Supplementary Materials

Supplement A: Definition of metabolic dysfunction-associated fatty liver disease

Metabolic dysfunction-associated fatty liver disease was defined as the presence of liver steatosis with at least one of the three following metabolic components: overweight or obesity (body mass index ≥ 25 kg/m^2), type 2 diabetes mellitus, and at least two metabolic risk abnormalities.[1-2] Although imaging tools are the preferred diagnostic procedure for hepatic steatosis, their availability is limited in 2009-2014 survey cycles of NHANES. Nevertheless, fatty liver scoring systems are acceptable alternatives for diagnosing hepatic steatosis.[3] The United States fatty liver index (USFLI) is a widely used hepatic steatosis scoring system in previous studies, and it was developed in the multi-ethnic US population from NHANES, with an area under the receiver operating characteristic curve of 0.80 (95% CI: 0.77-0.83).[4] Liver steatosis was defined as the USFLI score ≥ 30 in the this study, and USFLI was calculated as previously described.[4] The metabolic risk abnormalities included: (a) waist circumference ≥ 102 cm for males or ≥ 88 cm for females; (b) blood pressure ≥ 130/85 mmHg or currently taking specific medications; (c) plasma triglycerides ≥ 150 mg/dL or currently taking specific medications; (d) plasma high-density lipoprotein-cholesterol < 40 mg/dL for males and < 50 mg/dL for females or currently taking specific drugs; (e) prediabetes status (i.e., fasting glucose levels 100 to 125 mg/dL, or hemoglobin A1c 5.7-6.4%); (f) homeostasis model assessment of insulin resistance score ≥ 2.5.[2]

References:

1 M. Eslam, P. N. Newsome, S. K. Sarin, *et al.*, A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement, *J Hepatol*, 2020, **73**, 202-209.

2 Z. Q. Xie, H. X. Li, B. K. Wang, *et al.*, Trends in prevalence and all-cause mortality of metabolic dysfunction-associated fatty liver disease among adults in the past three decades: Results from the NHANES study, *Eur J Intern Med*, 2023, **110**, 62-70.

3 European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), and European Association for the Study of Obesity (EASO), EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease, *Diabetologia*, 2016, **59**, 1121-1140.

4 C. E. Ruhl and J. E. Everhart, Fatty liver indices in the multiethnic United States National Health and Nutrition Examination Survey, *Aliment Pharmacol Ther*, 2015, **41**, 65-76.

Supplement B: Definition of metabolic syndrome

The diagnostic criteria proposed by the Adult Treatment Program III of the National Cholesterol Education Program (ATP III) were applied as the definition of metabolic syndrome in this study.[1] Individuals with at least three of the following components were classified as metabolic syndrome: (a) Central obesity: waist circumstance ≥102 centimeters for males or ≥ 88 centimeters for females; (b) Elevated triglyceride: blood triglyceride (TG) ≥150mg/dL or current using medication to treat elevated TG; (c) Reduced high-density lipoprotein: blood high-density lipoprotein (HDL) < 40 mg/dL for males, blood HDL <50 mg/dL for females, or currently using medication for low HDL; (d) High blood pressure: systolic blood pressure ≥ 130 mmHg or (and) diastolic blood pressure ≥ 85 mmHg or currently using medication for high blood pressure; (e) Impaired fasting blood glucose: fasting blood glucose (FBG) ≥ 110 mg/dL or current use of medication to treat hyperglycemia.

References:

1 S. M. Grundy, H. B. Brewer, Jr., J. *et al.*, Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition, *Circulation*, 2004, **109**, 433-438.

Table S1 Comparison of background characteristics between excluded and included participants

Characteristics [a]	Overall (*n* = 5344)	Excluded (*n* = 3276)	Included (*n* = 2068)	*P* value [b]
Gender (%)				0.400
Female	2743 (51.46%)	1658 (50.94%)	1085 (52.24%)	
Male	2601 (48.54%)	1618 (49.06%)	983 (47.76%)	
Age (%)				0.400
20-39 years	1789 (36.58%)	1107 (37.54%)	682 (35.14%)	
40-59 years	1813 (35.80%)	1109 (35.21%)	704 (36.68%)	
60 and above years	1742 (27.62%)	1060 (27.25%)	682 (28.18%)	
Race/Ethnicity (%)				**<0.001**
Mexican American	745 (8.35%)	458 (8.61%)	287 (7.98%)	
Other Hispanic	532 (5.94%)	341 (6.25%)	191 (5.48%)	
Non-Hispanic White	2299 (66.71%)	1332 (64.79%)	967 (69.57%)	
Non-Hispanic Black	1128 (11.45%)	756 (12.93%)	372 (9.24%)	
Other Race	640 (7.54%)	389 (7.42%)	251 (7.72%)	
Education level (%)				0.300
Middle school or lower	1280 (16.34%)	801 (16.56%)	479 (16.02%)	
High School	2769 (52.91%)	1720 (53.65%)	1049 (51.80%)	
College or above	1295 (30.75%)	755 (29.80%)	540 (32.17%)	
Poverty-income ratio	2.95 (1.37, 5.00)	2.91 (1.34, 5.00)	3.00 (1.43, 5.00)	0.900
Marital status (%)				0.200
Married/Cohabited	3182 (62.93%)	1927 (61.63%)	1255 (64.88%)	
Never Married	1020 (18.90%)	637 (19.46%)	383 (18.06%)	
Other	1142 (18.17%)	712 (18.92%)	430 (17.05%)	
Smoking status (%)				0.400
Current	2137 (39.70%)	1294 (38.90%)	843 (40.91%)	
Former	198 (3.13%)	120 (3.34%)	78 (2.82%)	
Never	3009 (57.17%)	1862 (57.76%)	1147 (56.27%)	
Excessive alcohol consumption(%)				0.900
No	4780 (87.73%)	2924 (87.67%)	1856 (87.82%)	
Yes	564 (12.27%)	352 (12.33%)	212 (12.18%)	
Physical activity (%)				0.600
Inactive	1383 (22.64%)	878 (23.45%)	505 (21.43%)	
Low activity	1865 (35.48%)	1138 (34.91%)	727 (36.33%)	
Medium activity	754 (15.42%)	449 (15.24%)	305 (15.69%)	
High activity	1342 (26.46%)	811 (26.40%)	531 (26.55%)	
Caffeine intake (g/day)	0.12 (0.04, 0.24)	0.11 (0.04, 0.23)	0.12 (0.05, 0.24)	0.075
Energy intake (kcal/day)	1980.00 (1530.00, 2539.42)	1994.69 (1554.66, 2543.19)	1971.21 (1492.67, 2531.94)	0.052
Body mass index (kg/m²)	27.84 (24.18, 32.30)	27.90 (24.30, 32.30)	27.81 (24.00, 32.20)	0.600
FBG (mg/dL)	98.00 (91.00, 107.00)	98.00 (91.00, 108.00)	98.00 (91.00, 107.00)	0.900
HbA1c (%)	5.50 (5.20, 5.80)	5.50 (5.20, 5.80)	5.40 (5.20, 5.70)	0.200
SBP (mmHg)	118.67 (110.00, 129.33)	119.33 (110.90, 130.00)	118.67 (109.33, 128.67)	**0.029**
DBP (mmHg)	70.67 (64.00, 78.00)	71.33 (64.00, 78.67)	70.00 (63.33, 76.67)	**<0.001**
Survey cycle (%)				0.600
2009-2010	1936 (32.65%)	1189 (33.11%)	747 (31.95%)	
2011-2012	1622 (33.81%)	1005 (34.03%)	617 (33.49%)	
2013-2014	1786 (33.54%)	1082 (32.85%)	704 (34.56%)	

Notes: [a] Categorical variables were demonstrated as unweighted frequency (weighted percentage), while continuous variables were shown as median (inter-quartile range) due to their skewed distributions. [b] Categorical variables were compared using the chi-squared tests with Rao & Scott's second-order correction, while continuous variables were compared using the Wilcoxon rank-sum test for complex survey samples.

Abbreviations: FBG, fasting blood glucose; HbA1c, hemoglobin A1c; SBP, systolic blood pressure; DBP, diastolic blood pressure

Table S2 Comparison of clinical features among the included participants

Characteristics [a]	Overall (n = 2068)	Liver steatosis [b]			Advanced liver fibrosis [b]		
		No (n = 1367)	Yes (n = 701)	*P* value [c]	No (n = 1889)	Yes (n = 179)	*P* value [c]
WC (cm)	97.28 (87.30, 107.81)	92.10 (84.00, 99.73)	112.20 (103.00, 121.00)	**<0.001**	96.20 (87.00, 106.60)	113.80 (99.93, 130.65)	**<0.001**
TG (mg/dL)	101.00 (72.00, 147.00)	89.00 (65.00, 122.00)	139.00 (98.93, 199.40)	**<0.001**	99.00 (72.00, 145.00)	123.00 (82.00, 183.43)	**<0.001**
GGT (U/L)	19.00 (13.00, 28.00)	16.00 (12.00, 21.00)	28.00 (19.00, 41.00)	**<0.001**	18.00 (13.00, 27.00)	20.21 (15.00, 32.00)	**0.015**
AST (U/L)	23.00 (19.00, 27.00)	22.00 (19.00, 26.00)	25.00 (21.00, 31.00)	**<0.001**	23.00 (19.00, 27.00)	24.00 (21.00, 27.59)	**0.011**
ALT (U/L)	21.00 (17.00, 28.00)	20.00 (16.00, 24.00)	26.00 (20.00, 36.00)	**<0.001**	21.00 (17.00, 28.00)	20.00 (16.00, 26.00)	0.150
ALB (g/L)	4.30 (4.10, 4.50)	4.30 (4.10, 4.50)	4.20 (4.00, 4.40)	**<0.001**	4.30 (4.10, 4.50)	4.10 (3.90, 4.30)	**<0.001**
FBG (mg/dL)	98.00 (91.00, 107.00)	95.00 (89.00, 101.05)	107.00 (100.00, 123.00)	**<0.001**	98.00 (91.00, 105.00)	120.00 (110.00, 147.69)	**<0.001**
Insulin (μU/mL)	9.53 (6.13, 15.40)	7.22 (4.96, 10.28)	18.76 (13.99, 27.24)	**<0.001**	9.31 (6.00, 14.60)	15.87 (9.35, 24.93)	**<0.001**
HbA1c (%)	5.40 (5.20, 5.70)	5.40 (5.10, 5.60)	5.70 (5.40, 6.10)	**<0.001**	5.40 (5.20, 5.70)	6.20 (5.80, 7.20)	**<0.001**
PLT (10^9/L)	228.00 (194.00, 268.00)	226.00 (195.00, 262.12)	237.00 (191.00, 284.00)	**0.026**	231.00 (200.00, 270.33)	178.00 (149.09, 205.95)	**<0.001**
SBP (mmHg)	118.67 (109.33, 128.67)	116.00 (106.67, 125.33)	124.00 (114.67, 134.26)	**<0.001**	118.00 (108.67, 127.33)	131.33 (116.15, 142.96)	**<0.001**
DBP (mmHg)	70.00 (63.33, 76.67)	68.67 (62.67, 74.67)	72.67 (64.00, 78.67)	**<0.001**	70.00 (63.33, 76.67)	64.67 (58.00, 73.45)	**0.003**
Cr. (mg/dL)	103.31 (62.00, 161.00)	95.00 (57.00, 152.00)	124.00 (76.00, 175.00)	**<0.001**	103.00 (61.00, 162.00)	109.00 (78.72, 149.00)	0.140
MetS (%)				**<0.001**			**<0.001**
No	1443 (72.96%)	1174 (87.45%)	269 (41.34%)		1406.00 (76.53%)	37.00 (23.60%)	
Yes	625 (27.04%)	193 (12.55%)	432 (58.66%)		483.00 (23.47%)	142.00 (76.40%)	

Notes: [a] Categorical variables were demonstrated as unweighted frequency (weighted percentage), while continuous variables were shown as median (inter-quartile range) due to their skewed distributions. [b] Liver steatosis was defined by USFLI ≥30, while advanced liver fibrosis was indicated by NFS >0.676.[c] Categorical variables were compared using the chi-squared tests with Rao & Scott's second-order correction, while continuous variables were compared using the Wilcoxon rank-sum test for complex survey samples.

Abbreviation: WC, waist circumstance; TG, triglyceride; GGT, gamma-glutamyl transferase; ALT, alanine transaminase; AST, Aspartate transaminase; ALB, albumin; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; PLT, platelet count; SBP, systolic blood pressure; DBP, diastolic blood pressure; Cr, creatinine; MetS, metabolic syndrome.

Table S3 Distributions of urinary caffeine and caffeine metabolites among the included participants **(*n* = 2068)**

Metabolites	Abbreviation	LLOD (μmol/L)	DF (%)	GM (μmol/L)	Mean (μmol/L)	Percentiles		
						P25	P50	P75
1-methyluric acid	1-MU	0.050	100.00	55.29	108.75	24.50	59.60	133.00
3-methyluric acid	3-MU	0.100	83.12	0.52	1.36	0.17	0.54	1.45
7-methyluric acid	7-MU	0.040	99.23	11.29	29.60	4.66	13.51	33.46
1,3-dimethyluric acid	1,3-DMU	0.020	98.16	5.29	14.41	2.59	7.16	16.10
1,7-dimethyluric acid	1,7-DMU	0.020	98.50	17.50	47.92	7.69	25.22	61.91
3,7-dimethyluric acid	3,7-DMU	0.030	95.26	0.80	1.92	0.34	0.87	2.20
1,3,7-trimethyluric acid	1,3,7-TMU	0.005	95.21	0.83	2.52	0.29	1.18	3.06
1-methylxanthine	1-MX	0.030	100.00	22.26	50.43	9.35	25.81	64.73
3-methylxanthine	3-MX	0.040	99.47	23.98	55.71	11.50	27.85	64.12
7-methylxanthine	7-MX	0.020	99.90	38.16	87.81	17.11	41.80	105.00
1,3-dimethylxanthine (theophylline)	1,3-DMX	0.010	97.24	1.25	3.00	0.61	1.75	3.62
1,7-dimethylxanthine (paraxanthine)	1,7-DMX	0.006	98.79	10.19	22.65	4.80	14.61	30.99
3,7-dimethylxanthine (theobromine)	3,7-DMX	0.004	99.47	12.00	26.32	5.84	14.52	32.53
1,3,7-trimethylxanthine (caffeine)	1,3,7-TMX	0.003	96.91	1.94	5.36	0.79	2.75	6.94
5-acetylamino-6-amino-3-methyluracil	AAMU	0.100	99.61	51.91	112.78	22.50	60.60	143.00

Abbreviation: LLOD, lower limit of detection; DF, detection frequency; GM, geometric mean.

Table S4 Comparison of urinary caffeine and its metabolites among included participants **(*n* = 2068)**

Metabolites [a]	**Overall**	**Liver steatosis** [b]			**Advanced Liver fibrosis** [b]		
(**Unit:** μmol/mg Cr.)	**(*n* = 2068)**	**No (*n* = 1367)**	**Yes (*n* = 701)**	***P* value** [c]	**No (*n* = 1889)**	**Yes (*n* = 179)**	***P* value** [c]
1-MU	0.72 (0.32, 1.34)	0.73 (0.32, 1.36)	0.71 (0.33, 1.28)	0.900	0.72 (0.32, 1.34)	0.72 (0.27, 1.35)	0.900
3-MU	0.01 (0.00, 0.02)	0.01 (0.00, 0.02)	0.01 (0.00, 0.02)	0.900	0.01 (0.00, 0.02)	0.01 (0.00, 0.02)	0.200
7-MU	0.17 (0.07, 0.39)	0.17 (0.07, 0.43)	0.18 (0.07, 0.35)	0.700	0.17 (0.07, 0.39)	0.18 (0.07, 0.44)	0.500
1,3-DMU	0.09 (0.04, 0.16)	0.08 (0.03, 0.16)	0.10 (0.05, 0.17)	**0.004**	0.09 (0.04, 0.16)	0.09 (0.03, 0.17)	0.900
1,7-DMU	0.31 (0.12, 0.61)	0.28 (0.10, 0.57)	0.38 (0.18, 0.66)	**<0.001**	0.31 (0.12, 0.60)	0.36 (0.12, 0.81)	0.200
3,7-DMU	0.01 (0.01, 0.02)	0.01 (0.00, 0.03)	0.01 (0.01, 0.02)	0.700	0.01 (0.01, 0.03)	0.01 (0.00, 0.02)	**0.008**
1,3,7-TMU	0.01 (0.00, 0.03)	0.01 (0.00, 0.03)	0.02 (0.01, 0.04)	**<0.001**	0.01 (0.00, 0.03)	0.02 (0.01, 0.03)	0.120
1-MX	0.34 (0.14, 0.63)	0.35 (0.13, 0.64)	0.31 (0.14, 0.58)	0.130	0.35 (0.14, 0.64)	0.25 (0.09, 0.49)	**<0.001**
3-MX	0.35 (0.16, 0.75)	0.37 (0.17, 0.82)	0.32 (0.14, 0.64)	**0.019**	0.35 (0.16, 0.76)	0.32 (0.15, 0.67)	0.200
7-MX	0.55 (0.24, 1.18)	0.58 (0.27, 1.32)	0.46 (0.20, 0.89)	**<0.001**	0.56 (0.25, 1.22)	0.36 (0.16, 0.84)	**<0.001**
1,3-DMX	0.02 (0.01, 0.04)	0.02 (0.01, 0.04)	0.02 (0.01, 0.04)	0.200	0.02 (0.01, 0.04)	0.02 (0.00, 0.03)	**0.006**
1,7-DMX	0.15 (0.06, 0.33)	0.15 (0.06, 0.33)	0.16 (0.08, 0.33)	0.400	0.16 (0.06, 0.34)	0.11 (0.03, 0.19)	**<0.001**
3,7-DMX	0.18 (0.07, 0.39)	0.18 (0.07, 0.42)	0.17 (0.07, 0.36)	0.200	0.18 (0.07, 0.40)	0.11 (0.05, 0.23)	**<0.001**
1,3,7-TMX	0.03 (0.01, 0.08)	0.03 (0.01, 0.07)	0.04 (0.01, 0.09)	**<0.001**	0.03 (0.01, 0.08)	0.04 (0.01, 0.08)	0.600
AAMU	0.71 (0.31, 1.35)	0.70 (0.29, 1.35)	0.72 (0.34, 1.35)	0.300	0.72 (0.31, 1.35)	0.61 (0.23, 1.37)	0.500

Notes: [a] Continuous variables were shown as median (inter-quartile range) due to their skewed distributions. [b] Liver steatosis was defined by USFLI ≥30, while advanced liver fibrosis was indicated by NFS >0.676.[c] Continuous variables were compared using the Wilcoxon rank-sum test for complex survey samples.

Table S5 Association of individual urinary caffeine and its metabolites with liver steatosis in subgroup analyses

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
Subgroup: Males (*n* = 983)						
1-MU	1.03 (0.86, 1.22)	Reference	0.92 (0.45, 1.88)	0.86 (0.47, 1.57)	0.97 (0.54, 1.74)	0.868
3-MU	0.95 (0.80, 1.13)	Reference	1.04 (0.56, 1.91)	1.00 (0.55, 1.80)	0.72 (0.37, 1.41)	0.361
7-MU	0.92 (0.78, 1.07)	Reference	0.70 (0.44, 1.11)	0.80 (0.41, 1.53)	0.60 (0.32, 1.11)	0.161
1,3-DMU	**1.20 (1.03, 1.39)***	Reference	1.65 (0.94, 2.91)	1.79 (0.92, 3.49)	1.61 (0.85, 3.03)	0.148
1,7-DMU	**1.17 (1.01, 1.36)***	Reference	1.43 (0.76, 2.70)	1.61 (0.84, 3.07)	1.77 (0.91, 3.44)	0.098
3,7-DMU	0.95 (0.80, 1.12)	Reference	1.00 (0.59, 1.71)	1.34 (0.74, 2.40)	0.63 (0.37, 1.08)	0.251
1,3,7-TMU	**1.28 (1.10, 1.50)****	Reference	1.44 (0.73, 2.84)	1.89 (0.95, 3.76)	**3.13 (1.60, 6.09)****	**0.002**
1-MX	1.05 (0.91, 1.22)	Reference	1.09 (0.58, 2.04)	0.92 (0.47, 1.79)	1.13 (0.64, 2.00)	0.831
3-MX	0.86 (0.73, 1.02)	Reference	0.97 (0.59, 1.59)	0.93 (0.53, 1.65)	**0.43 (0.23, 0.83)***	**0.022**
7-MX	**0.83 (0.69, 0.99)***	Reference	0.74 (0.45, 1.22)	0.90 (0.48, 1.71)	**0.35 (0.19, 0.64)****	**0.007**
1,3-DMX	1.11 (0.95, 1.29)	Reference	1.04 (0.61, 1.79)	1.21 (0.70, 2.08)	1.38 (0.70, 2.71)	0.302
1,7-DMX	1.09 (0.95, 1.26)	Reference	1.90 (1.00, 3.59)	1.24 (0.68, 2.23)	1.45 (0.75, 2.77)	0.499
3,7-DMX	0.94 (0.80, 1.10)	Reference	0.99 (0.58, 1.70)	1.03 (0.60, 1.77)	0.58 (0.30, 1.10)	0.140
1,3,7-TMX	1.15 (1.00, 1.32)	Reference	1.14 (0.64, 2.04)	1.48 (0.81, 2.71)	1.83 (0.89, 3.77)	0.069
AAMU	1.10 (0.92, 1.31)	Reference	1.12 (0.72, 1.73)	1.24 (0.66, 2.32)	1.11 (0.60, 2.04)	0.704
Subgroup: Females (*n* = 1085)						
1-MU	0.80 (0.64, 1.01)	Reference	0.94 (0.49, 1.78)	1.05 (0.51, 2.15)	0.62 (0.29, 1.32)	0.299
3-MU	0.91 (0.75, 1.10)	Reference	0.51 (0.26, 1.00)	1.00 (0.53, 1.90)	0.72 (0.36, 1.44)	0.782
7-MU	0.92 (0.77, 1.08)	Reference	**0.43 (0.23, 0.81)***	0.84 (0.43, 1.65)	0.59 (0.30, 1.16)	0.444
1,3-DMU	1.01 (0.85, 1.21)	Reference	0.92 (0.50, 1.71)	0.88 (0.52, 1.47)	1.39 (0.72, 2.69)	0.387
1,7-DMU	1.02 (0.88, 1.19)	Reference	1.07 (0.57, 2.02)	1.00 (0.58, 1.72)	1.37 (0.73, 2.55)	0.395
3,7-DMU	1.05 (0.87, 1.26)	Reference	**0.44 (0.25, 0.79)***	0.81 (0.44, 1.50)	0.94 (0.52, 1.70)	0.664
1,3,7-TMU	1.11 (0.96, 1.28)	Reference	1.20 (0.64, 2.24)	1.10 (0.62, 1.94)	1.82 (1.02, 3.24)	0.069
1-MX	0.87 (0.73, 1.05)	Reference	1.48 (0.84, 2.61)	0.75 (0.35, 1.62)	0.73 (0.37, 1.44)	0.167
3-MX	0.88 (0.73, 1.05)	Reference	0.52 (0.26, 1.02)	0.75 (0.38, 1.48)	0.59 (0.33, 1.08)	0.258
7-MX	**0.82 (0.69, 0.98)***	Reference	**0.46 (0.24, 0.85)***	0.72 (0.37, 1.42)	**0.46 (0.25, 0.83)***	0.093
1,3-DMX	0.97 (0.82, 1.15)	Reference	1.17 (0.64, 2.15)	0.92 (0.52, 1.62)	1.07 (0.56, 2.02)	0.966
1,7-DMX	0.97 (0.83, 1.13)	Reference	1.20 (0.65, 2.22)	1.07 (0.62, 1.85)	0.99 (0.51, 1.90)	0.879

3,7-DMX	0.97 (0.83, 1.13)	Reference	0.56 (0.31, 1.03)	0.71 (0.38, 1.32)	0.96 (0.52, 1.76)	0.917
1,3,7-TMX	1.06 (0.92, 1.21)	Reference	1.31 (0.62, 2.77)	1.19 (0.68, 2.10)	1.63 (0.88, 3.01)	0.166
AAMU	0.85 (0.68, 1.05)	Reference	0.91 (0.53, 1.55)	1.04 (0.56, 1.94)	0.69 (0.39, 1.23)	0.326
Subgroup: Participants with metabolic syndrome (*n* = 625)						
1-MU	0.83 (0.61, 1.11)	Reference	0.93 (0.46, 1.89)	0.84 (0.38, 1.84)	0.66 (0.29, 1.50)	0.352
3-MU	0.86 (0.65, 1.15)	Reference	0.71 (0.29, 1.74)	0.72 (0.36, 1.41)	0.68 (0.28, 1.62)	0.455
7-MU	0.83 (0.65, 1.06)	Reference	0.49 (0.25, 1.00)	0.45 (0.20, 1.06)	0.41 (0.16, 1.05)	0.089
1,3-DMU	1.08 (0.86, 1.34)	Reference	1.54 (0.67, 3.55)	1.19 (0.63, 2.27)	1.53 (0.62, 3.77)	0.486
1,7-DMU	1.06 (0.87, 1.29)	Reference	1.50 (0.75, 2.98)	1.40 (0.66, 2.95)	1.27 (0.58, 2.80)	0.636
3,7-DMU	0.97 (0.76, 1.25)	Reference	0.60 (0.29, 1.23)	0.64 (0.37, 1.09)	0.92 (0.38, 2.23)	0.899
1,3,7-TMU	1.17 (0.98, 1.40)	Reference	1.52 (0.73, 3.17)	1.32 (0.59, 2.97)	2.08 (0.99, 4.35)	0.122
1-MX	0.93 (0.74, 1.17)	Reference	1.90 (0.94, 3.81)	0.76 (0.34, 1.72)	1.02 (0.48, 2.17)	0.521
3-MX	0.82 (0.62, 1.10)	Reference	0.68 (0.34, 1.37)	**0.40 (0.18, 0.88)***	0.47 (0.18, 1.21)	0.074
7-MX	0.79 (0.59, 1.05)	Reference	**0.38 (0.20, 0.69)****	0.50 (0.26, 1.00)	**0.35 (0.13, 0.93)***	0.083
1,3-DMX	1.04 (0.84, 1.28)	Reference	1.51 (0.75, 3.01)	1.21 (0.59, 2.45)	1.17 (0.53, 2.58)	0.861
1,7-DMX	1.00 (0.83, 1.22)	Reference	1.46 (0.74, 2.86)	1.16 (0.65, 2.07)	1.10 (0.46, 2.59)	0.972
3,7-DMX	0.95 (0.75, 1.20)	Reference	0.83 (0.48, 1.45)	**0.50 (0.28, 0.88)***	0.80 (0.35, 1.83)	0.381
1,3,7-TMX	1.11 (0.94, 1.31)	Reference	1.29 (0.52, 3.17)	1.29 (0.50, 3.34)	1.63 (0.67, 3.97)	0.304
AAMU	0.89 (0.67, 1.17)	Reference	0.94 (0.46, 1.93)	0.82 (0.40, 1.66)	0.86 (0.35, 2.11)	0.688
Subgroup: Participants without metabolic syndrome (*n* = 1443)						
1-MU	0.97 (0.80, 1.17)	Reference	0.89 (0.49, 1.61)	1.10 (0.61, 2.01)	0.84 (0.43, 1.64)	0.782
3-MU	0.97 (0.83, 1.13)	Reference	0.69 (0.39, 1.22)	1.07 (0.58, 1.99)	0.82 (0.43, 1.60)	0.893
7-MU	0.98 (0.85, 1.12)	Reference	0.57 (0.33, 0.99)	1.04 (0.59, 1.83)	0.75 (0.39, 1.44)	0.795
1,3-DMU	1.13 (0.95, 1.33)	Reference	1.04 (0.59, 1.84)	1.25 (0.72, 2.16)	1.57 (0.77, 3.22)	0.214
1,7-DMU	1.12 (0.96, 1.30)	Reference	1.30 (0.79, 2.16)	1.21 (0.64, 2.29)	1.85 (0.91, 3.78)	0.147
3,7-DMU	1.04 (0.89, 1.21)	Reference	0.75 (0.42, 1.33)	1.23 (0.69, 2.18)	0.90 (0.50, 1.60)	0.848
1,3,7-TMU	**1.19 (1.02, 1.39)***	Reference	1.41 (0.76, 2.63)	1.64 (0.86, 3.13)	**2.52 (1.29, 4.90)***	**0.015**
1-MX	0.98 (0.84, 1.14)	Reference	1.10 (0.67, 1.81)	0.89 (0.48, 1.65)	0.89 (0.50, 1.56)	0.546
3-MX	0.91 (0.78, 1.05)	Reference	0.64 (0.36, 1.12)	1.08 (0.59, 1.95)	0.61 (0.32, 1.17)	0.365
7-MX	0.88 (0.77, 1.01)	Reference	0.71 (0.46, 1.11)	1.17 (0.65, 2.13)	**0.54 (0.32, 0.91)***	0.143
1,3-DMX	1.04 (0.88, 1.24)	Reference	0.97 (0.52, 1.81)	0.95 (0.51, 1.79)	1.22 (0.65, 2.30)	0.591

1,7-DMX	1.05 (0.91, 1.21)	Reference	1.60 (0.95, 2.69)	1.16 (0.63, 2.14)	1.34 (0.70, 2.54)	0.610
3,7-DMX	0.97 (0.85, 1.11)	Reference	0.78 (0.45, 1.36)	1.21 (0.70, 2.10)	0.87 (0.49, 1.53)	0.986
1,3,7-TMX	1.08 (0.94, 1.23)	Reference	1.12 (0.61, 2.05)	1.32 (0.60, 2.94)	1.63 (0.83, 3.20)	0.170
AAMU	1.01 (0.83, 1.22)	Reference	1.08 (0.59, 2.00)	1.27 (0.75, 2.14)	0.92 (0.52, 1.64)	0.930

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and caffeine metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender (was not adjusted in the subgroup analysis stratified by gender), race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

Table S6 Association of individual urinary caffeine and its metabolites with advanced liver fibrosis in subgroup analyses

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
Subgroup: Males (*n* = 983)						
1-MU	0.84 (0.59, 1.21)	Reference	1.53 (0.47, 4.97)	0.88 (0.23, 3.37)	1.01 (0.32, 3.14)	0.778
3-MU	0.92 (0.71, 1.20)	Reference	1.92 (0.78, 4.72)	0.89 (0.37, 2.15)	0.68 (0.32, 1.42)	0.164
7-MU	0.84 (0.67, 1.07)	Reference	1.52 (0.59, 3.96)	0.68 (0.21, 2.22)	0.62 (0.26, 1.52)	0.168
1,3-DMU	0.92 (0.68, 1.23)	Reference	0.72 (0.26, 2.01)	0.68 (0.22, 2.11)	0.86 (0.32, 2.31)	0.746
1,7-DMU	0.93 (0.70, 1.23)	Reference	0.88 (0.31, 2.51)	0.87 (0.24, 3.15)	0.79 (0.28, 2.24)	0.689
3,7-DMU	0.90 (0.69, 1.17)	Reference	0.93 (0.37, 2.34)	0.99 (0.39, 2.49)	0.53 (0.20, 1.45)	0.270
1,3,7-TMU	0.99 (0.74, 1.32)	Reference	0.79 (0.29, 2.14)	1.40 (0.44, 4.46)	1.16 (0.37, 3.60)	0.595
1-MX	0.78 (0.56, 1.07)	Reference	0.53 (0.21, 1.34)	0.44 (0.15, 1.33)	0.56 (0.20, 1.61)	0.276
3-MX	0.79 (0.62, 1.01)	Reference	1.62 (0.60, 4.36)	0.41 (0.16, 1.07)	0.66 (0.29, 1.47)	0.060
7-MX	**0.71 (0.55, 0.90)***	Reference	0.66 (0.24, 1.81)	0.46 (0.20, 1.04)	**0.30 (0.12, 0.75)***	**0.016**
1,3-DMX	0.88 (0.66, 1.17)	Reference	0.79 (0.27, 2.33)	0.89 (0.33, 2.39)	0.58 (0.17, 2.01)	0.431
1,7-DMX	0.85 (0.63, 1.15)	Reference	1.09 (0.39, 3.04)	0.86 (0.30, 2.47)	0.52 (0.15, 1.77)	0.276
3,7-DMX	0.83 (0.66, 1.03)	Reference	0.79 (0.32, 1.93)	0.52 (0.19, 1.41)	0.50 (0.21, 1.18)	0.091
1,3,7-TMX	0.95 (0.73, 1.23)	Reference	0.98 (0.37, 2.62)	1.07 (0.39, 2.98)	1.04 (0.34, 3.14)	0.912
AAMU	0.81 (0.61, 1.07)	Reference	**0.24 (0.07, 0.80)***	0.45 (0.14, 1.44)	0.43 (0.16, 1.18)	0.238
Subgroup: Females (*n* = 1085)						
1-MU	0.66 (0.41, 1.05)	Reference	**0.18 (0.07, 0.42)*****	**0.32 (0.13, 0.77)***	**0.17 (0.05, 0.61)***	**0.028**
3-MU	0.87 (0.64, 1.19)	Reference	1.81 (0.84, 3.90)	1.37 (0.56, 3.38)	0.76 (0.27, 2.12)	0.556
7-MU	0.83 (0.65, 1.05)	Reference	0.96 (0.42, 2.17)	0.63 (0.24, 1.66)	0.45 (0.17, 1.21)	0.126
1,3-DMU	**0.71 (0.53, 0.94)***	Reference	0.51 (0.18, 1.43)	**0.32 (0.12, 0.89)***	**0.22 (0.06, 0.74)***	**0.022**
1,7-DMU	0.79 (0.61, 1.01)	Reference	0.93 (0.30, 2.89)	0.39 (0.13, 1.19)	0.30 (0.09, 1.07)	**0.043**
3,7-DMU	**0.75 (0.58, 0.97)***	Reference	0.69 (0.27, 1.80)	0.91 (0.40, 2.04)	0.36 (0.13, 1.00)	0.082
1,3,7-TMU	0.78 (0.60, 1.01)	Reference	0.46 (0.13, 1.59)	0.63 (0.21, 1.92)	**0.23 (0.06, 0.84)***	0.071
1-MX	**0.68 (0.49, 0.96)***	Reference	**0.44 (0.21, 0.91)***	**0.30 (0.10, 0.90)***	**0.19 (0.05, 0.67)***	**0.020**
3-MX	0.81 (0.62, 1.06)	Reference	0.73 (0.27, 1.94)	0.76 (0.32, 1.82)	0.41 (0.15, 1.11)	0.162

7-MX	**0.78 (0.61, 0.98)***	Reference	0.85 (0.36, 1.99)	0.88 (0.41, 1.85)	0.47 (0.18, 1.23)	0.150
1,3-DMX	**0.69 (0.53, 0.91)***	Reference	0.39 (0.14, 1.10)	**0.34 (0.15, 0.76)***	**0.17 (0.05, 0.61)***	**0.012**
1,7-DMX	**0.74 (0.59, 0.93)***	Reference	0.53 (0.22, 1.26)	**0.21 (0.07, 0.61)****	**0.20 (0.06, 0.61)***	**0.006**
3,7-DMX	**0.79 (0.65, 0.96)***	Reference	0.59 (0.29, 1.22)	**0.40 (0.18, 0.91)***	**0.33 (0.12, 0.88)***	**0.048**
1,3,7-TMX	0.81 (0.64, 1.03)	Reference	0.59 (0.19, 1.88)	0.54 (0.21, 1.38)	0.29 (0.07, 1.20)	0.105
AAMU	**0.67 (0.48, 0.95)***	Reference	0.88 (0.30, 2.53)	**0.26 (0.09, 0.74)***	**0.24 (0.06, 0.91)***	**0.016**
Subgroup: Participants with metabolic syndrome (*n* = 625)						
1-MU	0.78 (0.57, 1.07)	Reference	0.59 (0.22, 1.56)	0.68 (0.26, 1.75)	0.52 (0.19, 1.38)	0.251
3-MU	0.96 (0.78, 1.19)	Reference	1.39 (0.64, 3.02)	1.18 (0.61, 2.28)	0.83 (0.41, 1.65)	0.517
7-MU	0.89 (0.73, 1.08)	Reference	0.91 (0.42, 1.98)	0.61 (0.30, 1.25)	0.64 (0.29, 1.45)	0.182
1,3-DMU	0.86 (0.68, 1.08)	Reference	1.13 (0.41, 3.09)	0.68 (0.28, 1.61)	0.72 (0.32, 1.63)	0.243
1,7-DMU	0.88 (0.71, 1.09)	Reference	1.50 (0.49, 4.61)	1.01 (0.35, 2.88)	0.59 (0.25, 1.42)	0.156
3,7-DMU	0.88 (0.71, 1.08)	Reference	0.88 (0.46, 1.70)	1.16 (0.60, 2.25)	0.62 (0.27, 1.41)	0.368
1,3,7-TMU	0.90 (0.74, 1.10)	Reference	0.99 (0.36, 2.78)	1.52 (0.61, 3.79)	0.69 (0.31, 1.53)	0.593
1-MX	0.77 (0.59, 1.00)	Reference	0.71 (0.33, 1.53)	0.54 (0.24, 1.22)	0.44 (0.18, 1.09)	0.081
3-MX	0.91 (0.74, 1.11)	Reference	0.83 (0.36, 1.89)	0.53 (0.29, 1.00)	0.69 (0.32, 1.50)	0.193
7-MX	0.84 (0.68, 1.03)	Reference	0.87 (0.43, 1.75)	0.73 (0.42, 1.28)	0.62 (0.28, 1.38)	0.212
1,3-DMX	0.80 (0.64, 1.00)	Reference	0.70 (0.25, 1.98)	0.72 (0.30, 1.70)	0.40 (0.17, 1.00)	0.051
1,7-DMX	0.80 (0.63, 1.01)	Reference	0.93 (0.41, 2.09)	0.76 (0.33, 1.76)	0.33 (0.12, 1.00)	**0.042**
3,7-DMX	0.85 (0.72, 1.01)	Reference	0.78 (0.38, 1.60)	0.58 (0.31, 1.07)	0.67 (0.34, 1.31)	0.185
1,3,7-TMX	0.87 (0.72, 1.05)	Reference	0.88 (0.34, 2.27)	0.85 (0.33, 2.15)	0.64 (0.27, 1.49)	0.322
AAMU	0.79 (0.62, 1.02)	Reference	0.59 (0.20, 1.78)	0.41 (0.15, 1.13)	**0.43 (0.20, 0.92)***	**0.035**
Subgroup: Participants without metabolic syndrome (*n* = 1443)						
1-MU	0.72 (0.44, 1.20)	Reference	**0.19 (0.06, 0.63)***	**0.23 (0.07, 0.77)***	0.23 (0.06, 1.00)	0.061
3-MU	0.82 (0.55, 1.21)	Reference	3.59 (0.85, 15.11)	0.95 (0.28, 3.29)	1.06 (0.21, 5.20)	0.630
7-MU	0.78 (0.60, 1.02)	Reference	1.85 (0.65, 5.26)	0.62 (0.20, 1.87)	0.50 (0.12, 2.04)	0.156
1,3-DMU	0.74 (0.54, 1.00)	Reference	**0.10 (0.02, 0.47)****	0.36 (0.12, 1.06)	**0.20 (0.05, 0.80)***	0.166
1,7-DMU	0.82 (0.62, 1.09)	Reference	0.26 (0.06, 1.06)	0.36 (0.13, 1.00)	0.38 (0.09, 1.71)	0.327
3,7-DMU	0.70 (0.49, 1.00)	Reference	0.51 (0.18, 1.43)	0.41 (0.12, 1.34)	0.28 (0.08, 1.02)	0.073

1,3,7-TMU	0.81 (0.59, 1.13)	Reference	0.32 (0.09, 1.09)	0.53 (0.17, 1.68)	0.29 (0.05, 1.57)	0.247
1-MX	**0.67 (0.46, 0.96)***	Reference	**0.20 (0.08, 0.52)****	**0.18 (0.06, 0.59)***	**0.22 (0.06, 0.85)***	**0.043**
3-MX	0.75 (0.57, 1.00)	Reference	1.53 (0.54, 4.32)	0.60 (0.23, 1.58)	0.39 (0.09, 1.65)	0.111
7-MX	**0.67 (0.51, 0.88)***	Reference	0.40 (0.13, 1.17)	0.38 (0.13, 1.13)	**0.24 (0.08, 0.74)***	**0.044**
1,3-DMX	0.75 (0.55, 1.03)	Reference	0.47 (0.18, 1.20)	0.38 (0.11, 1.30)	0.19 (0.04, 0.94)	0.064
1,7-DMX	0.79 (0.62, 1.01)	Reference	0.71 (0.27, 1.82)	**0.18 (0.04, 0.69)***	0.27 (0.07, 1.08)	**0.035**
3,7-DMX	0.78 (0.61, 1.01)	Reference	0.38 (0.12, 1.16)	**0.20 (0.06, 0.69)***	**0.20 (0.05, 0.80)***	**0.029**
1,3,7-TMX	0.85 (0.64, 1.12)	Reference	0.49 (0.15, 1.58)	0.71 (0.26, 1.98)	0.34 (0.07, 1.70)	0.293
AAMU	**0.66 (0.46, 0.95)***	Reference	0.39 (0.12, 1.29)	**0.25 (0.07, 0.85)***	0.24 (0.06, 1.00)	**0.049**

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and its metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender (was not adjusted in the subgroup analysis stratified by gender), race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.

Table S7 Association of individual urinary caffeine and its metabolites with non-alcoholic fatty liver disease (***n*=1815**)

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
1-MU	0.97 (0.83, 1.14)	Reference	1.03 (0.67, 1.59)	1.12 (0.74, 1.71)	0.89 (0.55, 1.44)	0.740
3-MU	0.97 (0.83, 1.12)	Reference	0.83 (0.54, 1.28)	1.12 (0.73, 1.73)	0.87 (0.50, 1.48)	0.883
7-MU	0.92 (0.81, 1.06)	Reference	0.62 (0.39, 1.00)	0.87 (0.56, 1.36)	0.64 (0.35, 1.18)	0.300
1,3-DMU	1.15 (1.00, 1.32)	Reference	1.42 (0.88, 2.32)	1.37 (0.90, 2.07)	**1.88 (1.08, 3.28)***	0.055
1,7-DMU	1.14 (1.00, 1.30)	Reference	1.35 (0.86, 2.12)	1.46 (0.92, 2.31)	**1.84 (1.07, 3.19)***	**0.044**
3,7-DMU	1.00 (0.87, 1.16)	Reference	0.76 (0.50, 1.18)	1.09 (0.76, 1.56)	0.84 (0.52, 1.36)	0.832
1,3,7-TMU	**1.23 (1.08, 1.41)****	Reference	1.50 (0.89, 2.52)	**1.76 (1.08, 2.87)***	**2.79 (1.61, 4.84)****	**0.001**
1-MX	1.00 (0.88, 1.14)	Reference	1.46 (0.99, 2.15)	0.98 (0.60, 1.61)	1.07 (0.71, 1.62)	0.798
3-MX	0.89 (0.76, 1.02)	Reference	0.74 (0.50, 1.11)	0.85 (0.57, 1.26)	0.55 (0.31, 1.00)	0.083
7-MX	**0.84 (0.73, 0.98)***	Reference	0.71 (0.51, 1.00)	0.85 (0.55, 1.32)	**0.47 (0.27, 0.81)***	**0.030**
1,3-DMX	1.08 (0.94, 1.23)	Reference	1.16 (0.70, 1.92)	1.13 (0.73, 1.75)	1.39 (0.82, 2.36)	0.273
1,7-DMX	1.07 (0.95, 1.21)	Reference	1.57 (0.97, 2.56)	1.18 (0.75, 1.86)	1.39 (0.82, 2.36)	0.365
3,7-DMX	0.97 (0.85, 1.10)	Reference	0.73 (0.51, 1.05)	0.84 (0.60, 1.18)	0.78 (0.47, 1.30)	0.457
1,3,7-TMX	**1.14 (1.02, 1.27)***	Reference	1.40 (0.82, 2.39)	1.58 (0.93, 2.68)	**2.06 (1.27, 3.35)****	**0.008**
AAMU	1.03 (0.88, 1.20)	Reference	1.33 (0.93, 1.91)	1.33 (0.82, 2.14)	1.03 (0.63, 1.67)	0.926

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and its metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender, race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. In this additional analysis, participants with excessive alcohol consumption and viral hepatitis were excluded before analysis. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.

Table S8 Association of individual urinary caffeine and its metabolites with metabolic dysfunction-associated fatty liver disease (***n*=2068**)

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
1-MU	0.93 (0.81, 1.07)	Reference	1.01 (0.65, 1.56)	1.01 (0.66, 1.52)	0.80 (0.50, 1.27)	0.366
3-MU	0.93 (0.82, 1.06)	Reference	0.77 (0.50, 1.20)	1.04 (0.68, 1.58)	0.75 (0.46, 1.20)	0.481
7-MU	0.93 (0.82, 1.04)	Reference	**0.61 (0.43, 0.87)***	0.84 (0.59, 1.20)	0.61 (0.37, 1.00)	0.148
1,3-DMU	**1.14 (1.01, 1.28)***	Reference	1.33 (0.86, 2.07)	1.34 (0.94, 1.90)	1.59 (0.96, 2.65)	0.103
1,7-DMU	1.12 (1.00, 1.26)	Reference	1.36 (0.96, 1.92)	1.42 (0.91, 2.21)	1.65 (1.00, 2.69)	0.073
3,7-DMU	1.02 (0.90, 1.16)	Reference	0.73 (0.50, 1.06)	1.11 (0.78, 1.56)	0.85 (0.55, 1.30)	0.917
1,3,7-TMU	**1.22 (1.09, 1.37)****	Reference	1.43 (0.90, 2.26)	**1.64 (1.06, 2.53)***	**2.56 (1.59, 4.12)****	**0.001**
1-MX	0.98 (0.88, 1.09)	Reference	1.37 (0.93, 2.00)	0.91 (0.58, 1.45)	0.97 (0.65, 1.45)	0.474
3-MX	0.89 (0.78, 1.01)	Reference	0.79 (0.55, 1.14)	0.87 (0.60, 1.25)	**0.56 (0.34, 0.93)***	**0.048**
7-MX	**0.84 (0.74, 0.96)***	Reference	**0.63 (0.49, 0.81)****	0.85 (0.57, 1.27)	**0.43 (0.27, 0.69)****	**0.010**
1,3-DMX	1.07 (0.95, 1.21)	Reference	1.18 (0.74, 1.86)	1.15 (0.78, 1.70)	1.30 (0.78, 2.16)	0.375
1,7-DMX	1.06 (0.95, 1.18)	Reference	**1.66 (1.12, 2.45)***	1.22 (0.83, 1.78)	1.30 (0.81, 2.11)	0.513
3,7-DMX	0.97 (0.86, 1.10)	Reference	0.87 (0.60, 1.27)	0.94 (0.68, 1.30)	0.83 (0.51, 1.36)	0.519
1,3,7-TMX	**1.12 (1.01, 1.24)***	Reference	1.31 (0.83, 2.06)	1.43 (0.89, 2.30)	**1.86 (1.17, 2.96)***	**0.019**
AAMU	0.99 (0.87, 1.13)	Reference	1.07 (0.81, 1.42)	1.20 (0.78, 1.85)	0.88 (0.58, 1.33)	0.729

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and its metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender, race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.

Table S9 Association of individual urinary caffeine and its metabolites with liver steatosis defined by FLI(+) (***n*=2068**)

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
1-MU	0.89 (0.78, 1.01)	Reference	0.95 (0.62, 1.46)	1.04 (0.70, 1.55)	**0.64 (0.43, 0.95)***	0.052
3-MU	0.96 (0.84, 1.09)	Reference	0.90 (0.60, 1.36)	1.06 (0.65, 1.72)	0.81 (0.50, 1.33)	0.561
7-MU	0.96 (0.86, 1.08)	Reference	**0.61 (0.43, 0.88)***	0.94 (0.63, 1.41)	0.73 (0.48, 1.12)	0.461
1,3-DMU	1.03 (0.94, 1.12)	Reference	1.00 (0.68, 1.48)	1.17 (0.80, 1.71)	0.99 (0.68, 1.45)	0.812
1,7-DMU	1.03 (0.95, 1.12)	Reference	0.99 (0.70, 1.40)	1.26 (0.85, 1.87)	0.97 (0.66, 1.42)	0.797
3,7-DMU	0.97 (0.86, 1.09)	Reference	0.89 (0.60, 1.31)	1.15 (0.78, 1.69)	0.84 (0.56, 1.28)	0.686
1,3,7-TMU	1.06 (0.98, 1.15)	Reference	0.91 (0.59, 1.40)	1.22 (0.78, 1.91)	1.36 (0.90, 2.05)	0.067
1-MX	**0.90 (0.81, 0.99)***	Reference	1.31 (0.93, 1.87)	1.03 (0.72, 1.47)	**0.67 (0.48, 0.93)***	**0.013**
3-MX	0.91 (0.81, 1.03)	Reference	0.91 (0.63, 1.31)	0.88 (0.58, 1.34)	0.69 (0.44, 1.09)	0.128
7-MX	**0.85 (0.76, 0.96)***	Reference	0.73 (0.51, 1.04)	0.73 (0.48, 1.09)	**0.49 (0.32, 0.74)****	**0.006**
1,3-DMX	0.98 (0.90, 1.07)	Reference	0.81 (0.51, 1.29)	0.96 (0.60, 1.54)	0.87 (0.57, 1.31)	0.708
1,7-DMX	0.97 (0.90, 1.05)	Reference	1.25 (0.78, 2.01)	0.95 (0.63, 1.42)	0.91 (0.60, 1.38)	0.360
3,7-DMX	0.95 (0.86, 1.05)	Reference	0.95 (0.67, 1.35)	0.95 (0.69, 1.32)	0.87 (0.59, 1.28)	0.515
1,3,7-TMX	1.04 (0.96, 1.12)	Reference	0.82 (0.55, 1.22)	1.00 (0.60, 1.65)	1.18 (0.78, 1.77)	0.336
AAMU	0.93 (0.83, 1.04)	Reference	1.05 (0.73, 1.51)	1.10 (0.71, 1.71)	0.71 (0.47, 1.06)	0.153

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and its metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender, race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.

Table S10 Association of individual urinary caffeine and its metabolites with liver steatosis defined by FLI(+)/USFLI(+) (***n*=2068**)

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
1-MU	0.91 (0.80, 1.04)	Reference	1.04 (0.67, 1.61)	1.17 (0.79, 1.74)	0.69 (0.47, 1.03)	0.136
3-MU	0.96 (0.84, 1.10)	Reference	0.90 (0.60, 1.34)	0.95 (0.59, 1.55)	0.78 (0.48, 1.28)	0.409
7-MU	0.96 (0.86, 1.09)	Reference	**0.61 (0.43, 0.87)***	0.94 (0.62, 1.43)	0.70 (0.44, 1.09)	0.373
1,3-DMU	1.05 (0.96, 1.15)	Reference	1.00 (0.68, 1.47)	1.32 (0.90, 1.94)	1.09 (0.74, 1.61)	0.405
1,7-DMU	1.05 (0.97, 1.14)	Reference	0.99 (0.70, 1.40)	1.37 (0.92, 2.04)	1.07 (0.72, 1.59)	0.414
3,7-DMU	0.98 (0.87, 1.11)	Reference	0.91 (0.60, 1.38)	1.20 (0.79, 1.82)	0.86 (0.55, 1.36)	0.817
1,3,7-TMU	1.09 (1.00, 1.18)	Reference	0.96 (0.63, 1.46)	1.31 (0.85, 2.02)	**1.56 (1.03, 2.36)***	**0.018**
1-MX	0.92 (0.83, 1.02)	Reference	1.30 (0.92, 1.83)	1.03 (0.71, 1.50)	0.75 (0.54, 1.05)	0.051
3-MX	0.92 (0.81, 1.04)	Reference	0.84 (0.59, 1.20)	0.90 (0.58, 1.40)	0.67 (0.42, 1.06)	0.134
7-MX	**0.86 (0.76, 0.97)***	Reference	0.73 (0.51, 1.06)	0.77 (0.51, 1.17)	**0.48 (0.31, 0.76)****	**0.010**
1,3-DMX	1.00 (0.91, 1.09)	Reference	0.84 (0.54, 1.31)	1.05 (0.66, 1.67)	0.94 (0.61, 1.46)	0.952
1,7-DMX	0.99 (0.91, 1.07)	Reference	1.19 (0.75, 1.90)	0.96 (0.60, 1.52)	0.95 (0.62, 1.47)	0.580
3,7-DMX	0.96 (0.86, 1.07)	Reference	0.93 (0.62, 1.39)	0.94 (0.64, 1.37)	0.86 (0.55, 1.34)	0.528
1,3,7-TMX	1.06 (0.98, 1.15)	Reference	0.84 (0.57, 1.23)	1.07 (0.64, 1.80)	1.36 (0.89, 2.09)	0.129
AAMU	0.94 (0.84, 1.06)	Reference	1.06 (0.74, 1.52)	1.20 (0.78, 1.86)	0.74 (0.49, 1.13)	0.290

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and its metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender, race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.

Table S11 Association of individual urinary caffeine and its metabolites with advanced liver fibrosis among participants without excessive alcohol consumption and viral hepatitis (***n*=1815**)

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
1-MU	**0.74 (0.60, 0.92)***	Reference	**0.42 (0.19, 0.94)***	**0.37 (0.17, 0.80)***	**0.35 (0.16, 0.76)***	**0.013**
3-MU	0.87 (0.71, 1.05)	Reference	1.33 (0.79, 2.24)	1.01 (0.58, 1.75)	0.70 (0.38, 1.31)	0.232
7-MU	**0.83 (0.73, 0.95)***	Reference	1.09 (0.55, 2.14)	0.72 (0.45, 1.16)	**0.53 (0.31, 0.90)***	**0.014**
1,3-DMU	**0.79 (0.66, 0.95)***	Reference	0.45 (0.19, 1.08)	**0.42 (0.20, 0.85)***	**0.40 (0.19, 0.84)***	**0.021**
1,7-DMU	0.84 (0.72, 1.00)	Reference	0.82 (0.35, 1.96)	0.55 (0.23, 1.28)	0.48 (0.22, 1.05)	0.058
3,7-DMU	**0.80 (0.68, 0.93)****	Reference	0.77 (0.45, 1.31)	0.89 (0.48, 1.63)	**0.42 (0.22, 0.81)***	**0.027**
1,3,7-TMU	0.86 (0.72, 1.02)	Reference	0.61 (0.23, 1.62)	0.85 (0.39, 1.82)	0.46 (0.19, 1.09)	0.147
1-MX	**0.72 (0.60, 0.86)****	Reference	**0.45 (0.22, 0.91)***	**0.28 (0.14, 0.57)****	**0.32 (0.15, 0.67)****	**0.003**
3-MX	**0.81 (0.70, 0.93)****	Reference	0.95 (0.50, 1.80)	0.61 (0.38, 1.00)	**0.50 (0.31, 0.82)***	**0.007**
7-MX	**0.75 (0.66, 0.85)*****	Reference	0.79 (0.48, 1.30)	0.71 (0.39, 1.30)	**0.38 (0.22, 0.66)****	**0.005**
1,3-DMX	**0.77 (0.66, 0.90)****	Reference	0.57 (0.26, 1.26)	0.53 (0.25, 1.09)	**0.30 (0.13, 0.68)****	**0.006**
1,7-DMX	**0.79 (0.69, 0.91)****	Reference	0.76 (0.41, 1.39)	**0.51 (0.29, 0.91)***	**0.32 (0.16, 0.64)****	**0.002**
3,7-DMX	**0.82 (0.73, 0.91)****	Reference	0.64 (0.33, 1.25)	**0.41 (0.24, 0.72)****	**0.42 (0.24, 0.72)****	**0.003**
1,3,7-TMX	0.86 (0.74, 1.00)	Reference	0.62 (0.29, 1.33)	0.66 (0.30, 1.42)	0.46 (0.19, 1.07)	0.120
AAMU	**0.72 (0.59, 0.89)****	Reference	0.48 (0.20, 1.14)	**0.35 (0.17, 0.72)***	**0.33 (0.15, 0.70)***	**0.004**

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and its metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender, race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.

Table S12 Association of individual urinary caffeine and its metabolites with advanced liver fibrosis defined by FIB-4(+) (***n*=2068**)

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
1-MU	0.80 (0.60, 1.05)	Reference	0.54 (0.25, 1.14)	**0.36 (0.16, 0.80)***	**0.43 (0.21, 0.88)***	**0.023**
3-MU	0.97 (0.76, 1.24)	Reference	0.79 (0.36, 1.74)	1.11 (0.53, 2.32)	0.69 (0.29, 1.60)	0.590
7-MU	0.89 (0.75, 1.07)	Reference	1.10 (0.47, 2.57)	1.17 (0.58, 2.36)	0.76 (0.35, 1.63)	0.544
1,3-DMU	**0.81 (0.69, 0.96)***	Reference	0.52 (0.22, 1.26)	**0.26 (0.12, 0.56)****	**0.45 (0.21, 0.94)***	**0.020**
1,7-DMU	**0.85 (0.74, 0.99)***	Reference	0.43 (0.19, 1.00)	**0.34 (0.15, 0.75)***	**0.42 (0.19, 0.90)***	**0.030**
3,7-DMU	0.82 (0.66, 1.02)	Reference	1.06 (0.53, 2.12)	0.79 (0.29, 2.15)	0.50 (0.24, 1.03)	0.081
1,3,7-TMU	0.88 (0.76, 1.01)	Reference	**0.35 (0.15, 0.79)***	0.77 (0.36, 1.62)	**0.40 (0.19, 0.83)***	0.108
1-MX	**0.74 (0.63, 0.87)****	Reference	**0.41 (0.20, 0.87)***	**0.19 (0.09, 0.41)*****	**0.37 (0.19, 0.72)****	**0.001**
3-MX	0.88 (0.74, 1.04)	Reference	0.79 (0.31, 2.05)	1.09 (0.50, 2.36)	0.57 (0.28, 1.13)	0.272
7-MX	**0.81 (0.68, 0.97)***	Reference	1.02 (0.54, 1.92)	0.83 (0.30, 2.26)	0.58 (0.29, 1.18)	0.157
1,3-DMX	**0.81 (0.70, 0.94)***	Reference	0.60 (0.30, 1.21)	**0.43 (0.21, 0.88)***	**0.40 (0.19, 0.84)***	**0.012**
1,7-DMX	**0.80 (0.70, 0.91)****	Reference	**0.43 (0.24, 0.76)****	**0.38 (0.20, 0.71)****	**0.43 (0.24, 0.78)***	**0.016**
3,7-DMX	**0.85 (0.74, 0.98)***	Reference	0.80 (0.32, 2.02)	0.65 (0.26, 1.63)	**0.38 (0.19, 0.76)***	**0.011**
1,3,7-TMX	0.89 (0.77, 1.02)	Reference	0.42 (0.18, 1.00)	0.59 (0.26, 1.31)	0.53 (0.24, 1.14)	0.193
AAMU	**0.72 (0.58, 0.90)****	Reference	**0.37 (0.15, 0.89)***	**0.25 (0.11, 0.57)****	**0.35 (0.19, 0.66)****	**0.002**

Notes: [a], The caffeine and its metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and its metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender, race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.

Table S13 Association of urinary caffeine and its metabolites with advanced liver fibrosis defined by NFS(+)/FIB-4(+)/APRI(+) (***n*=2068**)

Metabolites	Continuous [a]	Quantile1 [b]	Quantile2	Quantile3	Quantile4	*P* for trend
1-MU	0.79 (0.63, 1.00)	Reference	0.48 (0.24, 1.00)	**0.46 (0.23, 0.94)***	**0.43 (0.20, 0.93)***	**0.047**
3-MU	0.91 (0.74, 1.11)	Reference	1.13 (0.63, 2.04)	1.13 (0.61, 2.08)	**0.75 (0.39, 1.42)**	0.445
7-MU	**0.83 (0.72, 0.96)***	Reference	1.09 (0.58, 2.07)	0.88 (0.52, 1.48)	0.63 (0.35, 1.14)	0.111
1,3-DMU	**0.84 (0.71, 0.98)***	Reference	0.55 (0.25, 1.22)	**0.35 (0.17, 0.70)****	0.57 (0.28, 1.16)	0.069
1,7-DMU	0.87 (0.75, 1.00)	Reference	0.63 (0.32, 1.26)	0.48 (0.23, 1.03)	0.56 (0.27, 1.16)	0.110
3,7-DMU	**0.81 (0.68, 0.97)***	Reference	0.89 (0.51, 1.55)	0.71 (0.39, 1.28)	0.54 (0.29, 1.00)	**0.047**
1,3,7-TMU	0.89 (0.76, 1.04)	Reference	0.60 (0.28, 1.29)	0.85 (0.40, 1.79)	0.59 (0.29, 1.22)	0.323
1-MX	**0.76 (0.65, 0.89)****	Reference	**0.39 (0.20, 0.75)***	**0.28 (0.14, 0.58)****	**0.39 (0.22, 0.71)****	**0.002**
3-MX	**0.82 (0.70, 0.96)***	Reference	0.78 (0.41, 1.49)	0.78 (0.48, 1.25)	**0.54 (0.33, 0.88)***	**0.040**
7-MX	**0.77 (0.67, 0.89)****	Reference	0.87 (0.53, 1.44)	0.73 (0.39, 1.37)	**0.54 (0.31, 0.94)***	**0.044**
1,3-DMX	**0.81 (0.70, 0.93)****	Reference	0.62 (0.30, 1.29)	**0.41 (0.19, 0.87)***	0.48 (0.23, 1.00)	**0.027**
1,7-DMX	**0.81 (0.72, 0.91)****	Reference	0.56 (0.29, 1.08)	**0.43 (0.25, 0.74)****	**0.46 (0.26, 0.82)***	**0.011**
3,7-DMX	**0.82 (0.73, 0.91)****	Reference	0.79 (0.45, 1.38)	**0.44 (0.24, 0.79)***	**0.48 (0.30, 0.78)****	**0.002**
1,3,7-TMX	0.89 (0.78, 1.01)	Reference	0.64 (0.32, 1.30)	0.68 (0.30, 1.55)	0.54 (0.26, 1.16)	0.185
AAMU	**0.74 (0.61, 0.91)****	Reference	0.45 (0.20, 1.00)	**0.37 (0.19, 0.74)***	**0.42 (0.22, 0.83)***	**0.017**

Notes: [a], The caffeine and caffeine metabolites were corrected with urinary creatinine and ln-transformed and then introduced into survey-weighted multivariate logistic regression models as continuous variables. [b], The caffeine and caffeine metabolites were corrected with urinary creatinine and classified into four groups based on quartile and then introduced into survey-weighted multivariate logistic regression models as categorical variables. The models were adjusted for all covariates, including age, gender, race/ethnicity, education level, marriage status, PIR, smoking status, daily alcohol intake, physical activity, BMI, hypertension, HbA1c, daily energy intake, and survey cycle. The results are depicted as odds ratios (95% confidence intervals). **Bold font** indicates statistically significant; *, P <0.05; **, P <0.01; ***, P <0.001.