

Supplementary Material

Exposure to endocrine-disrupting chemicals, iron metabolism and risk of metabolic dysfunction-associated steatotic liver disease: A nationwide cross-sectional study in China

Zongyao Li, Yongbin Zhao, Zhenyu Wu, Huijun Wang, Yanzhen Hu, Xiaofan Zhang, Xi Kang, Chang Su, Tao Zhang, Aidong Liu

Table of Contents

Supplemental Figure 1. Spearman correlations among the concentrations of chemical exposure.

Supplemental Figure 2. The directed acyclic graph of the association between serum EDC and MASLD.

Supplemental Figure 3. Regression coefficients of population MASLD incidence rate and 22 EDCs concentrations in gender and age stratification analysis.

Supplemental Figure 4. The joint effects of key EDC mixtures on MASLD in the gender and age stratified population in BKMR models.

Supplemental Table 1. The concentration distribution of EDCs with a detection frequency >50%.

Supplemental Table 2. Participant characteristics of the male population, CHNS 2015.

Supplemental Table 3. Participant characteristics of the female population, CHNS 2015.

Supplemental Table 4. Participant characteristics of the elder population, CHNS 2015.

Supplemental Table 5. Participant characteristics of the young and middle age population, CHNS 2015.

Supplemental Table 6. Associations between mixed EDC exposure and MASLD in overall population by 10000 WQS models.

Supplemental Table 7. Association between EDCs and MASLD in CHNS 2015 male and female subgroups.

Supplemental Table 8. Association between EDCs and MASLD in CHNS 2015 the elderly and young and middle age subgroups.

Supplemental Table 9. Association between key EDCs and SF in the overall population, males, females, old age, and young and middle age subgroups.

Supplemental Table 10. Association between SF and MASLD in the overall population, males, females, old age, and young and middle age subgroups.

Supplemental Table 11. The interaction of Ln-transformed key EDCs and SF on MASLD risk in the overall population, males, females, old age, and young and middle age subgroups.

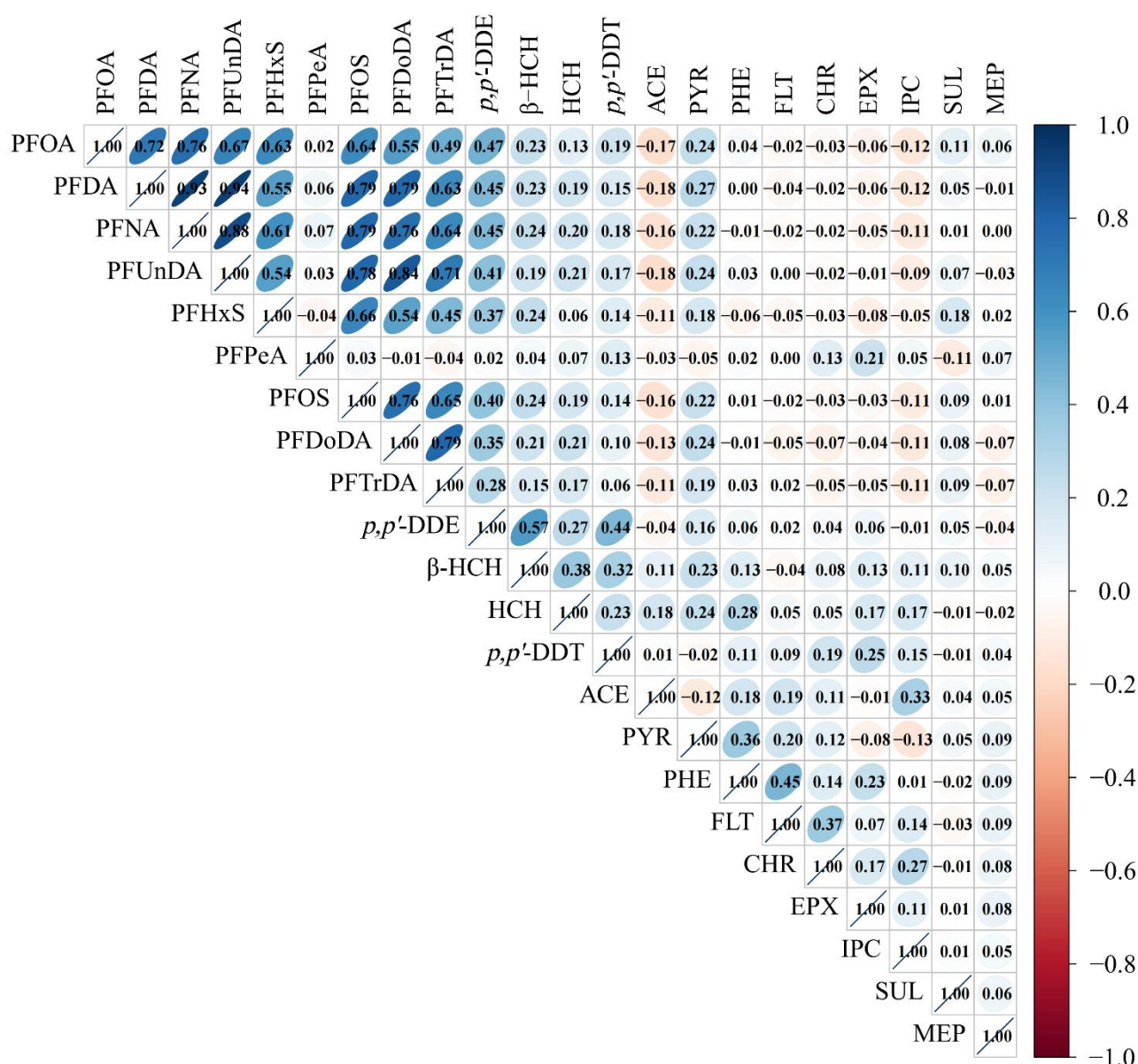
Supplemental Table 12. Mediating effects of SF on the associations between key EDCs and MASLD in different stratification.

Supplemental Table 13. Association between Ln-transformed EDCs in tertile and MASLD risk in overall population excluding all individuals with EDC concentrations above the 99th percentile.

Supplemental Table 14. Association between Ln-transformed EDCs in tertile and MASLD risk in overall population without multiple interpolation of covariates.

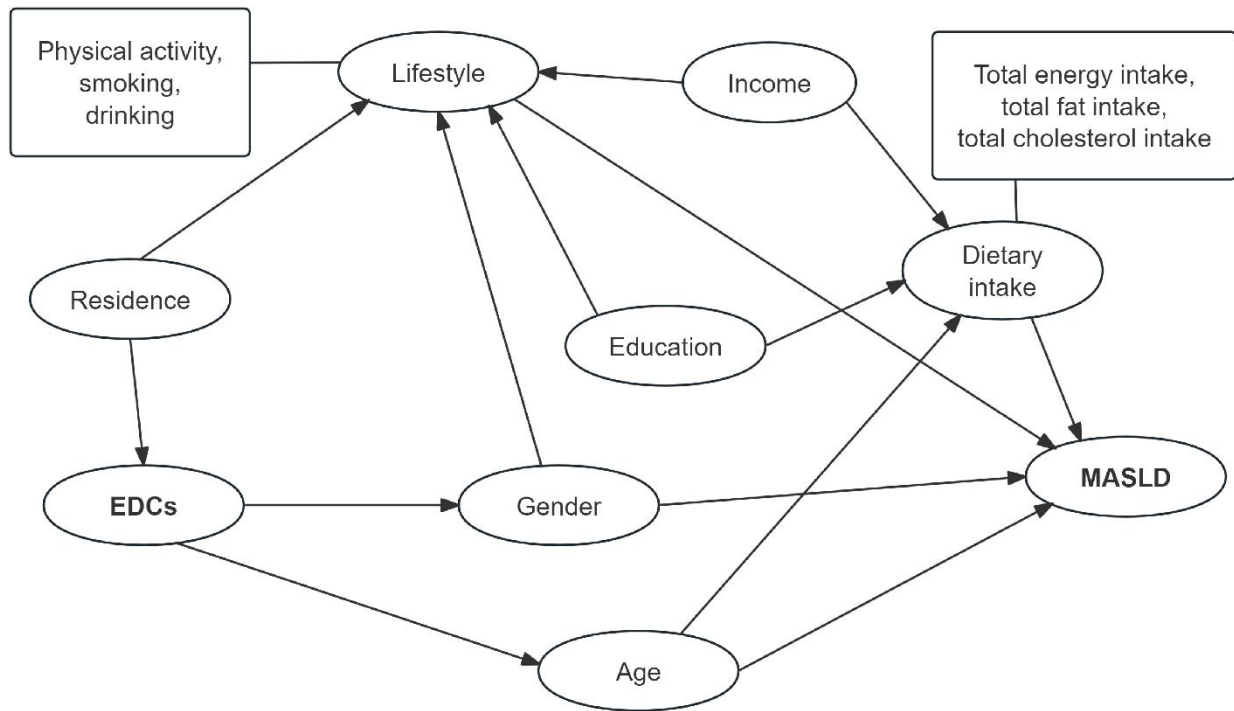
Supplemental Table 15. Association between mixtures of key EDCs and MASLD risk and the weight of each key EDCs in the QGC models.

Supplemental Figures



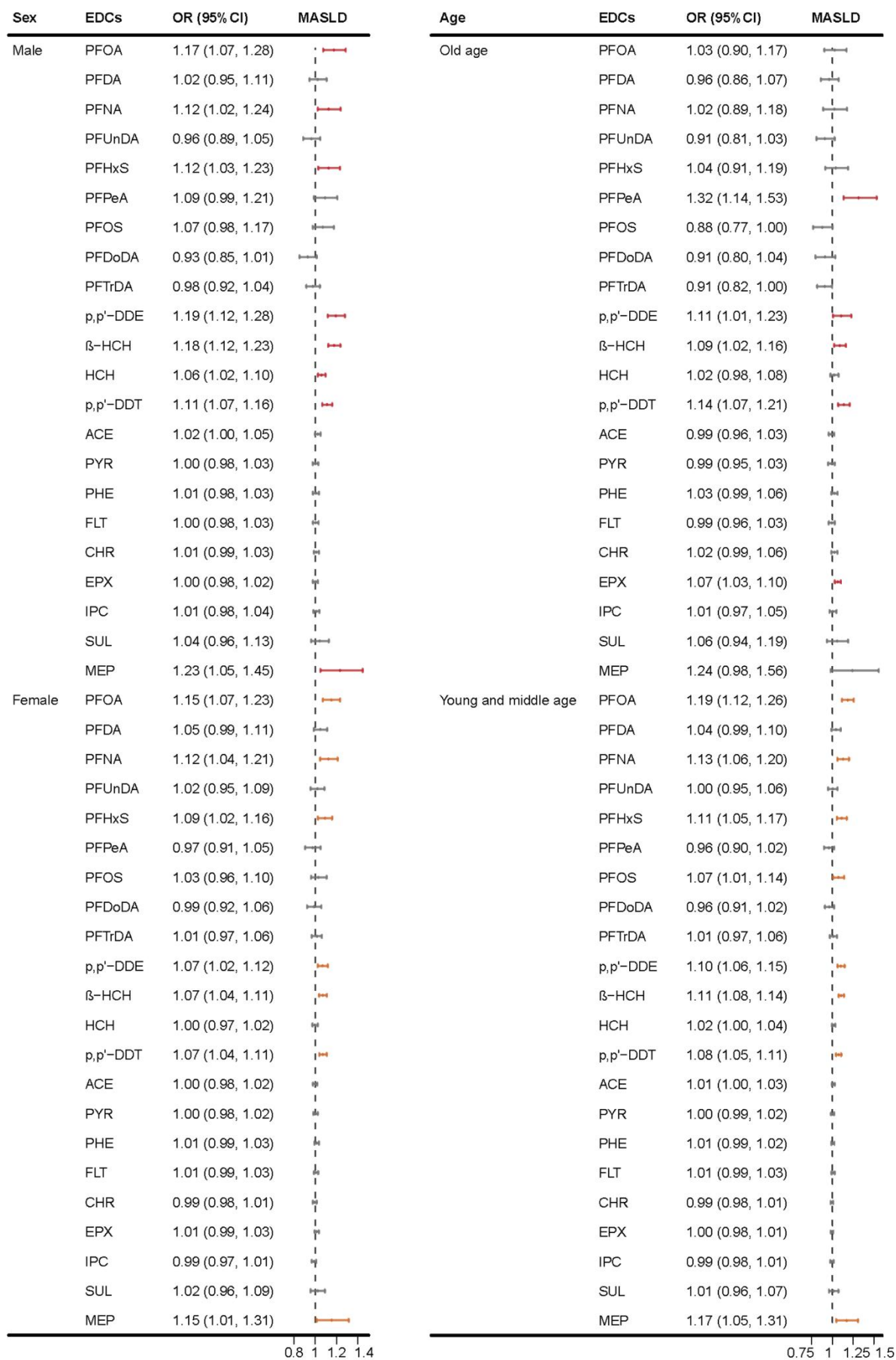
Supplemental Figure1. Spearman correlations among the concentrations of chemical exposure.

Abbreviations: PFOA, perfluorooctanoic acid; PFDA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFUnDA, perfluoroundecanoic acid; PFHxS, perfluorohexanesulfonate; PFPeA, perfluoro-n-pentanoic acid; PFOS, perfluorooctanesulfonate; PFDoDA, perfluorododecanoic acid; PFTrDA, perfluorotridecanoic acid; β -HCH, β -hexachlorocyclohexane; HCH, hexachlorocyclohexane; ACE, acenaphthene; PYR, pyrene; PHE, phenanthrene; FLT, fluoranthene; CHR, chrysene; EPX, etofenprox; IPC, isoprocarb; SUL, fipronil sulphone; MEP, monoethyl phthalate.



Supplemental Figure 2. The directed acyclic graph of the association between serum EDC and MASLD.

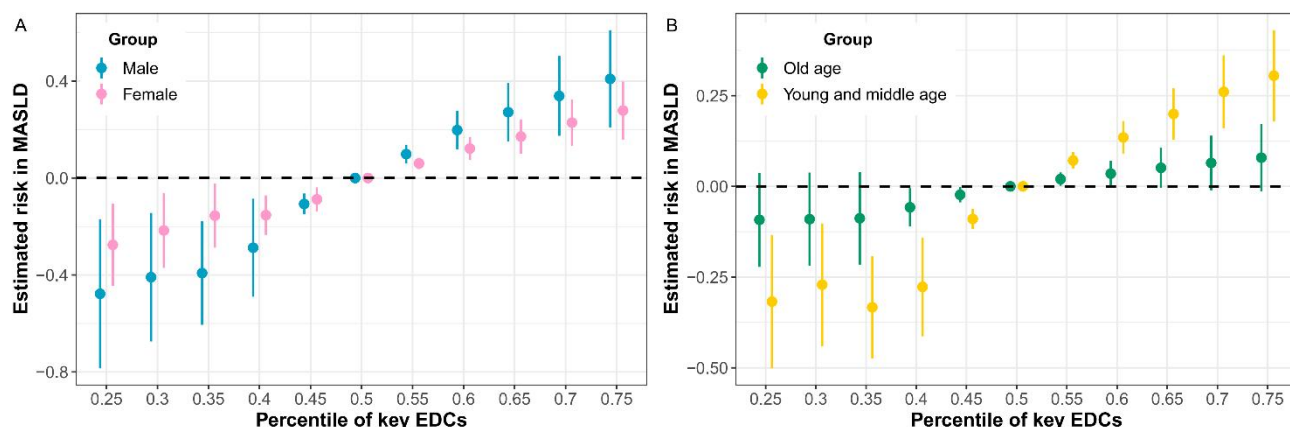
Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease.



Supplemental Figure 3. Regression coefficients of population MASLD incidence rate and 22 EDCs concentrations in gender and age stratification analysis.

Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease; PFOA, perfluorooctanoic acid; PFDA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFUnDA, perfluoroundecanoic acid; PFHxS, perfluorohexanesulfonate; PFPeA, perfluoro-n-pentanoic acid; PFOS, perfluorooctanesulfonate; PFDoDA, perfluorododecanoic acid; PFTrDA, perfluorotridecanoic acid; β -HCH, β -hexachlorocyclohexane; HCH, hexachlorocyclohexane; ACE, acenaphthene; PYR, pyrene; PHE, phenanthrene; FLT, fluoranthene; CHR, chrysene; EPX, etofenprox; IPC, isoprocarb; SUL, fipronil sulphone; MEP, monoethyl phthalate.

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).



Supplemental Figure 4. The joint effects of key EDC mixtures on MASLD in the gender and age stratified population in BKMR models.

Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease.

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Supplemental Tables

Supplemental Table 1. The concentration distribution of EDCs with a detection frequency >50%.

Chemical	LLOQ (ng/ml)	Detection rate (%)	Percentile (ng/ml)		
			P25	P50	P75
PFOA	0.05000	100.00	1.57494	3.31018	10.82966
PFDA	0.02500	97.33	0.01768	0.77285	0.18623
PFNA	0.05000	96.86	0.40257	0.91507	1.94989
PFUnDA	0.05000	92.69	0.22611	0.58553	1.29940
PFHxS	0.05000	91.03	0.18606	0.47336	1.13538
PFPeA	0.10000	90.40	0.43622	0.87012	1.55183
PFOS	1.00000	86.71	2.10120	4.91660	11.59390
PFDoDA	0.02500	70.03	< LOD	0.08155	0.20127
PFTTrDA	0.05000	67.07	< LOD	0.11893	0.31757
<i>p,p'</i> -DDE	0.00100	95.50	0.74900	2.29400	6.01500
β -HCH	0.00100	84.67	0.06400	0.28800	1.03100
HCH	0.00010	84.63	0.11400	0.39100	0.96900
<i>p,p'</i> -DDT	0.00100	59.33	< LOD	0.02403	0.08795
ACE	0.00050	69.03	< LOD	0.04200	0.84400
PYR	0.00050	65.65	< LOD	1.57620	1.18210
PHE	0.00100	58.06	< LOD	0.05100	0.33300
FLT	0.00005	55.62	< LOD	0.00640	0.04100
CHR	0.00001	52.43	< LOD	0.00511	0.03059
EPX	0.00005	61.58	< LOD	0.03940	0.34835
IPC	0.00050	50.37	< LOD	0.00550	0.52110
SUL	0.05000	86.56	0.10837	0.28116	0.68440
MEP	2.50000	56.75	< LOD	2.84700	4.52100

Abbreviations: EDCs, endocrine disrupting chemicals; LLOQ, lower limit of quantitation; PFOA, perfluorooctanoic acid; PFDA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFUnDA, perfluoroundecanoic acid; PFHxS, perfluorohexanesulfonate; PFPeA, perfluoro-n-pentanoic acid; PFOS, perfluorooctanesulfonate; PFDoDA, perfluorododecanoic acid; PFTTrDA, perfluorotridecanoic acid; β -HCH, β -hexachlorocyclohexane; HCH, hexachlorocyclohexane; ACE, acenaphthene; PYR, pyrene; PHE, phenanthrene; FLT, fluoranthene; CHR, chrysene; EPX, etofenprox; IPC, isoprocarb; SUL, fipronil sulphone; MEP, monoethyl phthalate.

Supplemental Table 2. Participant characteristics of the male population, CHNS 2015.

	Overall (n = 3042)	MASLD (n = 457)	Non-MASLD (n = 2585)	<i>P</i> value
Age, year	54.58 (13.45)	49.76 (13.37)	55.43 (13.28)	<0.001
Rural, n (%)	1972 (64.8)	274 (60.0)	1698 (65.7)	0.021
Education, n (%)				0.003
Junior high school and below	1849 (60.8)	249 (54.5)	1600 (61.9)	
High school and vocational high school	792 (26.0)	129 (28.2)	663 (25.6)	
University and above	401 (13.2)	79 (17.3)	322 (12.5)	
Annual household income, yuan (%)				0.404
Low	1150 (37.8)	162 (35.4)	988 (38.2)	
Medium	1094 (36.0)	166 (36.3)	928 (35.9)	
High	466 (15.3)	81 (17.7)	385 (14.9)	
Very high	332 (10.9)	48 (10.5)	284 (11.0)	
Smoker, n (%)	1678 (55.2)	244 (53.4)	1434 (55.5)	0.439
Alcohol user, n (%)	1651 (54.3)	249 (54.5)	1402 (54.2)	0.962
Physical activity, MET h/week	116.82 [47.56, 226.75]	113.33 [46.89, 195.28]	117.43 [47.60, 233.67]	0.326
Total energy intake, kcal	2106.74 [1680.42, 2656.65]	2135.93 [1719.21, 2735.51]	2100.06 [1669.94, 2647.34]	0.072
Total fat intake, g	80.13 [57.25, 109.50]	85.43 [61.56, 119.35]	79.20 [56.65, 107.98]	0.001
Total cholesterol intake, mg	233.01 [120.49, 374.31]	239.81 [120.00, 386.53]	232.29 [120.90, 371.80]	0.495
ALT, IU/L	12.30 [8.80, 17.60]	20.40 [14.70, 30.50]	11.30 [8.30, 15.60]	<0.001
AST, IU/L	16.50 [13.60, 20.50]	18.10 [13.90, 23.20]	16.30 [13.50, 20.10]	<0.001
Serum Ferritin, ng/mL	233.30 [148.22, 346.32]	291.50 [185.20, 435.60]	222.60 [142.00, 331.50]	<0.001

Data were presented as the mean (SD), median [IQR] or frequency (percentage).

Abbreviations: CHNS, China Health and Nutrition Survey; MASLD, metabolic dysfunction-associated steatotic liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Supplemental Table 3. Participant characteristics of the female population, CHNS 2015.

	Overall (n = 3947)	MASLD (n = 718)	Non-MASLD (n = 3229)	<i>P</i> value
Age, year	53.35 (13.59)	54.59 (11.99)	53.07 (13.90)	0.006
Rural, n (%)	2523 (63.9)	426 (59.3)	2097 (64.9)	0.005
Education, n (%)				0.023
Junior high school and below	2680 (67.9)	507 (70.6)	2173 (67.3)	
High school and vocational high school	848 (21.5)	155 (21.6)	693 (21.5)	
University and above	419 (10.6)	56 (7.8)	363 (11.2)	
Annual household income, yuan (%)				0.725
Low	1587 (40.2)	281 (39.1)	1306 (40.4)	
Medium	1416 (35.9)	269 (37.5)	1147 (35.5)	
High	542 (13.7)	93 (13.0)	449 (13.9)	
Very high	402 (10.2)	75 (10.4)	327 (10.1)	
Smoker, n (%)	68 (1.7)	12 (1.7)	56 (1.7)	1.000
Alcohol user, n (%)	254 (6.4)	37 (5.2)	217 (6.7)	0.143
Physical activity, MET h/week	107.80 [51.33, 203.57]	92.82 [49.83, 182.17]	111.53 [51.45, 207.15]	0.011
Total energy intake, kcal	1761.91 [1426.91, 2217.28]	1764.50 [1431.96, 2205.89]	1761.66 [1425.77, 2220.05]	0.642
Total fat intake, g	66.56 [47.56, 93.84]	67.58 [48.76, 95.60]	66.31 [47.45, 93.33]	0.303
Total cholesterol intake, mg	199.27 [100.06, 332.17]	208.32 [102.12, 334.40]	195.89 [99.62, 330.69]	0.327
ALT, IU/L	9.60 [7.00, 13.30]	14.80 [11.10, 21.50]	8.90 [6.65, 11.80]	<0.001
AST, IU/L	15.00 [12.40, 18.40]	16.40 [12.93, 20.90]	14.80 [12.30, 17.90]	<0.001
Serum Ferritin, ng/mL	103.40 [45.20, 189.20]	143.10 [63.92, 230.27]	96.60 [42.20, 178.10]	<0.001

Data were presented as the mean (SD), median [IQR] or frequency (percentage).

Abbreviations: CHNS, China Health and Nutrition Survey; MASLD, metabolic dysfunction-associated steatotic liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Supplemental Table 4. Participant characteristics of the elder population, CHNS 2015.

	Overall (n = 1535)	MASLD (n = 193)	Non-MASLD (n = 1342)	P value
Age, year	71.42 (5.19)	70.65 (4.97)	71.54 (5.22)	0.026
Female, n (%)	832 (54.2)	132 (68.4)	700 (52.2)	<0.001
Rural, n (%)	923 (60.1)	90 (46.6)	833 (62.1)	<0.001
Education, n (%)				0.024
Junior high school and below	1170 (76.2)	149 (77.2)	1021 (76.1)	
High school and vocational high school	263 (17.1)	24 (12.4)	239 (17.8)	
University and above	102 (6.6)	20 (10.4)	82 (6.1)	
Annual household income, yuan (%)				0.316
Low	781 (50.9)	86 (44.6)	695 (51.8)	
Medium	473 (30.8)	67 (34.7)	406 (30.3)	
High	160 (10.4)	23 (11.9)	137 (10.2)	
Very high	121 (7.9)	17 (8.8)	104 (7.7)	
Smoker, n (%)	372 (24.2)	30 (15.5)	342 (25.5)	0.003
Alcohol user, n (%)	349 (22.7)	28 (14.5)	321 (23.9)	0.005
Physical activity, MET h/week	57.52 [29.96, 127.37]	51.62 [29.23, 95.88]	59.42 [30.00, 131.70]	0.146
Total energy intake, kcal	1761.84 [1407.72, 2229.14]	1737.82 [1349.85, 2167.03]	1764.41 [1411.82, 2235.20]	0.333
Total fat intake, g	65.54 [46.27, 92.22]	66.41 [46.86, 89.62]	65.41 [46.24, 92.27]	0.932
Total cholesterol intake, mg	188.76 [94.21, 337.50]	204.27 [93.33, 341.58]	185.60 [95.06, 336.16]	0.856
ALT, IU/L	9.50 [7.00, 13.10]	14.70 [10.90, 19.90]	9.10 [6.70, 12.00]	<0.001
AST, IU/L	16.20 [13.30, 19.30]	16.80 [13.30, 21.30]	16.10 [13.30, 19.08]	0.054
Serum Ferritin, ng/mL	189.70 [117.45, 283.40]	216.90 [144.20, 312.10]	187.10 [114.50, 280.42]	0.002

Data were presented as the mean (SD), median [IQR] or frequency (percentage).

Abbreviations: CHNS, China Health and Nutrition Survey; MASLD, metabolic dysfunction-associated steatotic liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Supplemental Table 5. Participant characteristics of the young and middle age population, CHNS 2015.

	Overall (n = 5454)	MASLD (n = 982)	Non-MASLD (n = 4472)	<i>P</i> value
Age, year	48.95 (10.78)	49.19 (10.68)	48.89 (10.81)	0.434
Female, n (%)	3115 (57.1)	586 (59.7)	2529 (56.6)	0.079
Rural, n (%)	3572 (65.5)	610 (62.1)	2962 (66.2)	0.016
Education, n (%)				0.266
Junior high school and below	3359 (61.6)	607 (61.8)	2752 (61.5)	
High school and vocational high school	1377 (25.2)	260 (26.5)	1117 (25.0)	
University and above	718 (13.2)	115 (11.7)	603 (13.5)	
Annual household income, yuan (%)				0.956
Low	1956 (35.9)	357 (36.4)	1599 (35.8)	
Medium	2037 (37.3)	368 (37.5)	1669 (37.3)	
High	848 (15.5)	151 (15.4)	697 (15.6)	
Very high	613 (11.2)	106 (10.8)	507 (11.3)	
Smoker, n (%)	1374 (25.2)	226 (23.0)	1148 (25.7)	0.090
Alcohol user, n (%)	1556 (28.5)	258 (26.3)	1298 (29.0)	0.091
Physical activity, MET h/week	129.20 [60.00, 230.99]	116.20 [55.45, 202.15]	132.28 [61.12, 239.76]	<0.001
Total energy intake, kcal	1953.49 [1555.53, 2472.39]	1931.96 [1565.65, 2510.45]	1959.24 [1554.49, 2462.18]	0.635
Total fat intake, g	74.12 [52.56, 103.62]	75.93 [54.29, 107.81]	73.90 [52.11, 103.16]	0.058
Total cholesterol intake, mg	219.26 [113.12, 353.42]	225.38 [111.97, 356.94]	216.69 [113.36, 352.33]	0.603
ALT, IU/L	11.00 [7.80, 15.90]	17.50 [12.40, 26.40]	10.10 [7.40, 13.90]	<0.001
AST, IU/L	15.50 [12.70, 19.30]	17.00 [13.40, 21.90]	15.20 [12.60, 18.70]	<0.001
Serum Ferritin, ng/mL	146.80 [62.40, 257.80]	186.05 [90.42, 311.53]	139.00 [58.10, 245.00]	<0.001

Data were presented as the mean (SD), median [IQR] or frequency (percentage).

Abbreviations: CHNS, China Health and Nutrition Survey; MASLD, metabolic dysfunction-associated steatotic liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Supplemental Table 6. Associations between mixed EDC exposure and MASLD in overall population by 10000 WQS models.

Directions	Mixture effects	
	OR (95%CI)	<i>P</i> value
Positive	1.89 (1.61, 2.21)	<0.001

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease; WQS, weighted quantile sum.

Supplemental Table 7. Association between EDCs and MASLD in CHNS 2015 male and female subgroups.

	Male				Female			
	OR (95% CI)				OR (95% CI)			
	T1	T2	T3	<i>P</i> -trend	T1	T2	T3	<i>P</i> -trend
PFOA	Ref.	1.24 (0.96, 1.61)	1.59 (1.22, 2.08)	<0.001	Ref.	1.49 (1.21, 1.84)	1.61 (1.29, 2.01)	<0.001
PFDA	Ref.	1.00 (0.78, 1.29)	1.06 (0.81, 1.38)	0.673	Ref.	1.21 (0.98, 1.48)	1.16 (0.94, 1.44)	0.179
PFNA	Ref.	1.01 (0.78, 1.30)	1.32 (1.01, 1.72)	0.041	Ref.	1.17 (0.95, 1.44)	1.36 (1.10, 1.69)	0.005
PFUnDA	Ref.	0.87 (0.68, 1.11)	0.81 (0.63, 1.06)	0.125	Ref.	1.19 (0.97, 1.46)	1.07 (0.86, 1.32)	0.567
PFHxS	Ref.	1.57 (1.21, 2.04)	1.47 (1.11, 1.94)	0.009	Ref.	1.26 (1.02, 1.55)	1.35 (1.08, 1.68)	0.010
PFPeA	Ref.	1.21 (0.94, 1.56)	1.18 (0.92, 1.52)	0.207	Ref.	0.97 (0.80, 1.18)	0.87 (0.71, 1.06)	0.170
PFOS	Ref.	1.30 (1.01, 1.69)	1.21 (0.93, 1.59)	0.177	Ref.	1.31 (1.06, 1.62)	1.26 (1.01, 1.56)	0.048
PFDODA	Ref.	0.87 (0.68, 1.11)	0.75 (0.57, 0.97)	0.031	Ref.	1.18 (0.96, 1.44)	0.94 (0.76, 1.16)	0.560
PFTTrDA	Ref.	0.80 (0.62, 1.03)	0.84 (0.65, 1.09)	0.174	Ref.	1.22 (0.99, 1.49)	1.00 (0.81, 1.24)	0.962
<i>p,p'</i> -DDE	Ref.	1.93 (1.47, 2.54)	2.78 (2.09, 3.72)	<0.001	Ref.	1.30 (1.04, 1.61)	1.67 (1.32, 2.11)	<0.001
β -HCH	Ref.	1.66 (1.26, 2.19)	3.31 (2.51, 4.41)	<0.001	Ref.	1.25 (1.01, 1.55)	2.00 (1.58, 2.53)	<0.001
HCH	Ref.	1.27 (0.98, 1.65)	1.60 (1.24, 2.08)	<0.001	Ref.	0.98 (0.80, 1.20)	1.03 (0.84, 1.26)	0.805
<i>p,p'</i> -DDT	Ref.	1.08 (0.83, 1.42)	1.91 (1.51, 2.43)	<0.001	Ref.	0.99 (0.80, 1.23)	1.52 (1.25, 1.84)	<0.001
ACE	Ref.	0.98 (0.76, 1.27)	1.13 (0.88, 1.46)	0.316	Ref.	0.85 (0.69, 1.03)	0.97 (0.80, 1.18)	0.767
PYR	Ref.	1.02 (0.80, 1.31)	1.01 (0.79, 1.29)	0.947	Ref.	0.95 (0.78, 1.16)	0.93 (0.76, 1.13)	0.448
PHE	Ref.	0.82 (0.63, 1.06)	1.04 (0.82, 1.31)	0.838	Ref.	0.98 (0.79, 1.21)	1.06 (0.88, 1.28)	0.543
FLT	Ref.	1.00 (0.76, 1.29)	1.08 (0.86, 1.37)	0.505	Ref.	0.97 (0.78, 1.19)	1.09 (0.90, 1.31)	0.394
CHR	Ref.	1.08 (0.82, 1.41)	1.08 (0.86, 1.36)	0.490	Ref.	0.81 (0.64, 1.01)	1.00 (0.83, 1.20)	0.867
EPX	Ref.	0.96 (0.75, 1.23)	0.96 (0.76, 1.23)	0.765	Ref.	0.97 (0.79, 1.20)	1.15 (0.95, 1.39)	0.156
IPC	Ref.	0.89 (0.66, 1.19)	1.14 (0.91, 1.42)	0.304	Ref.	0.82 (0.65, 1.03)	0.94 (0.78, 1.12)	0.396
SUL	Ref.	0.90 (0.69, 1.17)	1.09 (0.84, 1.41)	0.463	Ref.	0.96 (0.78, 1.18)	1.08 (0.88, 1.33)	0.444
MEP	Ref.	0.78 (0.59, 1.01)	1.22 (0.96, 1.53)	0.125	Ref.	1.08 (0.87, 1.33)	1.23 (1.02, 1.48)	0.028

Models were adjusted for age (continuous), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease; CHNS, China Health and Nutrition Survey; PFOA, perfluorooctanoic acid; PFDA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFUnDA, perfluoroundecanoic acid; PFHxS, perfluorohexanesulfonate; PFPeA, perfluoro-n-pentanoic acid; PFOS, perfluorooctanesulfonate; PFDODA, perfluorododecanoic acid; PFTTrDA, perfluorotridecanoic acid; β -HCH, β -hexachlorocyclohexane; HCH, hexachlorocyclohexane; ACE, acenaphthene; PYR, pyrene; PHE, phenanthrene; FLT, fluoranthene; CHR, chrysene; EPX, etofenprox; IPC, isoprocarb; SUL, fipronil sulphone; MEP, monoethyl phthalate.

Supplemental Table 8. Association between EDCs and MASLD in CHNS 2015 the elderly and young and middle age subgroups.

	Old age				Young and middle age			
	OR (95% CI)				OR (95% CI)			
	T1	T2	T3	<i>P</i> -trend	T1	T2	T3	<i>P</i> -trend
PFOA	Ref.	1.05 (0.71, 1.56)	1.22 (0.81, 1.82)	0.334	Ref.	1.58 (1.32, 1.89)	1.71 (1.42, 2.06)	<0.001
PFDA	Ref.	1.11 (0.76, 1.63)	0.91 (0.61, 1.36)	0.655	Ref.	1.07 (0.90, 1.28)	1.09 (0.91, 1.30)	0.356
PFNA	Ref.	1.16 (0.79, 1.70)	1.03 (0.69, 1.52)	0.904	Ref.	1.16 (0.97, 1.39)	1.37 (1.14, 1.64)	<0.001
PFUnDA	Ref.	0.88 (0.61, 1.28)	0.76 (0.51, 1.13)	0.180	Ref.	1.03 (0.87, 1.22)	0.96 (0.80, 1.15)	0.632
PFHxS	Ref.	1.37 (0.92, 2.05)	1.19 (0.77, 1.84)	0.482	Ref.	1.40 (1.17, 1.67)	1.45 (1.21, 1.75)	<0.001
PFPeA	Ref.	1.80 (1.20, 2.74)	2.04 (1.37, 3.09)	<0.001	Ref.	0.98 (0.83, 1.16)	0.86 (0.72, 1.02)	0.091
PFOS	Ref.	1.09 (0.75, 1.59)	0.68 (0.44, 1.03)	0.062	Ref.	1.38 (1.15, 1.64)	1.29 (1.07, 1.55)	0.010
PFDODA	Ref.	1.11 (0.77, 1.60)	0.71 (0.47, 1.06)	0.102	Ref.	1.01 (0.86, 1.20)	0.87 (0.73, 1.04)	0.133
PFTTrDA	Ref.	0.72 (0.49, 1.04)	0.71 (0.48, 1.04)	0.074	Ref.	1.07 (0.91, 1.28)	0.96 (0.80, 1.15)	0.640
<i>p,p'</i> -DDE	Ref.	1.51 (1.01, 2.29)	1.51 (0.99, 2.30)	0.068	Ref.	1.28 (1.07, 1.54)	1.88 (1.57, 2.25)	<0.001
β -HCH	Ref.	1.17 (0.76, 1.80)	1.70 (1.12, 2.63)	0.011	Ref.	1.19 (0.98, 1.43)	2.11 (1.77, 2.52)	<0.001
HCH	Ref.	1.19 (0.81, 1.76)	1.35 (0.92, 2.00)	0.127	Ref.	1.09 (0.92, 1.29)	1.16 (0.97, 1.38)	0.100
<i>p,p'</i> -DDT	Ref.	1.23 (0.80, 1.89)	2.25 (1.54, 3.31)	<0.001	Ref.	1.00 (0.83, 1.20)	1.54 (1.31, 1.81)	<0.001
ACE	Ref.	0.84 (0.57, 1.22)	0.81 (0.56, 1.18)	0.273	Ref.	0.94 (0.79, 1.12)	1.07 (0.90, 1.27)	0.411
PYR	Ref.	1.17 (0.79, 1.73)	0.84 (0.58, 1.21)	0.400	Ref.	0.94 (0.79, 1.12)	1.00 (0.84, 1.18)	0.949
PHE	Ref.	1.12 (0.75, 1.68)	1.23 (0.86, 1.75)	0.245	Ref.	0.88 (0.74, 1.05)	1.01 (0.86, 1.18)	0.988
FLT	Ref.	1.25 (0.83, 1.85)	0.90 (0.63, 1.29)	0.668	Ref.	0.93 (0.78, 1.12)	1.13 (0.97, 1.33)	0.143
CHR	Ref.	1.17 (0.75, 1.81)	1.30 (0.92, 1.82)	0.127	Ref.	0.86 (0.71, 1.04)	0.99 (0.84, 1.15)	0.759
EPX	Ref.	1.35 (0.89, 2.05)	1.91 (1.34, 2.73)	<0.001	Ref.	0.90 (0.76, 1.07)	0.95 (0.80, 1.12)	0.491
IPC	Ref.	0.84 (0.51, 1.35)	1.09 (0.78, 1.52)	0.657	Ref.	0.88 (0.72, 1.06)	0.98 (0.84, 1.15)	0.729
SUL	Ref.	1.23 (0.82, 1.85)	1.26 (0.83, 1.90)	0.301	Ref.	0.86 (0.72, 1.02)	1.03 (0.87, 1.23)	0.634
MEP	Ref.	1.20 (0.80, 1.79)	1.46 (1.02, 2.08)	0.039	Ref.	0.91 (0.76, 1.09)	1.18 (1.00, 1.38)	0.060

Models were adjusted for sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease; CHNS, China Health and Nutrition Survey; PFOA, perfluorooctanoic acid; PFDA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFUnDA, perfluoroundecanoic acid; PFHxS, perfluorohexanesulfonate; PFPeA, perfluoro-n-pentanoic acid; PFOS, perfluorooctanesulfonate; PFDODA, perfluorododecanoic acid; PFTTrDA, perfluorotridecanoic acid; β -HCH, β -hexachlorocyclohexane; HCH, hexachlorocyclohexane; ACE, acenaphthene; PYR, pyrene; PHE, phenanthrene; FLT, fluoranthene; CHR, chrysene; EPX, etofenprox; IPC, isoprocarb; SUL, fipronil sulphone; MEP, monoethyl phthalate.

Supplemental Table 9. Association between key EDCs and SF in the overall population, males, females, old age, and young and middle age subgroups.

	Overall		Male		Female		Old age		Young and middle age	
	Beta (95%CI)	<i>P</i> value	Beta (95%CI)	<i>P</i> value	Beta (95%CI)	<i>P</i> value	Beta (95%CI)	<i>P</i> value	Beta (95%CI)	<i>P</i> value
β -HCH	0.032 (0.024, 0.041)	<0.001	0.019 (0.008, 0.030)	<0.001	0.022 (0.011, 0.033)	<0.001	0.014 (0.000, 0.028)	0.046	0.058 (0.048, 0.068)	<0.001
<i>p,p'</i> -DDT	0.023 (0.014, 0.031)	<0.001	0.013 (0.002, 0.024)	0.019	0.019 (0.007, 0.030)	0.002	0.024 (0.010, 0.038)	0.001	0.032 (0.021, 0.042)	<0.001
MEP	0.020 (-0.015, 0.056)	0.265	-0.003 (-0.047, 0.041)	0.906	0.018 (-0.031, 0.067)	0.474	-0.025 (-0.084, 0.034)	0.399	0.040 (-0.004, 0.083)	0.076
ACE	-0.003 (-0.008, 0.002)	0.226	-0.005 (-0.012, 0.002)	0.132	-0.002 (-0.009, 0.005)	0.611	-0.009 (-0.018, -0.001)	0.027	-0.001 (-0.007, 0.006)	0.831
PFOA	0.126 (0.108, 0.145)	<0.001	0.081 (0.058, 0.105)	<0.001	0.128 (0.103, 0.154)	<0.001	0.064 (0.033, 0.095)	<0.001	0.180 (0.158, 0.202)	<0.001
PFPeA	-0.013 (-0.033, 0.007)	0.200	-0.025 (-0.051, 0.001)	0.058	-0.009 (-0.036, 0.018)	0.519	-0.031 (-0.065, 0.003)	0.074	-0.005 (-0.03, 0.019)	0.679

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: EDCs, endocrine disrupting chemicals; SF, serum ferritin; β -HCH, β -hexachlorocyclohexane; MEP, monoethyl phthalate; ACE, acenaphthene; PFOA, perfluorooctanoic acid; PFPeA, perfluoro-n-pentanoic acid.

Supplemental Table 10. Association between SF and MASLD in the overall population, males, females, old age, and young and middle age subgroups.

	OR (95%CI)	P value
Overall	1.60 (1.48, 1.73)	<0.001
Male	1.85 (1.58, 2.16)	<0.001
Female	1.40 (1.28, 1.55)	<0.001
Old age	1.63 (1.30, 2.07)	<0.001
Young and middle age	1.50 (1.39, 1.63)	<0.001

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: SF, serum ferritin; MASLD, metabolic dysfunction-associated steatotic liver disease.

Supplemental Table 11. The interaction of Ln-transformed key EDCs and SF on MASLD risk in the overall population, males, females, old age, and young and middle age subgroups.

	<i>P</i> for interaction					
	β -HCH	<i>p,p'</i> -DDT	MEP	ACE	PFOA	PFPeA
Overall	0.290	0.289	0.419	0.431	0.181	0.393
Male	0.153	0.231	0.168	0.157	0.263	0.177
Female	0.647	0.666	0.845	0.766	0.614	0.800
Old age	0.544	0.592	0.446	0.508	0.487	0.591
Young and middle age	0.837	0.940	0.760	0.782	0.890	0.757

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: EDCs, endocrine disrupting chemicals; SF, serum ferritin; MASLD, metabolic dysfunction-associated steatotic liver disease; β -HCH, β -hexachlorocyclohexane; MEP, monoethyl phthalate; ACE, acenaphthene; PFOA, perfluorooctanoic acid; PFPeA, perfluoro-n-pentanoic acid.

Supplemental Table 12. Mediating effects of SF on the associations between key EDCs and MASLD in different stratification.

	Key EDCs	TE	NDE	NIE	Proportion mediated by SF	P value
		OR (95% CI)	OR (95% CI)	OR (95% CI)		
Male	PFOA	1.0192 (1.0101, 1.0271)	1.0139 (1.0042, 1.0217)	1.0052 (1.0032, 1.0075)	27.16%	<0.001
	β -HCH	1.0226 (1.0152, 1.0319)	1.0210 (1.0138, 1.0302)	1.0016 (1.0007, 1.0026)	6.97%	<0.001
	<i>p,p'</i> -DDT	1.0168 (1.0093, 1.0256)	1.0156 (1.0082, 1.0241)	1.0012 (1.0002, 1.0022)	7.15%	0.026
Female	PFOA	1.0206 (1.0108, 1.0294)	1.0151 (1.0053, 1.0239)	1.0054 (1.0035, 1.0074)	26.57%	<0.001
	β -HCH	1.0105 (1.0049, 1.0163)	1.0094 (1.0040, 1.0151)	1.0011 (1.0005, 1.0017)	10.38%	<0.001
	<i>p,p'</i> -DDT	1.0119 (1.0055, 1.0187)	1.0109 (1.0047, 1.0176)	1.0010 (1.0003, 1.0018)	8.48%	<0.001
Old age	β -HCH	1.0095 (1.0031, 1.0182)	1.0087 (1.0023, 1.0172)	1.0008 (1.0001, 1.0017)	8.14%	0.036
	<i>p,p'</i> -DDT	1.0181 (1.0082, 1.0300)	1.0165 (1.0069, 1.0280)	1.0015 (1.0004, 1.0030)	8.62%	<0.001
Young and middle age	PFOA	1.0243 (1.0171, 1.0321)	1.0154 (1.0081, 1.0236)	1.0088 (1.0067, 1.0110)	36.36%	<0.001
	β -HCH	1.0158 (1.0105, 1.0213)	1.0124 (1.0072, 1.0179)	1.0034 (1.0026, 1.0045)	21.48%	<0.001
	<i>p,p'</i> -DDT	1.0126 (1.0070, 1.0187)	1.0105 (1.0053, 1.0166)	1.0020 (1.0012, 1.0030)	16.28%	<0.001

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: SF, serum ferritin; EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease; TE, total effect; NDE, natural direct effect; NIE, natural indirect effect; β -HCH, β -hexachlorocyclohexane; PFOA, perfluorooctanoic acid.

Supplemental Table 13. Association between Ln-transformed EDCs in fertile and MASLD risk in overall population excluding all individuals with EDC concentrations above the 99th percentile.

	OR (95% CI)				
	Continuous	T1	T2	T3	<i>P</i> -trend
PFOA	1.20 (1.13, 1.27)	Reference	1.52 (1.27, 1.81)	1.70 (1.41, 2.04)	<0.001
PFDA	1.05 (1.00, 1.11)	Reference	1.15 (0.97, 1.36)	1.11 (0.93, 1.33)	0.254
PFNA	1.14 (1.07, 1.22)	Reference	1.19 (1.00, 1.42)	1.34 (1.12, 1.60)	0.002
PFUnDA	1.00 (0.94, 1.06)	Reference	1.02 (0.86, 1.21)	0.96 (0.81, 1.15)	0.671
PFHxS	1.15 (1.09, 1.22)	Reference	1.51 (1.26, 1.81)	1.63 (1.35, 1.98)	<0.001
PFPeA	1.01 (0.95, 1.08)	Reference	1.06 (0.90, 1.25)	1.01 (0.85, 1.20)	0.891
PFOS	1.10 (1.03, 1.17)	Reference	1.41 (1.18, 1.68)	1.35 (1.12, 1.62)	0.002
PFDoDA	0.97 (0.91, 1.03)	Reference	1.08 (0.92, 1.28)	0.90 (0.75, 1.07)	<0.001
PFTTrDA	1.01 (0.96, 1.05)	Reference	0.99 (0.84, 1.17)	0.94 (0.78, 1.12)	<0.001
<i>p,p'</i> -DDE	1.14 (1.09, 1.19)	Reference	1.43 (1.19, 1.71)	2.10 (1.74, 2.55)	0.067
β -HCH	1.13 (1.09, 1.16)	Reference	1.36 (1.13, 1.63)	2.48 (2.05, 3.01)	0.071
HCH	1.02 (1.00, 1.04)	Reference	1.08 (0.91, 1.28)	1.17 (0.99, 1.39)	0.224
<i>p,p'</i> -DDT	1.10 (1.06, 1.13)	Reference	0.96 (0.80, 1.15)	1.68 (1.44, 1.98)	0.437
ACE	1.01 (1.00, 1.03)	Reference	0.95 (0.80, 1.12)	1.05 (0.89, 1.24)	<0.001
PYR	1.00 (0.98, 1.02)	Reference	0.94 (0.79, 1.11)	0.90 (0.77, 1.06)	0.585
PHE	1.00 (0.98, 1.02)	Reference	0.83 (0.69, 0.99)	0.97 (0.83, 1.13)	0.239
FLT	1.00 (0.98, 1.02)	Reference	0.96 (0.80, 1.15)	1.05 (0.90, 1.23)	0.603
CHR	0.99 (0.98, 1.01)	Reference	0.88 (0.73, 1.06)	0.98 (0.84, 1.15)	0.543
EPX	1.01 (0.99, 1.02)	Reference	0.92 (0.78, 1.09)	1.07 (0.91, 1.26)	0.762
IPC	1.00 (0.98, 1.02)	Reference	0.86 (0.70, 1.05)	1.02 (0.87, 1.18)	0.404
SUL	1.05 (0.99, 1.11)	Reference	0.93 (0.78, 1.11)	1.16 (0.98, 1.38)	0.926
MEP	1.23 (1.10, 1.39)	Reference	1.00 (0.83, 1.19)	1.26 (1.08, 1.47)	0.005

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease; PFOA, perfluorooctanoic acid; PFDA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFUnDA, perfluoroundecanoic acid; PFHxS, perfluorohexanesulfonate; PFPeA, perfluoro-n-pentanoic acid; PFOS, perfluorooctanesulfonate; PFDoDA, perfluorododecanoic acid; PFTTrDA, perfluorotridecanoic acid; β -HCH, β -hexachlorocyclohexane; HCH, hexachlorocyclohexane; ACE, acenaphthene; PYR, pyrene; PHE, phenanthrene; FLT, fluoranthene; CHR, chrysene; EPX, etofenprox; IPC, isoprocarb; SUL, fipronil sulphone; MEP, monoethyl phthalate.

Supplemental Table 14. Association between Ln-transformed EDCs in tertile and MASLD risk in overall population without multiple interpolation of covariates.

	OR (95% CI)				<i>P</i> -trend
	Continuous	T1	T2	T3	
PFOA	1.18 (1.11, 1.25)	Reference	1.57 (1.31, 1.87)	1.75 (1.46, 2.10)	<0.001
PFDA	1.04 (0.99, 1.10)	Reference	1.08 (0.91, 1.28)	1.11 (0.93, 1.32)	0.257
PFNA	1.15 (1.08, 1.23)	Reference	1.18 (1.00, 1.41)	1.42 (1.19, 1.70)	<0.001
PFUnDA	0.99 (0.94, 1.05)	Reference	1.05 (0.89, 1.24)	0.95 (0.80, 1.13)	0.519
PFHxS	1.12 (1.06, 1.18)	Reference	1.49 (1.25, 1.78)	1.54 (1.28, 1.86)	<0.001
PFPeA	1.02 (0.96, 1.09)	Reference	1.16 (0.98, 1.37)	1.03 (0.87, 1.22)	0.796
PFOS	1.05 (0.99, 1.11)	Reference	1.34 (1.13, 1.60)	1.27 (1.06, 1.52)	0.012
PFDODA	0.97 (0.92, 1.02)	Reference	1.08 (0.91, 1.27)	0.90 (0.76, 1.07)	0.221
PFTTrDA	1.00 (0.96, 1.04)	Reference	1.01 (0.86, 1.19)	0.91 (0.77, 1.08)	0.288
<i>p,p'</i> -DDE	1.10 (1.06, 1.15)	Reference	1.47 (1.23, 1.76)	2.13 (1.77, 2.58)	<0.001
β -HCH	1.11 (1.08, 1.14)	Reference	1.28 (1.07, 1.53)	2.31 (1.92, 2.79)	<0.001
HCH	1.02 (1.00, 1.04)	Reference	1.08 (0.91, 1.27)	1.16 (0.98, 1.38)	0.076
<i>p,p'</i> -DDT	1.09 (1.06, 1.12)	Reference	1.06 (0.88, 1.26)	1.75 (1.49, 2.05)	<0.001
ACE	1.01 (0.99, 1.02)	Reference	0.91 (0.77, 1.07)	1.02 (0.87, 1.21)	0.785
PYR	1.00 (0.98, 1.02)	Reference	0.95 (0.81, 1.12)	0.94 (0.79, 1.10)	0.435
PHE	1.01 (0.99, 1.02)	Reference	0.88 (0.74, 1.04)	1.00 (0.86, 1.17)	0.936
FLT	1.01 (0.99, 1.03)	Reference	0.98 (0.82, 1.17)	1.16 (0.99, 1.35)	0.068
CHR	1.01 (0.99, 1.02)	Reference	0.95 (0.79, 1.14)	1.11 (0.95, 1.29)	0.210
EPX	1.01 (1.00, 1.03)	Reference	1.05 (0.88, 1.23)	1.07 (0.92, 1.26)	0.378
IPC	1.00 (0.98, 1.02)	Reference	0.84 (0.69, 1.02)	1.04 (0.89, 1.20)	0.763
SUL	1.02 (0.97, 1.08)	Reference	0.93 (0.79, 1.11)	1.06 (0.89, 1.26)	0.473
MEP	1.21 (1.09, 1.35)	Reference	0.99 (0.83, 1.18)	1.29 (1.10, 1.50)	0.002

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; EDCs, endocrine disrupting chemicals; PFOA, perfluorooctanoic acid; PFDA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFUnDA, perfluoroundecanoic acid; PFHxS, perfluorohexanesulfonate; PFPeA, perfluoro-n-pentanoic acid; PFOS, perfluorooctanesulfonate; PFDODA, perfluorododecanoic acid; PFTTrDA, perfluorotridecanoic acid; β -HCH, β -hexachlorocyclohexane; HCH, hexachlorocyclohexane; ACE, acenaphthene; PYR, pyrene; PHE, phenanthrene; FLT, fluoranthene; CHR, chrysene; EPX, etofenprox; IPC, isoprocarb; SUL, fipronil sulphone; MEP, monoethyl phthalate.

Supplemental Table 15. Association between mixtures of key EDCs and MASLD risk and the weight of each key EDCs in the QGC models.

	Key EDCs	Weight	OR (95%CI)	P value
Overall	β -HCH	0.335	2.11 (1.81, 2.45)	<0.001
	<i>p,p'</i> -DDT	0.268		
	PFOA	0.176		
	MEP	0.131		
	ACE	0.090		
	PFPeA	-1.000		
Male	β -HCH	0.374	2.45 (1.95, 3.07)	<0.001
	<i>p,p'</i> -DDT	0.238		
	ACE	0.124		
	MEP	0.111		
	PFOA	0.096		
	PFPeA	0.056		
Female	<i>p,p'</i> -DDT	0.301	1.79 (1.47, 2.18)	<0.001
	β -HCH	0.292		
	PFOA	0.216		
	MEP	0.146		
	ACE	0.045		
	PFPeA	-1.000		
Old age	<i>p,p'</i> -DDT	0.457	2.10 (1.44, 3.07)	<0.001
	β -HCH	0.233		
	PFOA	0.165		
	MEP	0.145		
	ACE	-0.812		
	PFPeA	-0.188		
Young and middle age	<i>p,p'</i> -DDT	0.304	1.87 (1.59, 2.20)	<0.001
	β -HCH	0.231		
	PFOA	0.217		
	MEP	0.131		
	ACE	0.117		
	PFPeA	-1.000		

Models were adjusted for age (continuous), sex (binary), residence (categorical), education (categorical), household income (categorical), smoking (binary), alcohol drinking (binary), physical activity (continuous), total energy intake (continuous), total fat intake (continuous), and total cholesterol intake (continuous).

Abbreviations: EDCs, endocrine disrupting chemicals; MASLD, metabolic dysfunction-associated steatotic liver disease; QGC, quantile-based G-computation; β -HCH, β -hexachlorocyclohexane; PFOA, perfluorooctanoic acid; MEP, monoethyl phthalate; ACE, acenaphthene; PFPeA, perfluoro-n-pentanoic acid.