

Supplementary Materials

Table S1. Measured and standard concentrations of the certified reference materials.

THMs	Measured Value ^a (ng/mL)	Standard Value ^b (ng/mL)	Reference Type	Coincidence (%)
Cr	6.76 ± 0.13	6.99 (5.24–8.74)	Serum ^c	96.76
Cd	4.95 ± 0.09	4.92 (3.94–5.90)	Serum ^c	100.59
Pb	3.68 ± 0.03	3.83 ± 0.18	Hair ^d	101.03
As	19.90 ± 0.55	19.70 (15.80–23.60)	Serum ^c	95.98

^a The measured value is the mean and standard deviation for three repeated measurements. ^b Standard values are provided by the company. ^c ClinChek® Serum Controls (trace elements level II, REF 8881, EVISA). ^d Human Hair Certified Reference Material (GBW09101b, China).

Table S2. Limit and precision of detection for four toxic heavy metals (THMs).

THMs	Instrument Detection Limit (ng/mL)	Dilutio n Factor	Method Detection Limit (ng/mL)	Repeatability Rel. Repeat. SD [#]	Reproducibility Rel. Repro. SD [*]
Cr	0.002	20	0.04	1.86%	2.38%
Cd	0.003	20	0.06	1.88%	2.32%
Pb	0.010	20	0.20	0.89%	2.24%
As	0.016	20	0.32	2.77%	3.70%

[#] Relative repeatability standard deviation: calculated by extracting 3 measurements from same day. ^{*} Relative reproducibility standard deviation: calculated by extracting 3 measurements from 3 different days.

Table S3. Main characteristics of included studies in the meta-analysis.

No.	Author ^a	Drug ^b	Published year	Area	Geographic area	Sample type	Sample size		THMs	NOS score
							Case	control		
[1]	Guo et al.	1	2013	China	Asia	serum	119	126	Cr, Cd, Pb, As	9
[2]	Arinola et al._1	0	2010	Nigeria	Africa	plasma	15	20	Cr, Cd, Pb	7
	Arinola et al._2	1	2010	Nigeria	Africa	plasma	20	20	Cr, Cd, Pb	7
[3]	Cai et al._1	0	2015	China	Asia	serum	61	61	Cr, Cd, Pb, As	8
	Cai et al._2	0	2015	China	Asia	serum	50	49	Cr, Cd, Pb, As	8
[4]	Li et al.	1	2018	China	Asia	serum	158	669	Cr, As	8

[5]	P.C. Stanley et al._1	0	2002	Nigeria	Africa	serum	20	20	Cd, Pb	6
	P.C. Stanley et al._2	1	2002	Nigeria	Africa	serum	20	20	Cd, Pb	6
	P.C. Stanley et al._3	1	2002	Nigeria	Africa	serum	20	20	Cd, Pb	6
[6]	Present study	0	-	China	Asia	serum	95	95	Cr, Cd, Pb, As	9

^a Arinola et al._1 The schizophrenic patients were newly diagnosed and not taking antipsychotic drugs. Arinola et al._2 The schizophrenic patients had used antipsychotic drugs for at least 2 weeks. Cai et al._1 The case and control were from a training set. Cai et al._2 The case and control were from a test set. P.C. Stanley et al._1 The schizophrenic patients before the start of treatment. P.C. Stanley et al._2 The schizophrenic patients at 3 weeks after treatment. P.C. Stanley et al._3 The schizophrenic patients at 7 weeks after treatment. ^b 0: patients with schizophrenia were not treated with antipsychotic drugs. 1: patients with schizophrenia were treated with antipsychotic drugs.

Table S4. Results of meta-analysis of 4 THMs.

THMs	Groups	No. of studies	Sample size		Test of association		Test of heterogeneity	
			Case	Control	SMD	95%CI	I ²	p
	Overall	5	518	1020	0.3246	0.0166–0.6326	83.0%	<0.01
Cr	Drug = 0	3	211	225	0.3134	-0.2770–0.9038	88.2%	0.7640
	Drug = 1	3	297	815	0.4063	0.2662–0.5464	0.0%	
Cd	Overall	6	538	1040	-0.0357	-0.4812–0.4098	92.6%	<0.01
	Drug = 0	4	241	245	0.2796	-0.2488–0.8079	86.2%	0.0978
	Drug = 1	4	317	835	-0.3763	-0.9452–0.1927	91.1%	
Pb	Overall	6	538	1040	0.2537	-0.2108–0.7183	93.5%	<0.01
	Drug = 0	4	241	245	0.4064	0.1371–0.6757	47.9%	0.3337
	Drug = 1	4	317	835	0.0240	-0.7033–0.7512	95.0%	
As	Overall	4	483	1000	0.4459	-1.1994–2.0912	99.4%	<0.01
	Drug = 0	2	206	205	-0.1397	-0.3889–0.1095	99.8%	0.4560
	Drug = 1	2	277	795	1.2972	-2.4727–5.0672	37.4%	

Reference

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- Cai, L., T.; Chen, J.; Yang, K.; Zhou, X.; Yan, W.; Chen, L.; Sun, L.; Li, S.; Qin, P.; Wang, et al. Serum trace element differences between Schizophrenia patients and controls in the Han Chinese population. *Sci Rep.* **2015**, *5*, 15013.
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5. Stanley, P.C.; V.C. Wakwe. Toxic trace metals in the mentally ill patients. *Niger Postgrad Med J.* 2002. 9, 199–204.

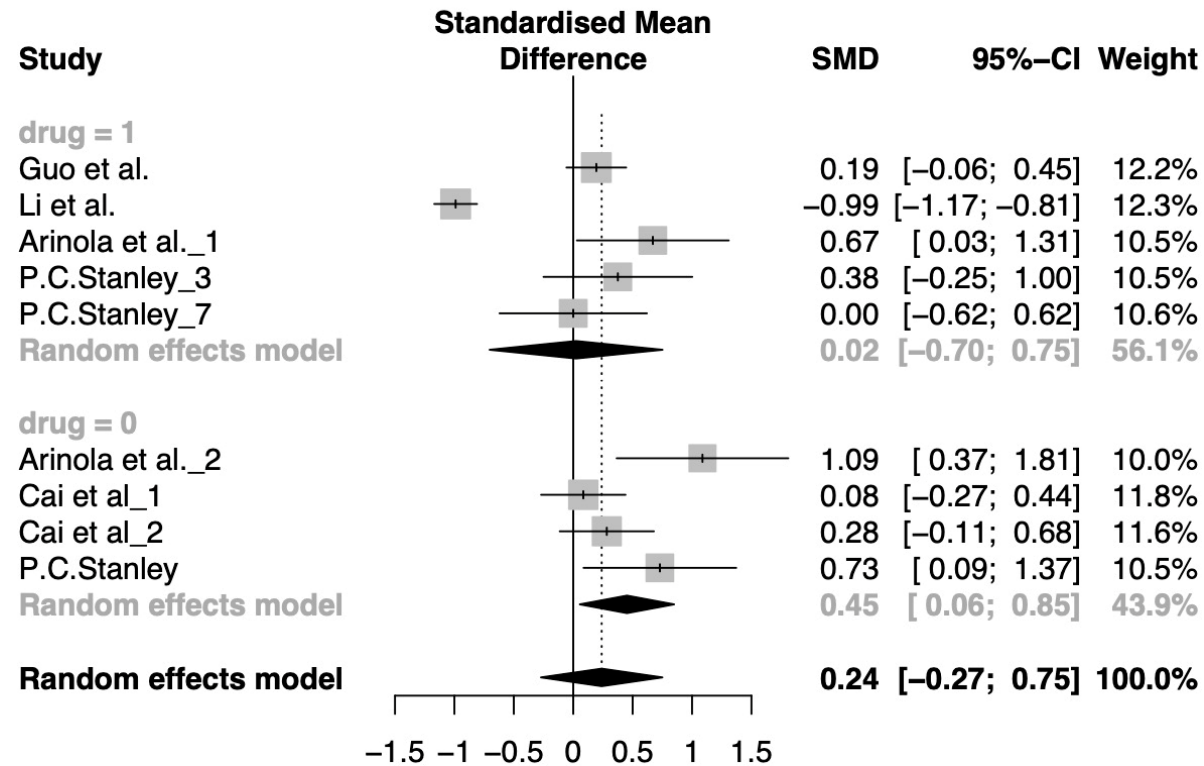
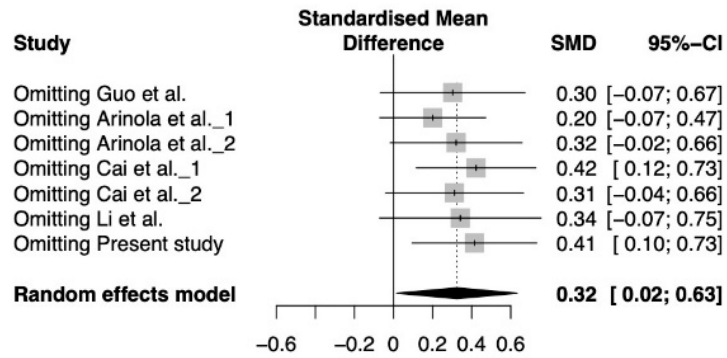
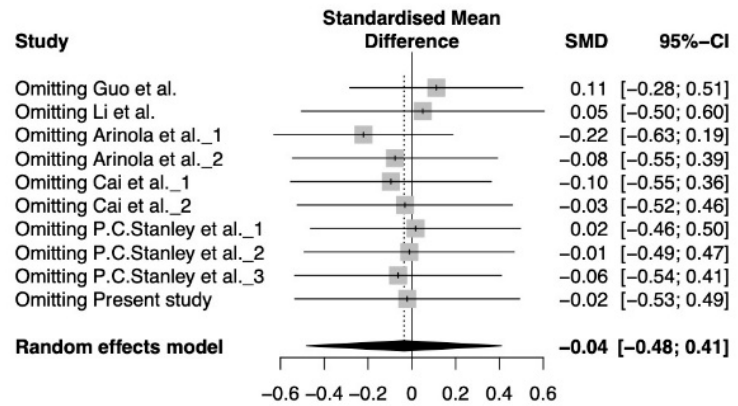


Figure S1. Forest plot of subgroup analysis stratified by whether the patients with schizophrenia treated with antipsychotic drugs (without present study). Overall pooled prevalence was calculated by random-effects module. Horizontal bars show 95% CIs. drug = 1, patients with schizophrenia were treated with antipsychotic drugs. drug = 0, patients with schizophrenia were not treated with antipsychotic drugs.

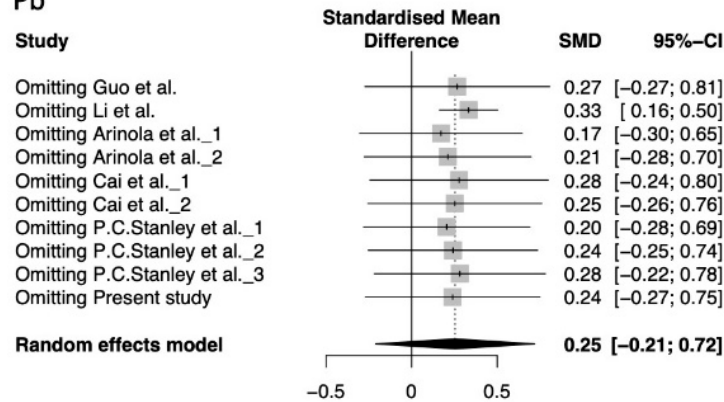
Cr



Cd



Pb



As

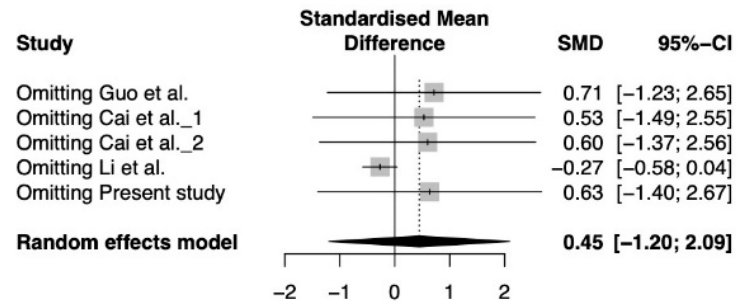


Figure S2. Sensitivity analysis through deletion of one study at a time to reflect the influence of the individual dataset to the pooled SMDs of the THM concentrations in patients with schizophrenia and healthy controls.