

Supplemental Information

Association Between Urinary Cobalt and All-Cause and Cause-Specific Mortality Among Chinese Older Adults: A Prospective Cohort Study

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Specific Classification Information for Covariates

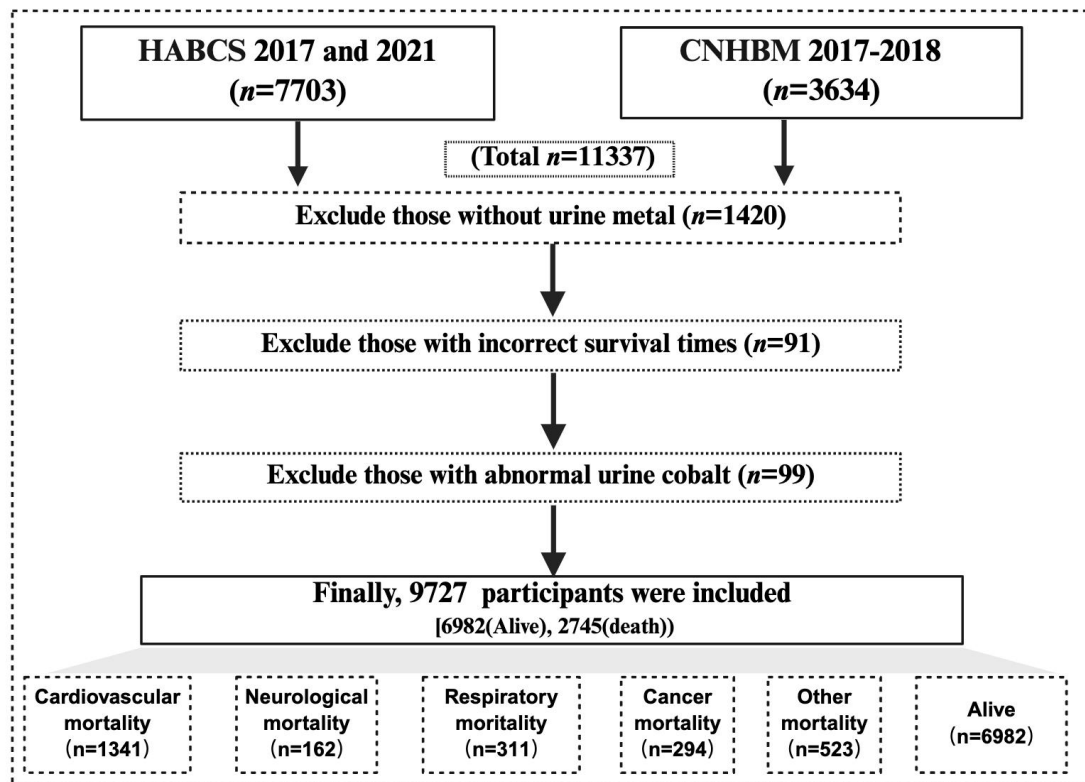
Educational status was defined as illiterate for participants who had never received formal education and educated otherwise. Economic status was assessed differently across cohorts. In the HABCS, it was evaluated using the question: “How do you rate your economic status compared with other local people?” with response options of “Very rich”, “Rich”, “Average”, “Poor”, and “Very poor”. In the CNHBM, it was based on annual household income categories: < 10,000 yuan, 10,000–30,000 yuan, 30,000–60,000 yuan, 60,000–100,000 yuan, and > 100,000 yuan. To harmonize these measures, we grouped “Very rich” and “Rich” in HABCS as “high”, and “Poor” and “Very poor” as “low”; the middle category remained “middle”. For CNHBM, households with annual income > 60,000 yuan were classified as “high”, those with < 10,000 yuan as “low”, and others as “middle”. Marital status was categorized as married (including partnered) or unmarried (never married, divorced, or widowed). BMI was calculated from measured height and weight and classified as underweight (< 18.5 kg/m²), normal (18.5–24 kg/m²), overweight (24–28 kg/m²), or obese (≥ 28 kg/m²). Hypertension was defined as either self-reported physician diagnosis or measured systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥ 90 mmHg. Diabetes was defined as self-reported diagnosis or fasting blood glucose > 7.0 mmol/L. Dyslipidemia was defined according to the Chinese Guidelines for the

Prevention and Treatment of Dyslipidemia in Adults (2016 Revision) as triglycerides $\geq$ 2.3 mmol/L, total cholesterol $\geq$ 6.2 mmol/L, LDL-C $\geq$ 4.1 mmol/L, or HDL-C $<$ 1.0 mmol/L. For the HABCS cohort, where direct LDL-C measurement was unavailable, it was estimated using the Friedewald formula: LDL-C = TC – HDL-C – TG/5. CKD was defined as an estimated glomerular filtration rate (eGFR) $\leq$ 60 mL/min/1.73 m², calculated using the CKD-EPI 2009 equation, in accordance with the KDOQI guidelines.

Supplementary Table S1 Spiked recoveries and relative standard deviations for 5 metals in urine.

Analyte	Background ($\mu\text{g/L}$)	2.5 $\mu\text{g/L}$		5 $\mu\text{g/L}$		10 $\mu\text{g/L}$	
		Recovery (%)	RSD (%)	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)
Co	1.75	99.9	1.9	101.5	0.6	99.6	0.8
As	2.03	100.7	3.0	103.3	2.4	98.7	1.2
Cd	1.47	101.7	1.6	102.4	1.3	100.2	0.6
Pb	3.21	104.7	5.9	101.5	1.8	101.8	0.9
Ni	3.83	104.1	3.7	101.7	1.0	99.8	2.9

Note. As, arsenic; Cd, cadmium; Pb, lead; Co, cobalt; Ni, nickel; RSD, relative standard deviation.



Supplementary Figure S1 Flowchart for the inclusion and exclusion of study participants

Supplementary Table S2 Basic characteristics of the study participants according to quartile groups of urinary cobalt levels

Characteristics	Overall	Q1	Q2	Q3	Q4	P-value
Participants, <i>n</i>	9,727	2,552	2,345	2,403	2,427	
Age (mean (<i>SD</i>))	77.820 (13.080)	76.158 (12.766)	76.505 (12.727)	78.020 (13.063)	80.641 (13.285)	< 0.001
Sex (%)						< 0.001
Male	4,589 (47.178)	1,111 (43.534)	1,107 (47.207)	1,217 (50.645)	1,154 (47.548)	
Female	5,138 (52.822)	1,441 (56.466)	1,238 (52.793)	1,186 (49.355)	1,273 (52.452)	
Education level (%)						< 0.001
Literate	5,725 (58.857)	1,543 (60.462)	1,434 (61.151)	1,434 (59.675)	1,314 (54.141)	
Illiterate	4,002 (41.143)	1,009 (39.538)	911 (38.849)	969 (40.325)	1,113 (45.859)	
Economic level (%)						< 0.001
Low	1,651 (16.973)	467 (18.299)	417 (17.783)	394 (16.396)	373 (15.369)	
Middle	6,287 (64.635)	1,610 (63.088)	1,472 (62.772)	1,541 (64.128)	1,664 (68.562)	
High	1,789 (18.392)	475 (18.613)	456 (19.446)	468 (19.476)	390 (16.069)	
Ethnicity(%)						0.121
Han	9,029 (92.824)	2,368 (92.790)	2,159 (92.068)	2,225 (92.593)	2,277 (93.820)	
Other	698 (7.176)	184 (7.210)	186 (7.932)	178 (7.407)	150 (6.180)	
Residential area (%)						< 0.001
Rural	2,258 (23.214)	713 (27.939)	609 (25.970)	551 (22.930)	385 (15.863)	
Urban	7,469 (76.786)	1,839 (72.061)	1,736 (74.030)	1,852 (77.070)	2,042 (84.137)	
Marital status (%)						< 0.001
Married	6,003 (61.715)	1,631 (63.911)	1,532 (65.330)	1,482 (61.673)	1,358 (55.954)	
Unmarried	3,724 (38.285)	921 (36.089)	813 (34.670)	921 (38.327)	1,069 (44.046)	
BMI (%)						< 0.001
Underweight	909 (9.345)	191 (7.484)	187 (7.974)	254 (10.570)	277 (11.413)	

Normal	4,661 (47.918)	1,187 (46.513)	1,097 (46.780)	1,143 (47.566)	1,234 (50.845)	0.011
Overweight	2,929 (30.112)	817 (32.014)	747 (31.855)	715 (29.754)	650 (26.782)	
Obesity	1,228 (12.625)	357 (13.989)	314 (13.390)	291 (12.110)	266 (10.960)	
Current smoking status (%)						0.067
No	7,655 (78.698)	2,058 (80.643)	1,843 (78.593)	1,845 (76.779)	1,909 (78.657)	
Yes	2,072 (21.302)	494 (19.357)	502 (21.407)	558 (23.221)	518 (21.343)	
Current drinking status (%)						0.568
No	7,386 (75.933)	1,944 (76.176)	1,777 (75.778)	1,784 (74.241)	1,881 (77.503)	
Yes	2,341 (24.067)	608 (23.824)	568 (24.222)	619 (25.759)	546 (22.497)	
Fruit consumption (%)						0.118
No	2,355 (24.211)	638 (25.000)	548 (23.369)	589 (24.511)	580 (23.898)	
Yes	7,372 (75.789)	1,914 (75.000)	1,797 (76.631)	1,814 (75.489)	1,847 (76.102)	
Vegetable consumption (%)						0.218
No	361 (3.711)	104 (4.075)	74 (3.156)	80 (3.329)	103 (4.244)	
Yes	9,366 (96.289)	2,448 (95.925)	2,271 (96.844)	2,323 (96.671)	2,324 (95.756)	
Meat consumption (%)						0.007
Yes	8,957 (92.084)	2,349 (92.045)	2,163 (92.239)	2,231 (92.842)	2,214 (91.224)	
No	770 (7.916)	203 (7.955)	182 (7.761)	172 (7.158)	213 (8.776)	
Hypertension (%)						0.097
Yes	6,763 (69.528)	1,809 (70.886)	1,571 (66.994)	1,660 (69.080)	1,723 (70.993)	
No	2,964 (30.472)	743 (29.114)	774 (33.006)	743 (30.920)	704 (29.007)	
Diabetes (%)						
Yes	1,639 (16.850)	412 (16.144)	428 (18.252)	415 (17.270)	384 (15.822)	
No	8,088 (83.150)	2,140 (83.856)	1,917 (81.748)	1,988 (82.730)	2,043 (84.178)	

Dyslipidemia (%)							< 0.001
Yes	3,111 (31.983)	888 (34.796)	802 (34.200)	732 (30.462)	689 (28.389)		
No	6,616 (68.017)	1,664 (65.204)	1,543 (65.800)	1,671 (69.538)	1,738 (71.611)		
Chronic kidney disease (%)							< 0.001
Yes	2,170 (22.309)	533 (20.886)	487 (20.768)	535 (22.264)	615 (25.340)		
No	7,557 (77.691)	2,019 (79.114)	1,858 (79.232)	1,868 (77.736)	1,812 (74.660)		
Cohort (%)							< 0.001
CNHBM	3,604 (37.052)	1,139 (44.632)	981 (41.834)	863 (35.913)	621 (25.587)		< 0.001
HABCS	6,123 (62.948)	1,413 (55.368)	1,364 (58.166)	1,540 (64.087)	1,806 (74.413)		
Metals level (µg/L)							
Urinary Co	0.220 (0.130, 0.398)	0.090 (0.049, 0.110)	0.170 (0.150, 0.197)	0.290 (0.252, 0.337)	0.559 (0.490, 0.820)		< 0.001
Urinary Cd	0.780 (0.390, 1.578)	0.420 (0.230, 0.802)	0.760 (0.412, 1.495)	1.014 (0.554, 2.022)	1.128 (0.567, 2.213)		< 0.001
Urinary Pb	1.230 (0.608, 2.785)	0.850 (0.435, 1.954)	1.200 (0.644, 2.740)	1.470 (0.800, 3.170)	1.500 (0.698, 3.295)		< 0.001
Urinary Cr	0.686 (0.320, 1.238)	0.500 (0.210, 0.959)	0.661 (0.312, 1.199)	0.732 (0.354, 1.270)	0.889 (0.466, 1.471)		< 0.001
Urinary As	21.562 (11.800, 40.518)	12.826 (7.316, 23.143)	21.380 (12.910, 37.570)	27.500 (16.089, 48.790)	28.660 (15.253, 52.515)		< 0.001

Supplementary Table S3 Basic characteristics of study participants according to their survival status

Characteristics	Overall	Alive	Death	<i>P</i> -value
Participants, n	9,727	6,982	2,745	
Age (mean (<i>SD</i>))	77.820 (13.080)	73.417 (10.605)	89.021 (12.059)	< 0.001
Sex (%)				0.032
Male	4,589 (47.178)	3,342 (47.866)	1,247 (45.428)	
Female	5,138 (52.822)	3,640 (52.134)	1,498 (54.572)	
Education level (%)				< 0.001
Literate	5,725 (58.857)	4,667 (66.843)	1,058 (38.543)	
Illiterate	4,002 (41.143)	2,315 (33.157)	1,687 (61.457)	
Economic level (%)				< 0.001
Low	1,651 (16.973)	1,268 (18.161)	383 (13.953)	
Middle	6,287 (64.635)	4,378 (62.704)	1,909 (69.545)	
High	1,789 (18.392)	1,336 (19.135)	453 (16.503)	
Ethnicity (%)				0.572
Han	9,029 (92.824)	6,474 (92.724)	2,555 (93.078)	
Other	698 (7.176)	508 (7.276)	190 (6.922)	
Residential area (%)				< 0.001
Rural	2,258 (23.214)	1,974 (28.273)	284 (10.346)	
Urban	7,469 (76.786)	5,008 (71.727)	2461 (89.654)	
Marital status (%)				< 0.001
Married	6,003 (61.715)	5,035 (72.114)	968 (35.264)	
Unmarried	3,724 (38.285)	1,947 (27.886)	1,777 (64.736)	
BMI (%)				<0.001
Underweight	909 (9.345)	384 (5.500)	525 (19.126)	
Normal	4,661 (47.918)	3,214 (46.033)	1,447 (52.714)	
Overweight	2,929 (30.112)	2,369 (33.930)	560 (20.401)	
Obesity	1,228 (12.625)	1,015 (14.537)	213 (7.760)	
Current smoking status (%)				< 0.001
Yes	2,072 (21.302)	1,580 (22.630)	492 (17.923)	
No	7,655 (78.698)	5,402 (77.370)	2,253 (82.077)	
Current drinking status (%)				< 0.001
Yes	2,341 (24.067)	1,851 (26.511)	490 (17.851)	
No	7,386 (75.933)	5,131 (73.489)	2,255 (82.149)	
Fruit consumption (%)				< 0.001
Yes	7,372 (75.789)	5,593 (80.106)	1,779 (64.809)	
No	2,355 (24.211)	1,389 (19.894)	966 (35.191)	
Vegetable consumption (%)				< 0.001
Yes	9,366 (96.289)	6,829 (97.809)	2,537 (92.423)	

No	3,61 (3.711)	153 (2.191)	208 (7.577)	
Meat consumption (%)				< 0.001
Yes	8,957 (92.084)	6,500 (93.097)	2,457 (89.508)	
No	7,70 (7.916)	482 (6.903)	288 (10.492)	
Hypertension (%)				< 0.001
Yes	6,763 (69.528)	4,777 (68.419)	1,986 (72.350)	
No	2,964 (30.472)	2,205 (31.581)	759 (27.650)	
Diabetes (%)				0.003
Yes	1,639 (16.850)	1,226 (17.559)	413 (15.046)	
No	8,088 (83.150)	5,756 (82.441)	2,332 (84.954)	
Dyslipidemia (%)				< 0.001
Yes	3,111 (31.983)	2,420 (34.661)	691 (25.173)	
No	6,616 (68.017)	4,562 (65.339)	2,054 (74.827)	
Chronic kidney disease (%)				< 0.001
Yes	2,170 (22.309)	1,102 (15.783)	1,068 (38.907)	
No	7,557 (77.691)	5,880 (84.217)	1,677 (61.093)	
Cohort (%)				< 0.001
CNHBM	3,604 (37.052)	3,221 (46.133)	383 (13.953)	
HABCS	6,123 (62.948)	3,761 (53.867)	2,362 (86.047)	

Supplementary Table S4 Results of hazard ratios and 95% confidence interval for the association between urinary cobalt and all-cause mortality and cause-specific mortality with different covariable models

Model	All-cause mortality	Cardiovascular mortality	Neurological mortality	Cancer mortality	Respiratory mortality	Other causes of mortality
Model1	1.250 (1.134–1.379)	1.262 (1.097–1.451)	1.749 (1.232–2.482)	1.186 (0.839–1.675)	0.955 (0.692–1.318)	1.283 (1.032–1.594)
Model2	1.244 (1.128–1.373)	1.269 (1.103–1.459)	1.669 (1.172–2.378)	1.160 (0.819–1.643)	0.936 (0.678–1.294)	1.267 (1.017–1.577)
Model3	1.246 (1.129–1.375)	1.262 (1.097–1.452)	1.658 (1.154–2.381)	1.183 (0.835–1.675)	0.950 (0.690–1.308)	1.269 (1.020–1.581)
Model4	1.244 (1.127–1.372)	1.262 (1.096–1.453)	1.644 (1.142–2.368)	1.180 (0.834–1.669)	0.950 (0.688–1.312)	1.257 (1.010–1.564)

Supplementary Table S5 Results of the association between urinary cobalt and all-cause and cause-specific mortality at different categories of urinary cobalt concentration variation (additionally adjusted for urinary arsenic and chromium)

Outcome	Unit	Events/Total	HR (95%CI)	P -value
All-cause mortality	Per unit	2,745/9,727	1.245 (1.128–1.374)	< 0.001
	Per IQR	2,745/9,727	1.060 (1.033–1.089)	< 0.001
	Q1	622/2,552	1.000 (ref)	
	Q2	618/2,345	1.124 (1.003–1.259)	0.044
	Q3	691/2,403	1.184 (1.056–1.328)	0.004
	Q4	814/2,427	1.302 (1.163–1.457)	< 0.001
	Per unit	162/9,727	1.596 (1.097–2.323)	0.015
	Per IQR	162/9,727	1.133 (1.025–1.253)	0.015
Neurological mortality	Q1	31/2,552	1.000 (ref)	
	Q2	33/2,345	1.352 (0.821–2.228)	0.237
	Q3	39/2,403	1.592 (0.968–2.616)	0.067
	Q4	59/2,427	2.208 (1.387–3.513)	0.001
	Per unit	1341/9,727	1.275 (1.108–1.467)	0.001
	Per IQR	1341/9,727	1.067 (1.028–1.108)	0.001
Cardiovascular mortality	Q1	316/2,552	1.000 (ref)	
	Q2	300/2,345	1.109 (0.944–1.303)	0.209
	Q3	336/2,403	1.191 (1.012–1.401)	0.035
	Q4	389/2,427	1.281 (1.091–1.503)	0.002
	Per unit	311/9,727	0.961 (0.696–1.326)	0.807
	Per IQR	311/9,727	0.989 (0.907–1.079)	0.807
Respiratory mortality	Q1	55/2,552	1.000 (ref)	
	Q2	82/2,345	1.637 (1.156–2.319)	0.005
	Q3	88/2,403	1.570 (1.102–2.238)	0.013
	Q4	86/2,427	1.373 (0.952–1.980)	0.090
	Per unit	294/9,727	1.180 (0.831–1.674)	0.355
	Per IQR	294/9,727	1.045 (0.952–1.148)	0.355
Cancer mortality	Q1	81/2,552	1.000 (ref)	
	Q2	76/2,345	0.961 (0.698–1.324)	0.809
	Q3	67/2,403	0.831 (0.590–1.171)	0.291
	Q4	70/2,427	0.911 (0.640–1.296)	0.603
	Per unit	523/9,727	1.249 (1.002–1.557)	0.048
Other causes of mortality	Per IQR	523/9,727	1.061 (1.001–1.126)	0.048
	Q1	125/2,552	1.000 (ref)	
	Q2	107/2,345	0.951 (0.731–1.238)	0.709
	Q3	127/2,403	1.025 (0.789–1.331)	0.853

	Q4	164/2,427	1.251 (0.970–1.612)	0.084
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Supplementary Table S6 Results of the association between urinary cobalt and all-cause and cause-specific mortality at different categories of urinary cobalt concentration variation (additionally adjusted for urinary nickel)

Outcome	Unit	Events/Total	HR (95%CI)	P -value
All-cause mortality	Per unit	2,745/9,727	1.244 (1.128–1.373)	< 0.001
	Per IQR	2,745/9,727	1.060 (1.033–1.089)	< 0.001
	Q1	622/2,552	1.000 (ref)	
	Q2	618/2,345	1.119 (1.000–1.254)	0.051
	Q3	691/2,403	1.176 (1.050–1.318)	0.005
	Q4	814/2,427	1.291 (1.154–1.445)	< 0.001
	Per unit	162/9,727	1.634 (1.134–2.356)	0.008
	Per IQR	162/9,727	1.141 (1.034–1.258)	0.008
Neurological mortality	Q1	31/2,552	1.000 (ref)	
	Q2	33/2,345	1.387 (0.843–2.285)	0.198
	Q3	39/2,403	1.661 (1.010–2.731)	0.046
	Q4	59/2,427	2.357 (1.488–3.732)	< 0.001
	Per unit	1341/9,727	1.262 (1.096–1.453)	0.001
	Per IQR	1341/9,727	1.064 (1.025–1.105)	0.001
	Q1	316/2,552	1.000 (ref)	
	Q2	300/2,345	1.096 (0.933–1.287)	0.264
Cardiovascular mortality	Q3	336/2,403	1.167 (0.992–1.372)	0.062
	Q4	389/2,427	1.247 (1.063–1.462)	0.007
	Per unit	294/9,727	1.179 (0.834–1.668)	0.351
	Per IQR	294/9,727	1.045 (0.952–1.147)	0.351
	Q1	81/2,552	1.000 (ref)	
	Q2	76/2,345	0.957 (0.695–1.317)	0.786
	Q3	67/2,403	0.825 (0.587–1.161)	0.270
	Q4	70/2,427	0.905 (0.638–1.284)	0.576
Cancer mortality	Per unit	311/9,727	0.930 (0.674–1.283)	0.656
	Per IQR	311/9,727	0.981 (0.899–1.069)	0.656
	Q1	55/2,552	1.000 (ref)	
	Q2	82/2,345	1.622 (1.146–2.295)	0.006
	Q3	88/2,403	1.534 (1.078–2.181)	0.017
	Q4	86/2,427	1.333 (0.927–1.916)	0.121
	Per unit	523/9,727	1.258 (1.010–1.565)	0.040
Respiratory mortality	Q1	55/2,552	1.000 (ref)	
	Q2	82/2,345	1.622 (1.146–2.295)	0.006
	Q3	88/2,403	1.534 (1.078–2.181)	0.017
	Q4	86/2,427	1.333 (0.927–1.916)	0.121
Other causes	Per unit	523/9,727	1.258 (1.010–1.565)	0.040

of mortality	Per IQR	523/9,727	1.063 (1.003–1.128)	0.040
	Q1	125/2,552	1.000 (ref)	
	Q2	107/2,345	0.951 (0.731–1.237)	0.706
	Q3	127/2,403	1.024 (0.790–1.329)	0.856
	Q4	164/2,427	1.252 (0.973–1.611)	0.080

Supplementary Table S7 Results of the association between urinary cobalt and all-cause and cause-specific mortality at different categories of urinary cobalt concentration variation (excluding dyslipidemia as a covariate)

Outcome	Unit	Events/Total	HR (95%CI)	P -value
All-cause mortality	Per unit	2,745/9,727	1.244 (1.127–1.372)	< 0.001
	Per IQR	2,745/9,727	1.060 (1.033–1.089)	< 0.001
	Q1	622/2,552	1.000 (ref)	
	Q2	618/2,345	1.120 (1.000–1.254)	0.050
	Q3	691/2,403	1.177 (1.050–1.319)	0.005
	Q4	814/2,427	1.294 (1.156–1.447)	< 0.001
	Per unit	162/9,727	1.641 (1.137–2.371)	0.008
Neurological mortality	Per IQR	162/9,727	1.142 (1.035–1.260)	0.008
	Q1	31/2,552	1.000 (ref)	
	Q2	33/2,345	1.389 (0.843–2.288)	0.197
	Q3	39/2,403	1.676 (1.020–2.753)	0.041
	Q4	59/2,427	2.330 (1.472–3.689)	< 0.001
	Per unit	1,341/9,727	1.262 (1.096–1.453)	0.001
	Per IQR	1,341/9,727	1.064 (1.025–1.105)	0.001
Cardiovascular mortality	Q1	316/2,552	1.000 (ref)	
	Q2	300/2,345	1.097 (0.934–1.288)	0.261
	Q3	336/2,403	1.168 (0.993–1.373)	0.061
	Q4	389/2,427	1.249 (1.066–1.465)	0.006
	Per unit	311/9,727	0.958 (0.695–1.320)	0.791
	Per IQR	311/9,727	0.988 (0.907–1.077)	0.791
	Q1	55/2,552	1.000 (ref)	
Respiratory mortality	Q2	82/2,345	1.623 (1.147–2.296)	0.006
	Q3	88/2,403	1.544 (1.086–2.197)	0.016
	Q4	86/2,427	1.359 (0.946–1.954)	0.097
	Per unit	294/9,727	1.180 (0.834–1.669)	0.350
	Per IQR	294/9,727	1.045 (0.953–1.147)	0.350
	Q1	81/2,552	1.000 (ref)	
	Q2	76/2,345	0.957 (0.695–1.317)	0.786
Cancer mortality				

	Q3	67/2,403	0.826 (0.587–1.161)	0.271
	Q4	70/2,427	0.905 (0.638–1.285)	0.578
	Per unit	523/9,727	1.257 (1.010–1.564)	0.041
	Per IQR	523/9,727	1.063 (1.003–1.127)	0.041
Other causes of mortality	Q1	125/2,552	1.000 (ref)	
	Q2	107/2,345	0.951 (0.731–1.237)	0.709
	Q3	127/2,403	1.025 (0.790–1.329)	0.854
	Q4	164/2,427	1.254 (0.975–1.613)	0.078

Supplementary Table S8 Results of the association between urinary cobalt and all-cause and cause-specific mortality at different categories of urinary cobalt concentration variation (excluding participants with follow-up duration <1 year)

Outcome	Unit	Events/Total	HR (95%CI)	P -value
All-cause mortality	Per unit	2,105/9,087	1.207 (1.074–1.357)	0.002
	Per IQR	2,105/9,087	1.050 (1.019–1.082)	0.002
	Q1	459/2,274	1.000 (ref)	
	Q2	509/2,272	1.125 (0.989–1.280)	0.072
	Q3	545/2,270	1.138 (0.998–1.297)	0.054
	Q4	592/2,271	1.198 (1.050–1.367)	0.007
	Per unit	120/9,087	1.748 (1.148–2.661)	0.009
	Per IQR	120/9,087	1.156 (1.036–1.289)	0.009
Neurological mortality	Q1	23/2,274	1.000 (ref)	
	Q2	25/2,272	1.290 (0.723–2.302)	0.388
	Q3	30/2,270	1.540 (0.863–2.748)	0.144
	Q4	42/2,271	2.306 (1.337–3.975)	0.003
	Per unit	1,034/9,087	1.190 (1.003–1.410)	0.046
	Per IQR	1,034/9,087	1.046 (1.001–1.093)	0.046
	Q1	239/2,274	1.000 (ref)	
	Q2	244/2,272	1.056 (0.880–1.267)	0.558
Cardiovascular mortality	Q3	269/2,270	1.116 (0.927–1.342)	0.246
	Q4	282/2,271	1.122 (0.931–1.351)	0.228
	Per unit	233/9,087	0.787 (0.518–1.196)	0.261
	Per IQR	233/9,087	0.940 (0.843–1.047)	0.261
	Q1	44/2,274	1.000 (ref)	
	Q2	64/2,272	1.393 (0.942–2.061)	0.097
	Q3	70/2,270	1.315 (0.884–1.957)	0.177
	Q4	55/2,271	0.942 (0.612–1.451)	0.787
Respiratory mortality	Per unit	246/9,087	1.095 (0.732–1.640)	0.659
	Per IQR	246/9,087	1.024 (0.922–1.137)	0.659
Cancer mortality	Per unit	246/9,087	1.095 (0.732–1.640)	0.659
	Per IQR	246/9,087	1.024 (0.922–1.137)	0.659

	Q1	60/2,274	1.000 (ref)	
	Q2	73/2,272	1.138 (0.802–1.614)	0.469
	Q3	60/2,270	0.940 (0.644–1.371)	0.747
	Q4	53/2,271	0.895 (0.598–1.340)	0.590
	Per unit	397/9,087	1.377 (1.078–1.758)	0.010
	Per IQR	397/9,087	1.086 (1.020–1.157)	0.010
Other causes of mortality	Q1	85/2,274	1.000 (ref)	
	Q2	85/2,272	1.009 (0.742–1.370)	0.956
	Q3	97/2,270	1.043 (0.767–1.418)	0.788
	Q4	130/2,271	1.369 (1.016–1.844)	0.039

Supplementary Table S9 Results of the association between urinary cobalt and all-cause and cause-specific mortality at different categories of urinary cobalt concentration variation (adjusted for urinary creatinine by dividing metal concentration by urinary creatinine concentration)

Outcome	Unit	Events/Total	HR (95%CI)	P -value
	Per unit	2,729/9,727	1.039 (1.009–1.069)	0.010
	Per IQR	2,729/9,727	1.012 (1.003–1.022)	0.010
All-cause mortality	Q1	2,966/2,432	1.000 (ref)	
	Q2	3,033/2,432	1.023 (0.910–1.150)	0.703
	Q3	3,115/2,432	1.040 (0.927–1.167)	0.505
	Q4	3,342/2,431	1.269 (1.134–1.421)	0.001
	Per unit	164/9,727	1.050 (0.932–1.183)	0.425
	Per IQR	164/9,727	1.016 (0.977–1.056)	0.425
Neurological mortality	Q1	10/2,432	1.000 (ref)	
	Q2	24/2,432	1.965 (0.936–4.126)	0.074
	Q3	45/2,432	2.760 (1.382–5.514)	0.004
	Q4	85/2,431	4.401 (2.243–8.636)	0.001
	Per unit	1,326/9,727	1.048 (1.007–1.091)	0.023
	Per IQR	1,326/9,727	1.015 (1.002–1.029)	0.023
Cardiovascular mortality	Q1	268/2,432	1.000 (ref)	
	Q2	284/2,432	0.956 (0.808–1.131)	0.598
	Q3	333/2,432	0.998 (0.847–1.175)	0.979
	Q4	441/2,431	1.207 (1.028–1.417)	0.022
	Per unit	311/9,727	1.029 (0.944–1.122)	0.517
Respiratory mortality	Per IQR	311/9,727	1.009 (0.982–1.038)	0.517
	Q1	62/2,432	1.000 (ref)	
	Q2	74/2,432	1.092 (0.777–1.533)	0.612

Cancer mortality	Q3	86/2,432	1.167 (0.837–1.628)	0.362
	Q4	89/2,431	1.081 (0.767–1.521)	0.657
	Per unit	293/9,727	0.855 (0.692–1.056)	0.146
	Per IQR	293/9,727	0.951 (0.888–1.018)	0.146
	Q1	90/2,432	1.000 (ref)	
	Q2	78/2,432	0.882 (0.649–1.198)	0.421
	Q3	61/2,432	0.719 (0.516–1.001)	0.051
	Q4	64/2,431	0.911 (0.647–1.284)	0.595
	Per unit	517/9,727	1.029 (0.964–1.099)	0.385
	Per IQR	517/9,727	1.009 (0.988–1.031)	0.385
Other causes of mortality	Q1	92/2,432	1.000 (ref)	
	Q2	115/2,432	1.114 (0.845–1.468)	0.443
	Q3	132/2,432	1.100 (0.839–1.443)	0.489
	Q4	178/2,431	1.315 (1.008–1.716)	0.043

Supplementary Table S10 Association between urinary cobalt and cardiovascular mortality (ICD: I00–I09, I11, I13, I20–I51, I60–I69) and lung cancer mortality (ICD: C34) across different urinary cobalt concentration ranges

Outcome	Unit	Events/Total	HR (95%CI)	P -value
Lung cancer mortality	Per unit	82/9,727	1.053 (0.520–2.133)	0.886
	Per IQR	82/9,727	1.014 (0.839–1.225)	0.886
	Q1	18/2,552	1.000 (ref)	
	Q2	20/2,345	1.151 (0.601–2.206)	0.671
	Q3	25/2,403	1.474 (0.775–2.805)	0.237
	Q4	19/2,427	1.165 (0.580–2.340)	0.667
	Per unit	1,183/9,727	1.279 (1.103–1.483)	0.001
	Per IQR	1,183/9,727	1.068 (1.027–1.111)	0.001
New cardiovascular mortality	Q1	278/2,552	1.000 (ref)	
	Q2	257/2,345	1.070 (0.900–1.272)	0.444
	Q3	298/2,403	1.169 (0.984–1.389)	0.076
	Q4	350/2,427	1.249 (1.055–1.479)	0.010

Supplementary Table S11 Results of the association between urinary cobalt and all-cause and cause-specific mortality at different categories of urinary cobalt concentration variation (excluding participants with pre-existing cardiovascular, neurological, cancer, and respiratory diseases)

Outcome	Unit	Events/Total	HR (95%CI)	P -value
Total mortality	Per IQR	2,046/7,846	1.057 (1.026–1.089)	0.000
	<i>Q1</i>	434/1,965	1.000 (ref)	
	<i>Q2</i>	472/1,958	1.096 (0.960–1.251)	0.176
	<i>Q3</i>	524/1,983	1.123 (0.982–1.284)	0.090
	<i>Q4</i>	616/1,940	1.263 (1.107–1.442)	0.001
	<i>P for trend</i>		< 0.001	
Neurological mortality	Per IQR	132/7,846	1.141 (1.027–1.268)	0.014
	<i>Q1</i>	23/1,965	1.000 (ref)	
	<i>Q2</i>	27/1,958	1.277 (0.726–2.247)	0.396
	<i>Q3</i>	29/1,983	1.370 (0.771–2.434)	0.283
	<i>Q4</i>	53/1,940	2.334 (1.393–3.910)	0.001
	<i>P for trend</i>		0.001	
Cardiovascular mortality	Per IQR	962/7,846	1.063 (1.018–1.110)	0.006
	<i>Q1</i>	209/1,965	1.000 (ref)	
	<i>Q2</i>	222/1,958	1.095 (0.904–1.328)	0.353
	<i>Q3</i>	251/1,983	1.163 (0.958–1.412)	0.127
	<i>Q4</i>	280/1,940	1.221 (1.007–1.480)	0.042
	<i>P for trend</i>		0.038	
Cancer mortality	Per IQR	223/7,846	1.070 (0.969–1.181)	0.184
	<i>Q1</i>	52/1,965	1.000 (ref)	
	<i>Q2</i>	64/1,958	1.128 (0.776–1.638)	0.529
	<i>Q3</i>	53/1,983	0.912 (0.610–1.365)	0.654
	<i>Q4</i>	54/1,940	1.039 (0.685–1.575)	0.857
	<i>P for trend</i>		0.879	
Respiratory mortality	Per IQR	221/7,846	0.951 (0.854–1.059)	0.358
	<i>Q1</i>	44/1,965	1.000 (ref)	
	<i>Q2</i>	56/1,958	1.238 (0.828–1.850)	0.298
	<i>Q3</i>	59/1,983	1.064 (0.704–1.608)	0.770
	<i>Q4</i>	62/1,940	1.048 (0.689–1.593)	0.828
	<i>P for trend</i>		0.93	
Other causes of mortality	Per IQR	420/7,846	1.058 (0.993–1.128)	0.082
	<i>Q1</i>	94/1,965	1.000 (ref)	
	<i>Q2</i>	85/1,958	0.915 (0.679–1.233)	0.559
	<i>Q3</i>	106/1,983	1.016 (0.758–1.362)	0.916

<i>Q4</i>	135/1,940	1.247 (0.937–1.658)	0.130
<i>P for trend</i>		0.075	

Supplementary Table S12 Results of the association between urinary cobalt and all-cause and cause-specific mortality at different categories of urinary cobalt concentration variation (included respiratory drug use condition)

Outcome	Unit	Events/Totals	HR (95%CI)	<i>P</i> -value
Total mortality	Per IQR	2,745/9,727	1.060 (1.033–1.089)	< 0.001
	<i>Q1</i>	622/2,552	1.000 (ref)	
	<i>Q2</i>	618/2,345	1.120 (1.000–1.254)	0.050
	<i>Q3</i>	691/2,403	1.179 (1.052–1.321)	0.005
	<i>Q4</i>	814/2,427	1.293 (1.156–1.446)	0.000
	<i>P for trend</i>		< 0.001	
	Per IQR	162/9,727	1.142 (1.036–1.260)	0.008
Neurological mortality	<i>Q1</i>	31/2,552	1.000 (ref)	
	<i>Q2</i>	33/2,345	1.390 (0.844–2.289)	0.196
	<i>Q3</i>	39/2,403	1.671 (1.017–2.746)	0.043
	<i>Q4</i>	59/2427	2.368 (1.496–3.749)	0.000
	<i>P for trend</i>		< 0.001	
	Per IQR	1,341/9,727	1.064 (1.025–1.105)	0.001
Cardiovascular mortality	<i>Q1</i>	316/2,552	1.000 (ref)	
	<i>Q2</i>	300/2,345	1.096 (0.933–1.288)	0.262
	<i>Q3</i>	336/2,403	1.169 (0.995–1.375)	0.058
	<i>Q4</i>	389/2,427	1.249 (1.065–1.464)	0.006
	<i>P for trend</i>		0.004	
	Per IQR	294/9,727	1.045 (0.953–1.147)	0.348
Cancer mortality	<i>Q1</i>	81/2,552	1.000 (ref)	
	<i>Q2</i>	76/2,345	0.962 (0.699–1.324)	0.811
	<i>Q3</i>	67/2,403	0.828 (0.589–1.165)	0.280
	<i>Q4</i>	70/2,427	0.909 (0.640–1.290)	0.593
	<i>P for trend</i>		0.585	
	Per IQR	311/9,727	0.990 (0.908–1.079)	0.818
Respiratory mortality	<i>Q1</i>	55/2,552	1.000 (ref)	
	<i>Q2</i>	82/2,345	1.617 (1.142–2.288)	0.007
	<i>Q3</i>	88/2,403	1.550 (1.089–2.206)	0.015
	<i>Q4</i>	86/2,427	1.346 (0.936–1.935)	0.109

	<i>P for trend</i>		0.261	
	Per IQR	523/9,727	1.063 (1.002–1.127)	0.042
	<i>Q1</i>	125/2,552	1.000 (ref)	
Other causes of mortality	<i>Q2</i>	107/2,345	0.951 (0.731–1.237)	0.709
	<i>Q3</i>	127/2,403	1.023 (0.789–1.327)	0.863
	<i>Q4</i>	164/2,427	1.252 (0.973–1.610)	0.081
	<i>P for trend</i>		0.038	
