

Supplementary Tables

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Table S1 Distribution of urinary TCS and TCC concentrations (ng/mL) in participants.

pollutants	DF (%)	Percentile				
		5th	25th	50th	75th	95th
TCS	59.46	<LOD	<LOD	0.056	0.236	2.060
TCC	21.07	<LOD	<LOD	<LOD	<LOD	0.107

Abbreviation: DF, detection frequency; deviation; LOD, limits of detection; TCS, triclosan; TCC, triclocarban.

Table S2 Association of triclosan and triclocarban exposure with type 2 diabetes mellitus/gestational diabetes mellitus reported for different populations.

Population	Sample size	TCS&T2DM/GDM	TCC&T2DM/GDM	Reference
Henan Rural Cohort Study	956	↑	—	This study
NHANES 2013-2014	900	—	↑(women)	Xie et al. (2020)
SWAN Multi-Pollutant Study (MPS)	1299	—	/	Li et al. (2021)
NHANES 2005-2014	8498	↓	/	Ward et al. (2020)
Cambridge Baby Growth Study (CBGS)	232	↓*	/	Fisher et al. (2018)
Pregnancy Environment and Lifestyle Study (PETALS)	111	↑*	/	Zhu et al. (2022)
Shanghai Birth Cohort Study	620	↑*	/	Ouyang et al. (2018)

Abbreviation: TCS, triclosan; TCC, triclocarban; T2DM, type 2 diabetes mellitus; GDM, gestational diabetes mellitus.

↑: positive association; ↓: negative association; —: no association; /: not studied; *: TCS&GDM.

Table S3 CpG sites and *OR* (95%CI) for T2DM in univariate logistic regression model.

CpG site	Position	Distance2TSS	<i>OR</i> (95%CI)	<i>P</i> -value
Chr17:76355136	31	1024	1.004(0.970,1.038)	0.835
Chr17:76355146	41	1014	1.076(0.935,1.239)	0.306
Chr17:76355149	44	1011	1.039(0.942,1.146)	0.442
Chr17:76355152	47	1008	1.001(0.922,1.087)	0.985
Chr17:76355179	74	981	1.004(0.949,1.061)	0.898
Chr17:76355183	78	977	1.116(0.930,1.339)	0.238
Chr17:76355192	87	968	1.367(1.071,1.745)	0.012
Chr17:76355202	97	958	0.925(0.734,1.166)	0.508
Chr17:76355204	99	956	1.213(0.933,1.578)	0.148
Chr17:76355207	102	953	1.105(0.943,1.295)	0.218
Chr17:76355210	105	950	0.982(0.807,1.194)	0.853
Chr17:76355225	120	935	1.026(0.809,1.302)	0.831
Chr17:76355227	122	933	1.067(0.836,1.360)	0.603
Chr17:76355234	129	926	1.000(0.833,1.200)	0.998
Chr17:76355241	136	919	1.045(0.784,1.393)	0.764
Chr17:76355245	140	915	1.187(0.974,1.446)	0.090
Chr17:76355251	146	909	1.243(0.978,1.580)	0.075
Chr17:76355258	153	902	1.087(0.868,1.361)	0.468
Chr17:76355268	163	892	0.954(0.782,1.164)	0.643
Chr17:76355280	175	880	0.901(0.745,1.089)	0.279
Chr17:76355282	177	878	0.731(0.568,0.941)	0.015
Chr17:76355286	181	874	0.833(0.659,1.053)	0.126
Chr17:76355288	183	872	0.997(0.772,1.287)	0.979
Chr17:76355299	194	861	0.982(0.784,1.230)	0.874
Chr17:76355312	207	848	0.912(0.694,1.198)	0.506
Chr17:76355314	209	846	0.953(0.730,1.244)	0.724
Chr17:76355318	213	842	1.238(0.933,1.641)	0.138
Chr17:76355323	218	837	1.100(0.933,1.297)	0.258
Chr17:76355328	223	832	0.942(0.681,1.303)	0.718
Chr17:76355343	238	817	1.096(0.833,1.441)	0.513
Chr17:76355346	241	814	1.021(0.794,1.314)	0.870
Chr17:76355350	245	810	1.396(1.004,1.941)	0.047
Chr17:76356054	23	106	0.998(0.780,1.276)	0.985
Chr17:76356056	25	104	1.264(0.872,1.831)	0.216
Chr17:76356067	36	93	1.186(0.960,1.466)	0.114
Chr17:76356069	38	91	1.180(0.860,1.620)	0.305
Chr17:76356072	41	88	1.216(0.851,1.738)	0.282
Chr17:76356084	53	76	1.013(0.863,1.189)	0.876
Chr17:76356088	57	72	1.177(0.816,1.700)	0.383
Chr17:76356092	61	68	1.162(0.807,1.675)	0.420
Chr17:76356099	68	61	0.990(0.667,1.468)	0.959
Chr17:76356109	78	51	1.042(0.744,1.459)	0.811

Chr17:76356113	82	47	1.028(0.698,1.515)	0.889
Chr17:76356119	88	41	1.421(1.035,1.952)	0.030
Chr17:76356124	93	36	1.227(0.886,1.699)	0.219
Chr17:76356133	102	27	0.934(0.636,1.372)	0.727
Chr17:76356152	121	8	1.179(0.813,1.711)	0.385
Chr17:76356158	127	2	1.194(0.839,1.699)	0.325
Chr17:76356161	130	-1	1.289(0.959,1.733)	0.093
Chr17:76356163	132	-3	1.057(0.738,1.514)	0.762
Chr17:76356170	139	-10	0.957(0.728,1.259)	0.755
Chr17:76356172	141	-12	1.012(0.687,1.491)	0.952
Chr17:76356176	145	-16	1.537(1.125,2.101)	0.007
Chr17:76356178	147	-18	1.088(0.822,1.441)	0.555
Chr17:76356190	159	-30	0.521(0.412,0.660)	<0.001
Chr17:76356194	163	-34	0.911(0.688,1.206)	0.513
Chr17:76356197	166	-37	0.867(0.640,1.174)	0.356
Chr17:76356199	168	-39	0.435(0.305,0.622)	<0.001
Chr17:76356204	173	-44	1.337(0.913,1.960)	0.136
Chr17:76356211	180	-51	1.214(0.908,1.623)	0.190
Chr17:76356226	195	-66	0.813(0.579,1.143)	0.234
Chr17:76356228	197	-68	0.941(0.681,1.302)	0.715
Chr17:76356232	201	-72	0.893(0.628,1.269)	0.527
Chr17:76354927	27	1233	0.999(0.985,1.014)	0.943
Chr17:76354934	34	1226	1.005(0.992,1.018)	0.473
Chr17:76354947	47	1213	1.002(0.989,1.014)	0.778
Chr17:76354955	55	1205	1.003(0.991,1.016)	0.614
Chr17:76354963	63	1197	0.998(0.983,1.013)	0.785
Chr17:76354965	65	1195	1.001(0.987,1.016)	0.866
Chr17:76354981	81	1179	0.990(0.964,1.017)	0.480
Chr17:76354984	84	1176	1.001(0.987,1.015)	0.862
Chr17:76354990	90	1170	0.998(0.972,1.025)	0.874
Chr17:76355009	109	1151	1.000(0.986,1.013)	0.969
Chr17:76355014	114	1146	1.003(0.990,1.015)	0.692
Chr17:76355017	117	1143	0.999(0.984,1.015)	0.906
Chr17:76355020	120	1140	1.000(0.985,1.015)	0.996
Chr17:76355029	129	1131	1.000(0.985,1.015)	0.990
Chr17:76355044	144	1116	1.000(0.987,1.013)	0.981
Chr17:76355061	161	1099	1.001(0.990,1.013)	0.812
Chr17:76355068	168	1092	0.998(0.986,1.011)	0.811
Chr17:76355089	189	1071	0.999(0.987,1.012)	0.918
Chr17:76355115	215	1045	0.998(0.985,1.010)	0.711
Chr17:76354582	44	1578	1.025(1.002,1.048)	0.032
Chr17:76354588	50	1572	1.018(0.989,1.047)	0.220
Chr17:76354596	58	1564	1.048(1.007,1.092)	0.021
Chr17:76354621	83	1539	1.000(0.982,1.018)	0.992

Chr17:76354638	100	1522	1.022(0.995,1.049)	0.111
Chr17:76354663	125	1497	1.013(0.985,1.041)	0.364
Chr17:76354669	131	1491	0.998(0.977,1.020)	0.869
Chr17:76354724	186	1436	1.002(0.984,1.021)	0.839
Chr17:7635732	194	1428	1.013(0.990,1.036)	0.277
Chr17:76354741	203	1419	1.007(0.992,1.024)	0.356
Chr17:76354763	225	1397	1.001(0.982,1.019)	0.944

Each tested CpG site was named as its genomic position.

Chr: The chromosome on which the fragment is located; Genomic Position: The position of the fragment on the reference genome; Position: The position of the CpG site on the target genomic region; Distance to TSS: The distance of the site on the reference genome relative to the transcription start site (TSS), and the minus sign indicates that the site is upstream of the TSS.

Abbreviations: CI, confidence interval; OR, odds ratio; T2DM, type 2 diabetes mellitus.

$P < 0.05$ /93 is considered as statistically significant with two-tailed test.

Table S4 Genomic region and *OR* (95%CI) for T2DM in univariate logistic regression model.

Genomic region	Length	Distance to TSS	<i>OR</i> (95%CI)
Chr17:76355106_Chr17:76355374	269	786	1.083(0.769,1.524)
Chr17:76356032_Chr17:76356279	248	-119	1.117(0.499,2.500)
Chr17:76354901_Chr17:76355135	235	1025	0.999(0.984,1.014)
Chr17:76354539_Chr17: 76354788	250	1372	1.014(0.983,1.047)

Genomic region: Genomic region was named as the start site to the end site on the chromosome.

Length: The product's size (bp); Distance to TSS: The distance of the site on the reference genome relative to the transcription start site (TSS), and the minus sign indicates that the site is upstream of the TSS.

Abbreviations: T2DM, type 2 diabetes mellitus.

P < 0.05/4 is considered as statistically significant with two-tailed test.

Table S5 Association between Ln-TCScrea and methylation level of Chr17:76356190 or Chr17:76356199.

SOCS-3 DNA methylation	β (95%CI)		
	model 1	model 2	model 3
Methylation of Chr17:76356190	-0.027(-0.043,-0.012)	-0.026(-0.042,-0.010)	-0.025(-0.040,-0.009)
Methylation of Chr17:76356199	-0.010(-0.020,0.000)	-0.010(-0.019,0.000)	-0.009(-0.019,0.001)

Abbreviation: TCS, triclosan.

model 1: crude model.

model 2: adjusted age, gender, educational level, marital status, average monthly income, smoking status, alcohol status, physical activity, high-fat diet, vegetable and fruit intake, and family history of T2DM.

model 3: model 2 +BMI, PP, TC, TG.

Table S6 Mediation analysis of the association of Ln-TCScrea with T2DM and glucose metabolism-related indicators by methylation level of Chr17:76356190 or Chr17:76356199.

Mediator	Total effect	Indirect effect	Direct effect	PE
Methylation of Chr17:76356190				
T2DM	0.124(0.060,0.188)	0.018(0.006,0.038)	0.109(0.044,0.175)	14.54%
FBG	0.135(0.072,0.197)	0.012(0.004,0.024)	0.123(0.061,0.185)	8.83%
INS	0.157(0.011,0.303)	0.012(-0.001,0.034)	0.146(-0.001,0.292)	/
HbA1c	0.067(0.028,0.106)	0.003(0.000,0.009)	0.064(0.025,0.103)	/
Ln-HOMA2- β	-0.023(-0.038,-0.008)	-0.002(-0.005,-0.001)	-0.021(-0.035,-0.006)	10.00%
Ln-HOMA2-IR	0.015(0.004,0.025)	0.002(0.001,0.004)	0.013(0.002,0.023)	11.67%
Methylation of Chr17:76356199				
T2DM	0.124(0.060,0.188)	0.009(0.000,0.023)	0.118(0.053,0.184)	/
FBG	0.135(0.072,0.197)	0.003(-0.000,0.012)	0.132(0.069,0.194)	/
INS	0.157(0.011,0.303)	0.005(-0.003,0.022)	0.152(0.006,0.298)	/
HbA1c	0.067(0.028,0.106)	0.002(-0.000,0.006)	0.065(0.026,0.105)	/
Ln-HOMA2- β	-0.023(-0.038,-0.008)	-0.001(-0.003,0.000)	-0.022(-0.037,-0.007)	/
Ln-HOMA2-IR	0.015(0.004,0.025)	0.001(0.000,0.002)	0.014(0.003,0.025)	/

Abbreviation: TCS, triclosan; T2DM, type 2 diabetes mellitus; FBG, fasting blood glucose; INS, insulin; HbA1c, glycosylated hemoglobin A1c; HOMA2- β , homeostasis model assessment 2 of β cell function; HOMA2-IR, homeostasis model assessment 2 of insulin resistance.

PE* = indirect effect / total effect.

adjusted age, gender, educational level, marital status, average monthly income, smoking status, alcohol status, physical activity, high-fat diet, vegetable and fruit intake, family history of T2DM, BMI, PP, TC, and TG.

Table S7 The results of subgroup analysis.

characteristics	<i>OR (95%CI)</i>	<i>P</i> -interaction
	T2DM	
Age, years		0.858
<55	1.151(1.015,1.305)	
55-65	1.107(1.004,1.221)	
>65	1.165(1.015,1.337)	
Gender		0.109
men	1.198(1.082,1.326)	
women	1.091(1.003,1.188)	
Educational level		0.877
never attended school	1.157(0.998,1.342)	
primary school	1.127(1.001,1.269)	
junior secondary and above	1.148(1.039,1.269)	
Average monthly income		0.884
CNY <500	1.129(1.022,1.248)	
CNY 500~	1.137(1.010,1.282)	
CNY 1000~	1.160(1.016,1.323)	
Physical activity		0.901
low	1.145(1.005,1.305)	
moderate	1.156(1.042,1.283)	
high	1.118(0.998,1.253)	
Smoking status		0.344
current smoker	1.257(1.061,1.490)	
never/past-smoker	1.121(1.044,1.204)	
Alcohol status		0.720
current drinker	1.153(0.968,1.373)	
never/past-drinker	1.138(1.060,1.221)	
BMI		0.482
<18.5	/	
18.5-23.9	1.186(1.073,1.311)	
>23.9	1.093(1.007,1.185)	

Abbreviation: TCS, triclosan; T2DM, type 2 diabetes mellitus.

Table S8 Sensitivity analysis (excluding patients who had diabetes treatment in the last two weeks) (n=784).

Outcome	<i>OR/ β (95%CI)</i>		
	model 1	model 2	model 3
T2DM	1.072(0.999,1.151)	1.073(0.997,1.154)	1.069(0.983,1.163)
FBG	0.074(0.017,0.131)	0.073(0.016,0.129)	0.059(0.007,0.111)
INS	0.162(-0.004,0.329)	0.170(0.004,0.3636)	0.134(-0.022,0.290)
HbA1c	0.026(-0.008,0.060)	0.026(-0.008,0.061)	0.019(-0.013,0.050)
Ln-HOMA2-β	-0.012(-0.027,0.002)	-0.012(-0.026,0.003)	-0.010(-0.024,0.004)
Ln-HOMA2-IR	0.011(-0.001,0.024)	0.011(-0.001,0.024)	0.008(-0.004,0.020)

Abbreviation: TCS, triclosan; T2DM, type 2 diabetes mellitus; FBG, fasting blood glucose; INS, insulin; HbA1c, glycosylated hemoglobin A1c; HOMA2-β, homeostasis model assessment 2 of β cell function; HOMA2-IR, homeostasis model assessment 2 of insulin resistance.

model 1: crude model.

model 2: adjusted age, gender, educational level, marital status, average monthly income, smoking status, alcohol status, physical activity, high-fat diet, vegetable and fruit intake, and family history of T2DM.

model 3: model 2 +BMI, PP, TC, TG.

Table S9 Liquid chromatography gradient elution program

time (min)	0.00	0.50	1.00	3.00	5.00	8.00	8.10	10.00
A pure water (%)	65%	65%	40%	40%	0	0	65%	65%
B methanol (%)	35%	35%	60%	60%	100%	100%	35%	35%

Table S10 HPLC-MS/MS optimized parameters for TCS and TCC.

pollutants	Molecular weight	Retention time (min)	Parent ion (m/z)	Product ion (m/z)	Cone voltage (eV)	Collision energy (eV)
TCS	289.54	5.43	289.02	34.58	20	14
TCC	315.58	6.38	314.93	125.55	10	20

Abbreviation: TCS, triclosan; TCC, triclocarban.

Table S11 Spiked recoveries, coefficients of variation and detection limits of TCS and TCC.

pollutants	Recoveries (%)	Intra-day precision			Inter-day precision			LOD (ng/mL)	
		RSD (%)			RSD (%)				
		1	5	10	1	5	10		
TCS	126.70	11.13	8.18	7.85	15.42	13.64	12.04	0.0293	
TCC	–	15.82	13.64	11.13	15.40	14.72	11.60	0.0066	

Abbreviation: LOD, limits of detection; TCS, triclosan; TCC, triclocarban.