment for  
 166 insulin resistance (ln) in multivariable-adjusted restricted cubic splines. Beta indicates change in  
 167 predicted homeostatic model assessment for insulin resistance (ln) for a unit change in metal. Beta =0  
 168 means no association between exposures and the outcome; beta >0 means a positive association between  
 169 exposures and outcomes; beta <0 means a negative association between exposures and outcomes. The  
 170 solid red lines correspond to the central estimates, and the red-shaded regions indicate the 95%  
 171 confidence intervals. The model was adjusted for survey cycle of NHANES (2011-2012, 2013-2014, and  
 172 2015-2016), age (continuous), sex, body mass index (continuous), race (Mexican American, other  
 173 Hispanic, non-Hispanic White, non-Hispanic Black, and other race), alcohol consumption ( $\geq 12$   
 174 drinks/year and < 12 drinks/year), and hypertension (yes or no). NHANES, National Health and Nutrition  
 175 Examination Survey; CI, confidence interval.

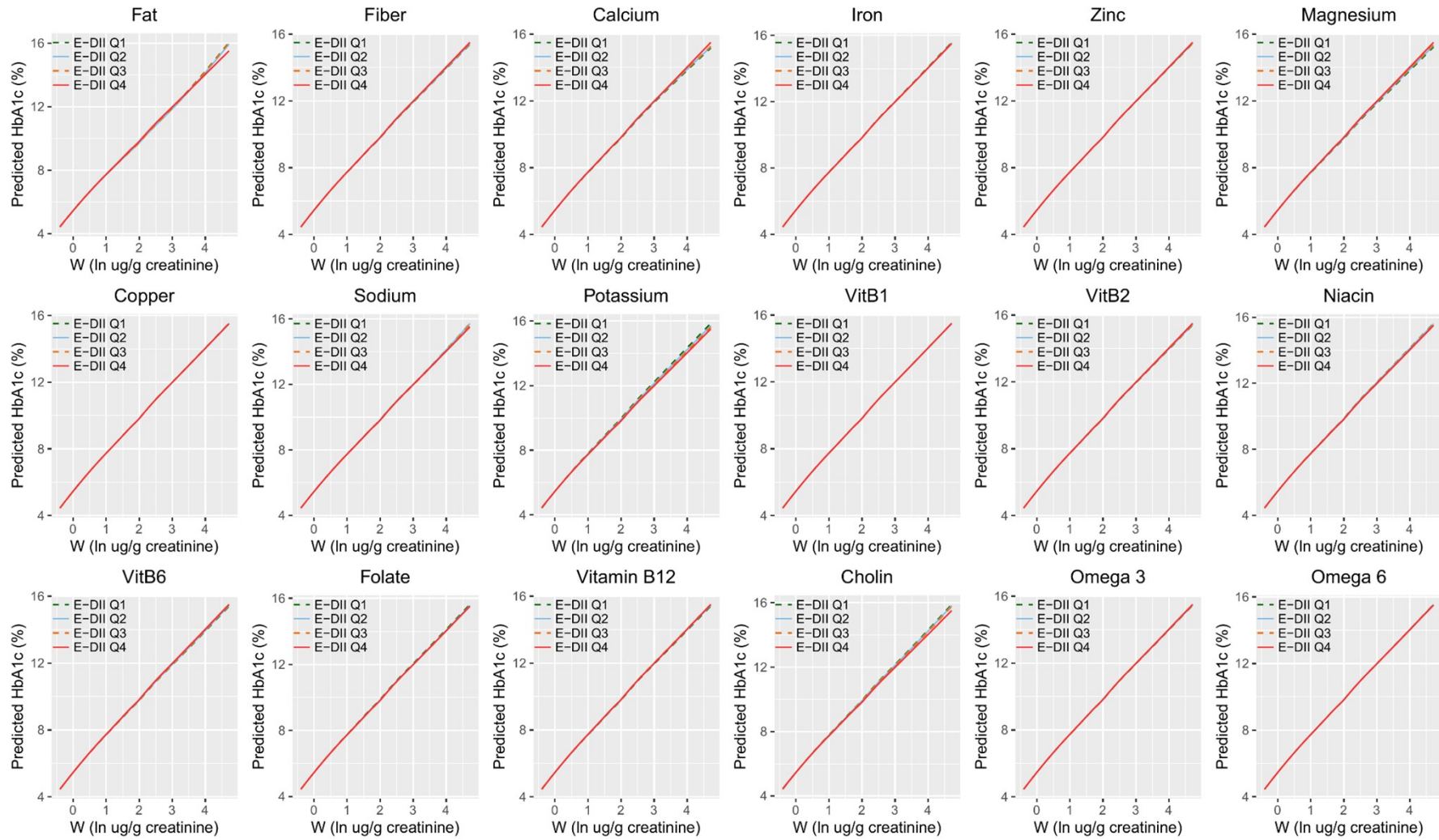


176 Figure S7. The Cd-hemoglobin A1c (%) relationships in the “E-DII Q4” group and in the hypothetically  
177 “E-DII Q1-3” group. E-DII, energy-adjusted diet inflammatory index.





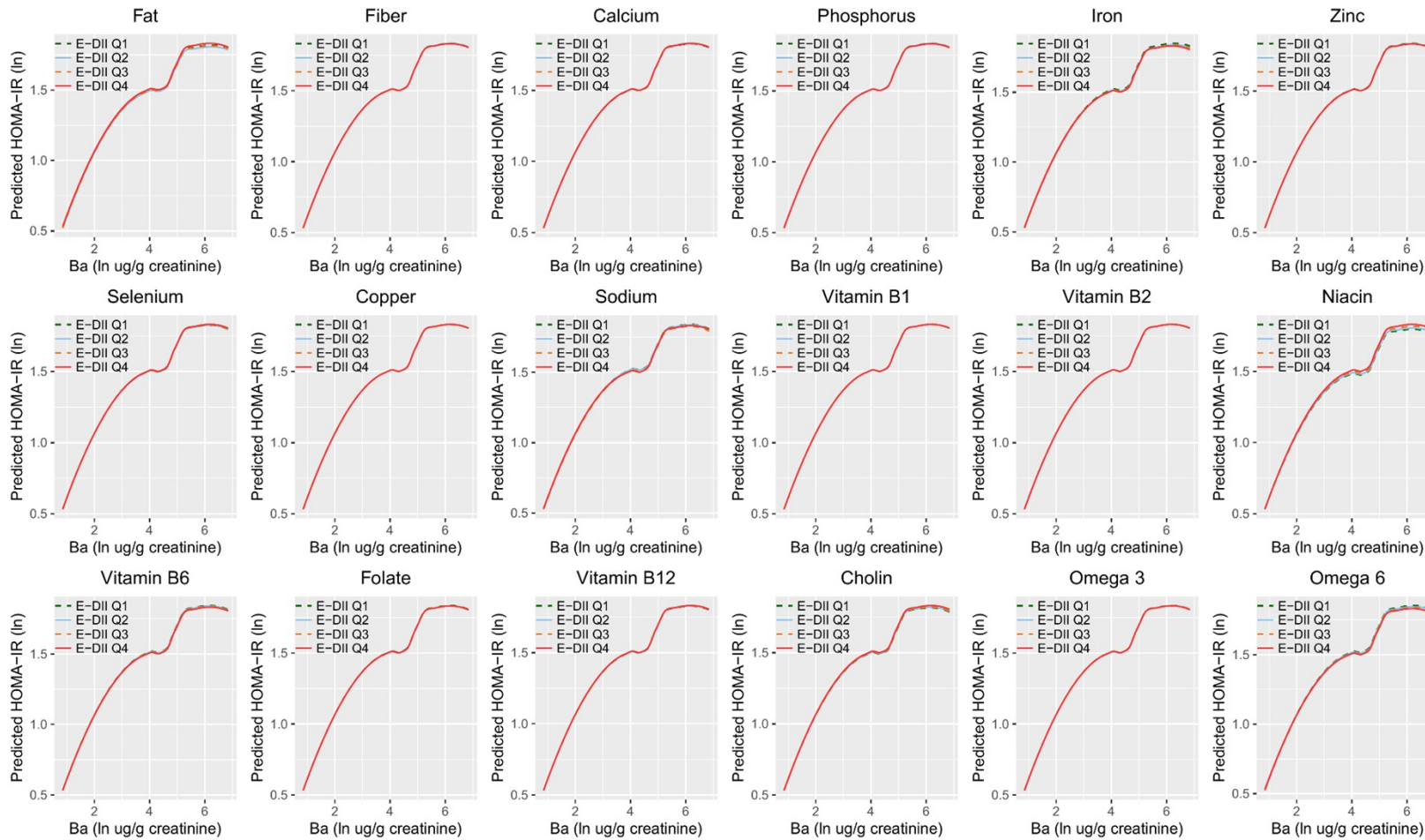
178 Figure S8. The W-hemoglobin A1c (%) relationships in the “E-DII Q4” group and in the hypothetically “E-DII Q1-3” group. E-DII, energy-adjusted diet inflammatory index.



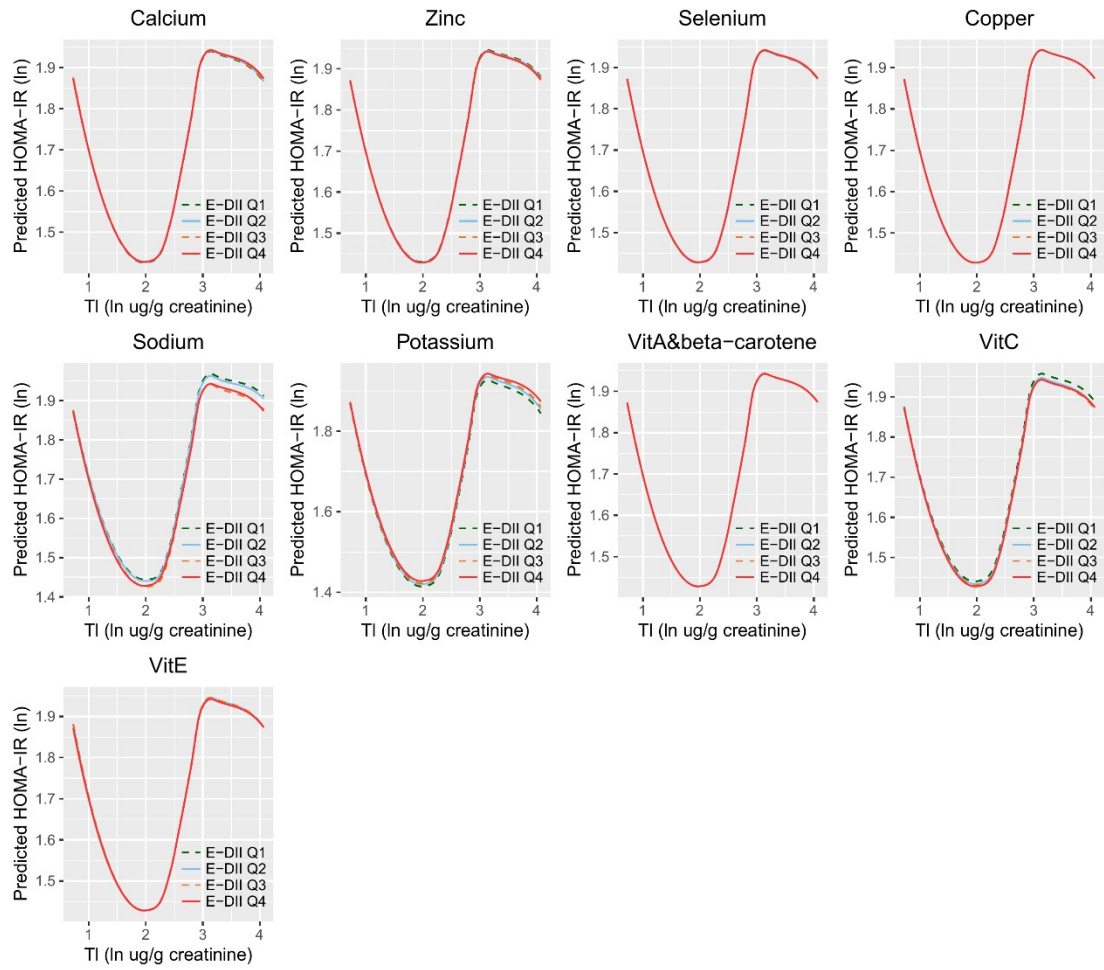


179 Figure S9. The Ba- homeostatic model assessment for insulin resistance (HOMA-IR) (ln) relationships in the “E-DII Q4” group and in the hypothetically “E-DII Q1-3” group.

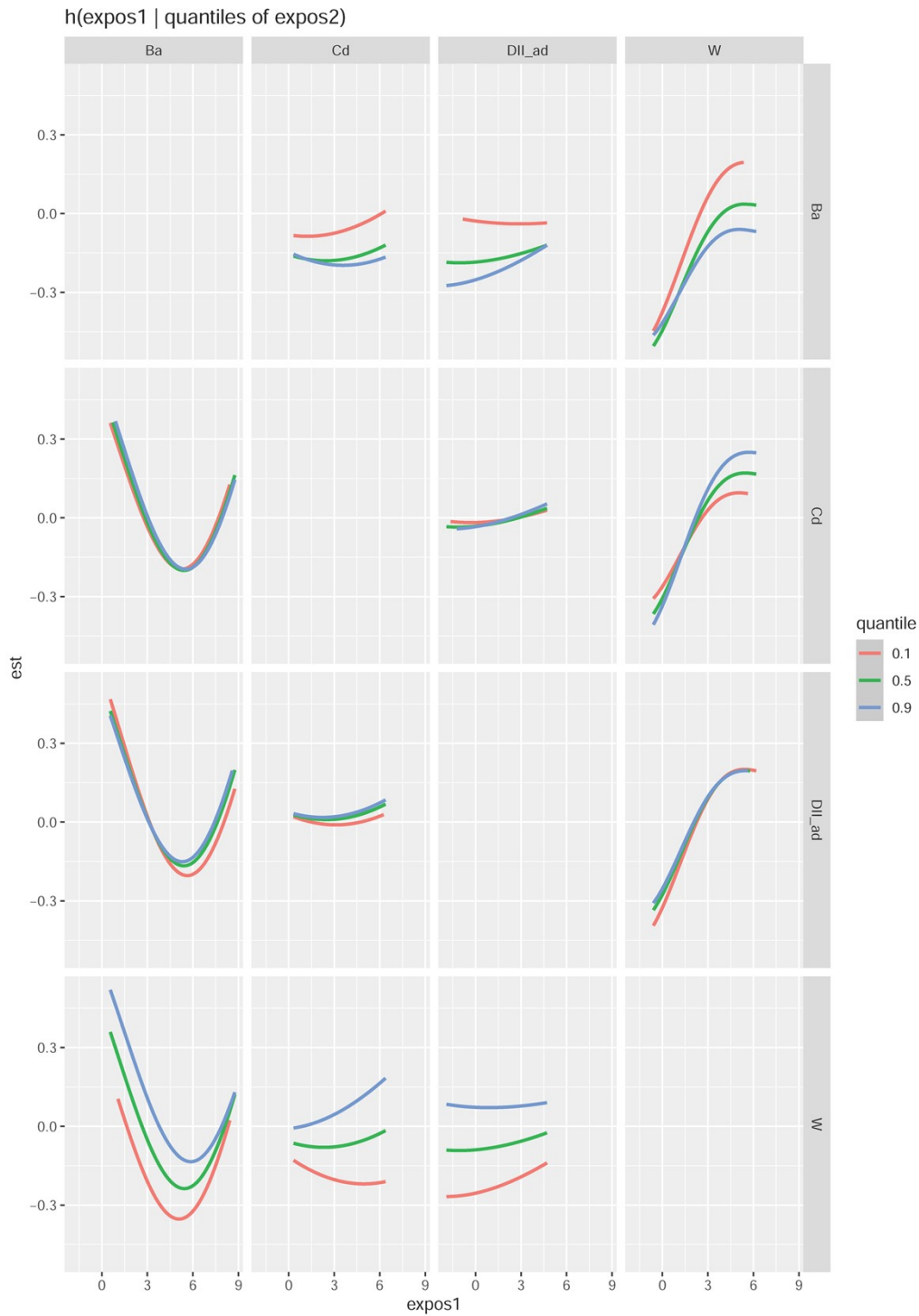
180 E-DII, energy-adjusted diet inflammatory index.



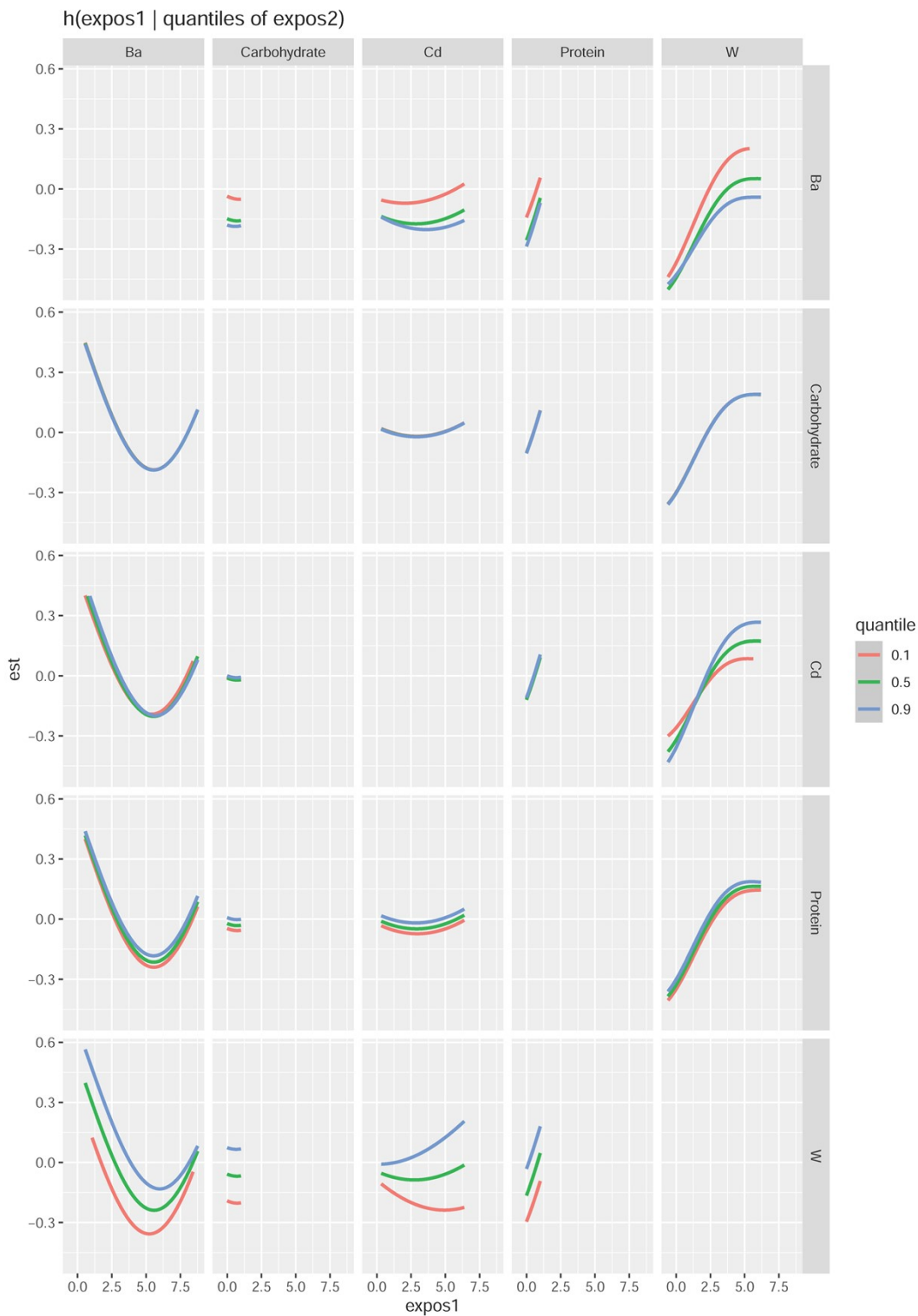
181 Figure S10. The TI- homeostatic model assessment for insulin resistance (ln) relationships in the “E-DII  
182 Q4” group and in the hypothetically “E-DII Q1-3” group. E-DII, energy-adjusted diet inflammatory  
183 index.



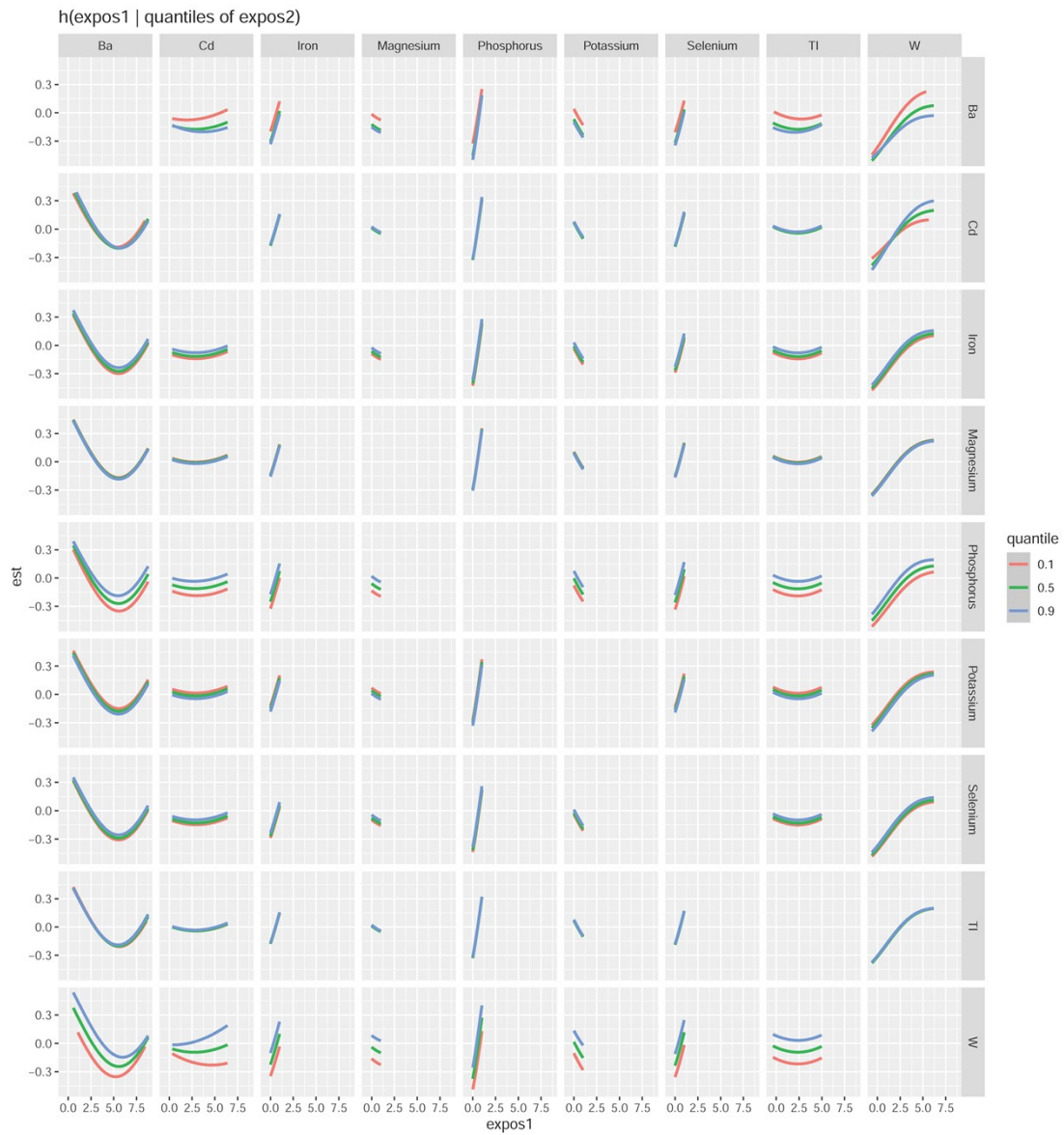
184 Figure S11. Impact of E-DII and metal interactions on diabetes. Bivariate exposure–response functions  
 185 for each of the exposure presented on the upper coordinate axis when the other variables presented on  
 186 the right longitudinal axis holding at different quantiles (10th, 50th, and 90th percentiles) and the other  
 187 variables were held at the median. Model adjusted for survey cycle of NHANES (2011-2012, 2013-2014,  
 188 and 2015-2016), age (continuous), sex, body mass index (continuous), race (Mexican American, other  
 189 Hispanic, non-Hispanic White, non-Hispanic Black, and other race), alcohol consumption ( $\geq 12$   
 190 drinks/year and  $< 12$  drinks/year), and hypertension (yes or no). DII-ad, adjusted energy diet  
 191 inflammatory index.



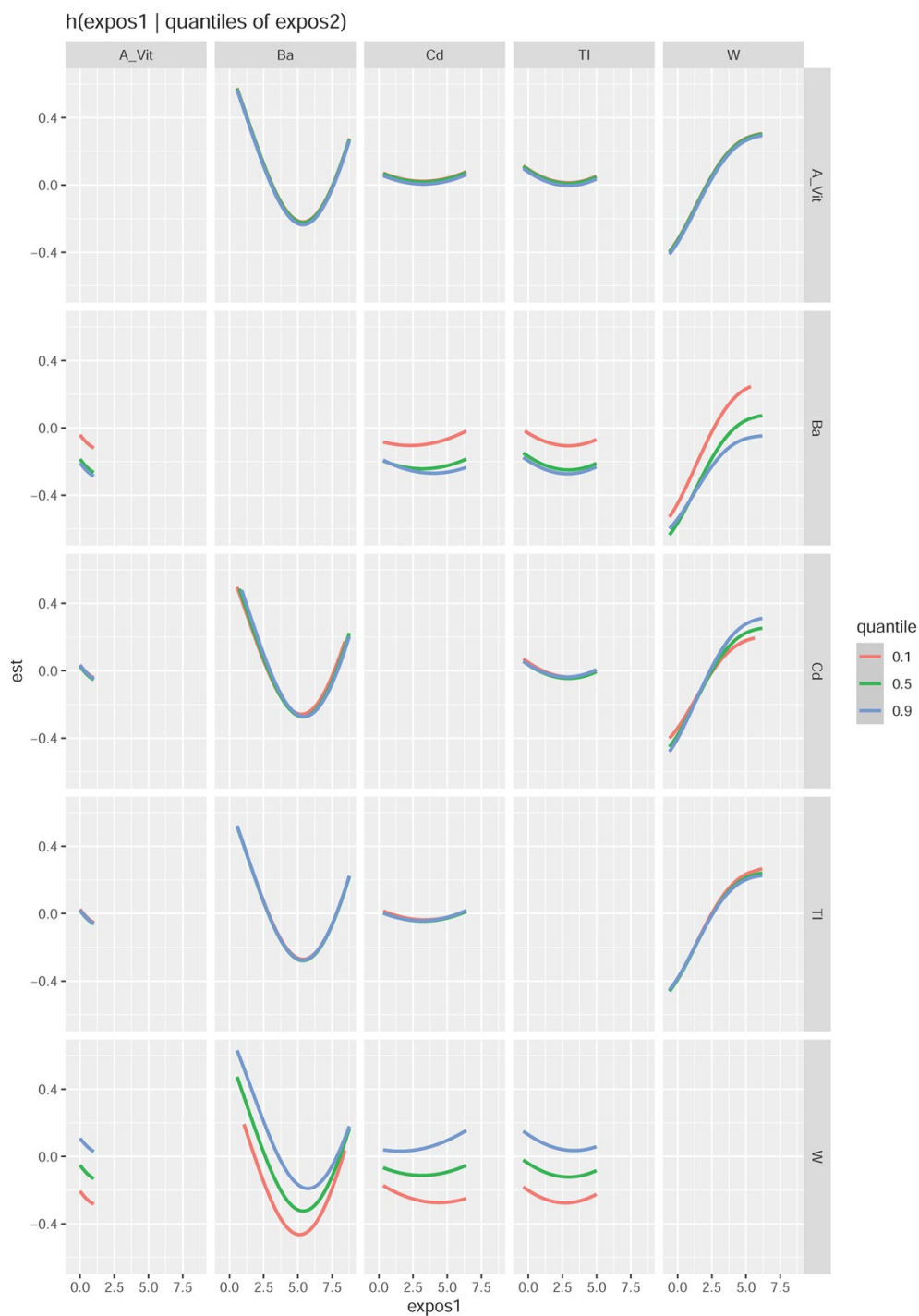
192 Figure S12. Impact of macro-nutrients and metal interactions on diabetes. Bivariate exposure–response  
 193 functions for each of the exposure presented on the upper coordinate axis when the other variables  
 194 presented on the right longitudinal axis holding at different quantiles (10th, 50th, and 90th percentiles)  
 195 and the other variables were held at the median. Model adjusted for survey cycle of NHANES (2011-  
 196 2012, 2013-2014, and 2015-2016), age (continuous), sex, body mass index (continuous), race (Mexican  
 197 American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race), alcohol  
 198 consumption ( $\geq 12$  drinks/year and  $< 12$  drinks/year), and hypertension (yes or no).



199 Figure S13. Impact of minerals and metal interactions on diabetes. Bivariate exposure–response  
 200 functions for each of the exposure presented on the upper coordinate axis when the other variables  
 201 presented on the right longitudinal axis holding at different quantiles (10th, 50th, and 90th percentiles)  
 202 and the other variables were held at the median. Model adjusted for survey cycle of NHANES (2011-  
 203 2012, 2013-2014, and 2015-2016), age (continuous), sex, body mass index (continuous), race (Mexican  
 204 American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race), alcohol  
 205 consumption ( $\geq 12$  drinks/year and  $< 12$  drinks/year), and hypertension (yes or no).



206 Figure S14. Impact of A vitamins and metal interactions on diabetes. Bivariate exposure–response  
 207 functions for each of the exposure presented on the upper coordinate axis when the other variables  
 208 presented on the right longitudinal axis holding at different quantiles (10th, 50th, and 90th percentiles)  
 209 and the other variables were held at the median. Model adjusted for survey cycle of NHANES (2011-  
 210 2012, 2013-2014, and 2015-2016), age (continuous), sex, body mass index (continuous), race (Mexican  
 211 American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race), alcohol  
 212 consumption ( $\geq 12$  drinks/year and  $< 12$  drinks/year), and hypertension (yes or no).



213 Reference

- 214 1. Qiu Z, Chen X, Geng T, et al. Associations of serum carotenoids with risk of  
215 cardiovascular mortality among individuals with type 2 diabetes: results from NHANES.  
216 *Diabetes care*, 2022, **45**: 1453-1461.