

## *Supplementary materials*

# **Exposure to Volatile Organic Compounds in Relation to Visceral Adiposity Index and Lipid Accumulation Product among Adults: NHANES 2011-2018**

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## **Text S1. Assessment of covariates**

The DEMO module of the NHANES database provides demographic information, including gender (male or female), age (continuous), race (Hispanic, non-Hispanic White, non-Hispanic Black, and other races), education level (high school graduate and below, and above high school), and PIR (continuous). BMI was categorized into three levels: normal weight ( $< 25 \text{ kg/m}^2$ ), overweight ( $25\text{--}30 \text{ kg/m}^2$ ), and obesity ( $\geq 30 \text{ kg/m}^2$ ). Having smoked at least 100 cigarettes in a lifetime was defined as a self-reported smoker. Serum cotinine is a biomarker of nicotine exposure with a lower limit of detection of 0.015 ng/mL. Serum cotinine concentration was used to determine whether an individual is tobacco-free ( $< 0.015 \text{ ng/mL}$ ) or tobacco-exposed ( $\geq 0.015 \text{ ng/mL}$ ). Average daily alcohol consumption in the past 12 months (continuous) was calculated based on the alcohol use data [1]. Different types of physical activity have different metabolic equivalent (MET) values. Physical activity was calculated based on the type of activity, MET value, weekly frequency, and duration. Physical activity was finally categorized into three levels: no physical activity ( $< 1 \text{ MET-h/wk}$ ), moderate physical activity ( $1\text{--}48 \text{ MET-h/wk}$ ), and vigorous physical activity ( $> 48 \text{ MET-h/wk}$ ) [2]. HEI-2015 is an indicator that assesses whether a set of foods aligns with the 2015-2020 Dietary Guidelines for Americans, with a maximum score of 100, and a higher score indicates a healthier diet [3]. The HEI-2015 (continuous) in this study was assessed based on data from the first 24 hour dietary recall interview. Participants were considered to have diabetes if they met one of the following conditions: fasting blood glucose  $\geq 126 \text{ mg/dL}$ , HbA1c level  $\geq 6.5\%$ , oral glucose tolerance test  $\geq 200 \text{ mg/dL}$ , a self-reported medical diagnosis, or current use of oral hypoglycemic medication or insulin [4]. Hypertension was defined as a systolic blood pressure  $\geq 140 \text{ mmHg}$  or a diastolic blood pressure  $\geq 90 \text{ mmHg}$ , or receiving a medical diagnosis from a healthcare professional [5]. Self-reported medical diagnoses of congestive heart failure, coronary heart disease, angina pectoris, heart attack, or stroke were defined as CVD [6].

**Table S1. Parent compounds, LLODs, detection rates, and descriptive statistics (*n* = 2015) for urinary mVOCs included in the analysis.**

VOC metabolites	Abbreviation	Parent compound	LLOD (µg/L)	Detection rate (%)	Median [IQR] (ng/mL)
2-methylhippuric acid	2MHA	Xylene	5	92.36	33.80 [13.35, 82.60]
3- and 4-methylhippuric acid	3-4MHA	Xylene	8	99.60	230.00 [93.40, 600.50]
N-acetyl-S-(2-carbamoyl-ethyl)-L-cysteine	AAMA	Acrylamide	2.2	99.95	53.80 [28.75, 108.00]
N-acetyl-S-(N-methylcarbamoyl)-L-cysteine	AMCC	N, N-Dimethylformamide	6.26	99.90	166.00 [85.45, 323.00]
2-aminothiazoline-4-carboxylic acid	ATCA	Cyanide	15	93.45	105.00 [50.65, 205.00]
N-acetyl-S-(benzyl)-L-cysteine	BMA	Toluene	0.5	99.80	6.75 [3.66, 13.30]
N-acetyl-S-(n-propyl)-L-cysteine	BPMA	1-Bromopropane	1.2	79.55	4.13 [1.51, 10.95]
N-acetyl-S-(2-carboxyethyl)-L-cysteine	CEMA	Acrolein	6.96	99.55	100.00 [53.50, 189.00]
N-acetyl-S-(2-cyanoethyl)-L-cysteine	CYMA	Acrylonitrile	0.5	87.84	1.71 [0.87, 14.60]
N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine	DHBMA	1,3-Butadiene	5.25	100.00	325.00 [197.00, 501.50]
N-acetyl-S-(2-hydroxypropyl)-L-cysteine	2HPMA	Propylene oxide	5.3	97.22	32.40 [17.30, 62.20]
N-acetyl-S-(3-hydroxypropyl)-L-cysteine	3HPMA	Acrolein	13	99.90	224.00 [121.50, 444.50]
Mandelic acid	MA	Styrene	12	99.06	136.00 [80.15, 232.00]
N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine	MHBMA3	1,3-Butadiene	0.6	97.22	4.47 [2.38, 9.22]
Phenylglyoxylic acid	PGA	Ethylbenzene, styrene	12	99.90	226.00 [135.00, 364.00]
N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine	HMPMA	Crotonaldehyde	1.7	100.00	214.00 [123.00, 388.00]

**Table S2. Weighted baseline characteristics of included participants divided by VAI-weighted tertiles.**

	<b>Tertile 1</b>	<b>Tertile 2</b>	<b>Tertile 3</b>	<b><i>p</i>-Value</b>
<b>N</b>	663	686	666	
<b>Sex, <i>n</i> (%)</b>				0.173
Male	361 (53.85)	355 (48.03)	341 (54.25)	
Female	302 (46.15)	331 (51.97)	325 (45.75)	
<b>Age (years, mean (SD))</b>	44.99 (18.00)	48.35 (16.29)	49.35 (15.51)	0.001
<b>PIR (median [IQR])</b>	3.23 [1.76, 5.00]	3.04 [1.42, 4.74]	2.56 [1.31, 4.62]	0.003
<b>Race, <i>n</i> (%)</b>				0.001
Hispanic	99 (9.72)	179 (15.21)	183 (15.18)	
Non-Hispanic White	245 (68.54)	274 (68.94)	298 (70.29)	
Non-Hispanic Black	204 (14.14)	141 (9.13)	98 (7.10)	
Other race	115 (7.60)	92 (6.71)	87 (7.43)	
<b>Education, <i>n</i> (%)</b>				0.008
High school graduate and below	238 (30.95)	300 (37.53)	329 (42.96)	
Above high school	425 (69.05)	386 (62.47)	337 (57.04)	
<b>BMI, <i>n</i> (%)</b>				< 0.001
< 25 kg/m <sup>2</sup>	321 (50.11)	160 (22.36)	95 (12.33)	
25-30 kg/m <sup>2</sup>	194 (27.91)	254 (37.77)	201 (31.67)	
≥ 30 kg/m <sup>2</sup>	148 (21.98)	272 (39.87)	370 (56.01)	
<b>Smoker, <i>n</i> (%)</b>				0.111
No	397 (60.23)	371 (54.83)	340 (51.46)	
Yes	266 (39.77)	315 (45.17)	326 (48.54)	
<b>Cotinine, <i>n</i> (%)</b>				0.760
< 0.015 ng/mL	206 (36.21)	234 (35.48)	203 (33.31)	
≥ 0.015 ng/mL	457 (63.79)	452 (64.52)	463 (66.69)	
<b>Alcohol consumption per day (drinks, median [IQR])</b>	0.16 [0.01, 0.86]	0.07 [0.00, 0.44]	0.07 [0.00, 0.49]	0.002
<b>HEI-2015 (mean (SD))</b>	52.47 (14.31)	49.29 (13.71)	49.01 (13.30)	0.004
<b>Physical activity, <i>n</i> (%)</b>				< 0.001
No	116 (14.71)	160 (18.24)	203 (25.28)	
Moderate	290 (40.30)	311 (48.53)	295 (47.87)	
Vigorous	257 (44.99)	215 (33.23)	168 (26.85)	
<b>Hypertension, <i>n</i> (%)</b>				< 0.001
No	430 (73.14)	375 (56.76)	332 (54.20)	
Yes	233 (26.86)	311 (43.24)	334 (45.80)	

<b>Diabetes, <i>n</i> (%)</b>				< 0.001
No	589 (93.99)	555 (83.81)	424 (71.50)	
Yes	74 (6.01)	131 (16.19)	242 (28.50)	
<b>CVD, <i>n</i> (%)</b>				0.001
No	617 (94.77)	619 (93.50)	568 (87.93)	
Yes	46 (5.23)	67 (6.50)	98 (12.07)	
<b>2MHA</b>	26.64 [13.26, 75.45]	33.05 [12.52, 81.03]	36.64 [13.66, 84.70]	0.298
<b>3-4MHA</b>	210.52 [79.43, 564.15]	250.83 [90.68, 616.65]	254.10 [97.25, 580.29]	0.136
<b>AAMA</b>	57.83 [36.71, 102.69]	49.46 [31.68, 99.62]	51.46 [34.25, 97.03]	0.221
<b>AMCC</b>	164.10 [87.72, 244.43]	167.47 [102.33, 292.52]	183.78 [111.15, 354.51]	0.010
<b>ATCA</b>	99.16 [53.34, 188.85]	104.42 [56.44, 200.73]	103.69 [54.17, 196.11]	0.674
<b>BMA</b>	6.88 [4.24, 13.30]	6.39 [3.87, 10.50]	6.17 [3.93, 10.56]	0.094
<b>BPMA</b>	5.14 [2.12, 11.01]	3.82 [1.73, 10.25]	4.04 [1.55, 10.33]	0.188
<b>CEMA</b>	80.86 [53.36, 137.35]	92.07 [57.29, 147.91]	99.95 [66.02, 181.84]	< 0.001
<b>CYMA</b>	1.46 [0.92, 3.43]	1.42 [0.85, 8.33]	1.66 [0.88, 45.26]	0.028
<b>DHBMA</b>	303.84 [242.20, 400.15]	305.13 [237.25, 388.00]	325.04 [248.33, 412.81]	0.193
<b>2HPMA</b>	30.56 [19.00, 52.72]	29.38 [19.48, 51.89]	30.19 [18.28, 55.22]	0.776
<b>3HPMA</b>	195.76 [124.01, 328.30]	183.82 [125.48, 318.60]	219.06 [131.37, 422.29]	0.036
<b>MA</b>	127.97 [97.17, 181.00]	123.96 [90.02, 178.60]	134.20 [94.75, 200.04]	0.069
<b>MHBMA3</b>	3.60 [2.51, 6.19]	3.43 [2.41, 5.76]	4.11 [2.70, 10.26]	< 0.001
<b>PGA</b>	217.41 [165.56, 289.98]	215.36 [158.76, 296.24]	222.87 [156.62, 321.94]	0.566
<b>HMPMA</b>	172.28 [141.74, 238.81]	175.29 [136.76, 254.45]	196.53 [145.37, 363.05]	0.001

**Table S3. Weighted baseline characteristics of included participants divided by LAP-weighted tertiles**

	<b>Tertile 1</b>	<b>Tertile 2</b>	<b>Tertile 3</b>	<b><i>p</i>-Value</b>
<b>N</b>	647	725	643	
<b>Sex, <i>n</i> (%)</b>				0.292
Male	337 (49.13)	375 (51.50)	345 (55.39)	
Female	310 (50.87)	350 (48.50)	298 (44.61)	
<b>Age (years, mean (SD))</b>	43.00 (17.46)	49.21 (16.81)	50.44 (14.84)	< 0.001
<b>PIR (median [IQR])</b>	3.15 [1.74, 5.00]	3.11 [1.46, 5.00]	2.58 [1.33, 4.37]	0.003
<b>Race, <i>n</i> (%)</b>				0.002
Hispanic	105 (10.29)	174 (14.40)	182 (15.43)	
Non-Hispanic White	249 (69.77)	268 (66.07)	300 (72.03)	
Non-Hispanic Black	167 (11.87)	179 (11.69)	97 (6.74)	
Other race	126 (8.07)	104 (7.84)	64 (5.79)	

<b>Education, <i>n</i> (%)</b>				0.009
High school graduate and below	231 (31.81)	320 (35.81)	316 (43.86)	
Above high school	416 (68.19)	405 (64.19)	327 (56.14)	
<b>BMI, <i>n</i> (%)</b>				< 0.001
< 25 kg/m <sup>2</sup>	408 (64.40)	140 (17.46)	28 (3.17)	
25-30 kg/m <sup>2</sup>	183 (27.26)	306 (44.18)	160 (25.68)	
≥ 30 kg/m <sup>2</sup>	56 (8.35)	279 (38.36)	455 (71.15)	
<b>Smoker, <i>n</i> (%)</b>				0.096
No	394 (60.66)	393 (54.23)	321 (51.68)	
Yes	253 (39.34)	332 (45.77)	322 (48.32)	
<b>Cotinine, <i>n</i> (%)</b>				0.681
< 0.015 ng/mL	188 (33.63)	247 (36.65)	208 (34.68)	
≥ 0.015 ng/mL	459 (66.37)	478 (63.35)	435 (65.32)	
<b>Alcohol consumption per day (drinks, median [IQR])</b>	0.14 [0.01, 0.71]	0.08 [0.00, 0.57]	0.05 [0.00, 0.43]	0.007
<b>HEI-2015 (mean (SD))</b>	52.13 (14.43)	51.03 (13.63)	47.57 (13.13)	< 0.001
<b>Physical activity, <i>n</i> (%)</b>				0.001
No	105 (14.45)	184 (20.62)	190 (23.07)	
Moderate	291 (41.87)	317 (45.01)	288 (49.78)	
Vigorous	251 (43.68)	224 (34.24)	165 (27.15)	
<b>Hypertension, <i>n</i> (%)</b>				< 0.001
No	466 (77.22)	391 (61.69)	280 (45.06)	
Yes	181 (22.78)	334 (38.31)	363 (54.94)	
<b>Diabetes, <i>n</i> (%)</b>				< 0.001
No	598 (95.51)	573 (85.94)	397 (67.82)	
Yes	49 (4.49)	152 (14.06)	246 (32.18)	
<b>CVD, <i>n</i> (%)</b>				0.008
No	602 (94.87)	649 (92.46)	553 (88.92)	
Yes	45 (5.13)	76 (7.54)	90 (11.08)	
<b>2MHA</b>	28.00 [13.43, 79.90]	39.16 [13.11, 88.21]	31.25 [12.56, 77.44]	0.357
<b>3-4MHA</b>	222.72 [80.31, 616.57]	253.89 [83.19, 616.21]	193.58 [94.00, 528.29]	0.658
<b>AAMA</b>	59.19 [36.43, 110.19]	51.14 [33.15, 92.76]	49.57 [33.31, 92.19]	0.053
<b>AMCC</b>	163.22 [81.31, 272.18]	175.20 [106.03, 293.17]	176.52 [112.55, 330.08]	0.025
<b>ATCA</b>	100.69 [57.03, 184.59]	105.59 [56.70, 211.88]	101.74 [50.47, 183.08]	0.210
<b>BMA</b>	7.04 [4.27, 12.82]	6.37 [3.84, 11.41]	5.90 [3.99, 10.52]	0.059
<b>BPMA</b>	5.57 [2.23, 12.15]	3.86 [1.76, 9.23]	3.82 [1.47, 9.50]	0.009
<b>CEMA</b>	77.73 [51.63, 140.71]	95.11 [57.77, 150.89]	98.63 [67.27, 170.31]	< 0.001
<b>CYMA</b>	1.49 [0.94, 6.74]	1.42 [0.85, 4.40]	1.56 [0.86, 28.31]	0.385

<b>DHBMA</b>	301.12 [238.76, 396.54]	306.68 [242.06, 395.38]	327.45 [249.90, 416.17]	0.098
<b>2HPMA</b>	32.74 [21.10, 57.44]	30.62 [17.79, 52.48]	27.28 [18.22, 52.31]	0.037
<b>3HPMA</b>	199.10 [123.38, 368.50]	185.63 [124.62, 319.93]	205.64 [131.68, 343.78]	0.359
<b>MA</b>	127.41 [91.80, 185.08]	128.91 [95.08, 180.94]	128.67 [92.17, 188.51]	0.972
<b>MHBMA3</b>	3.57 [2.46, 6.65]	3.62 [2.52, 6.22]	3.91 [2.61, 8.63]	0.245
<b>PGA</b>	218.78 [166.80, 291.81]	219.54 [165.81, 303.67]	212.93 [153.87, 310.56]	0.545
<b>HMPMA</b>	172.54 [140.44, 249.43]	173.17 [135.83, 266.20]	196.52 [146.08, 338.54]	0.008

**Table S4. Weighted median [IQR] concentrations of mVOCs (µg/g Cr) in urine grouped by sex.**

<b>mVOCs</b>	<b>Total</b>	<b>Male (<i>n</i> = 1057)</b>	<b>Female (<i>n</i> = 958)</b>	<b><i>p</i>-Value</b>
2MHA	32.42 [13.20, 79.90]	31.22 [13.53, 69.86]	34.22 [12.55, 94.59]	0.161
3-4MHA	232.13 [84.16, 591.00]	217.08 [80.88, 510.56]	256.77 [87.98, 714.06]	0.019
AAMA	53.24 [33.87, 100.25]	52.41 [32.79, 101.85]	53.57 [34.72, 94.78]	0.768
AMCC	169.05 [102.33, 301.13]	156.49 [91.51, 249.13]	188.13 [116.72, 352.14]	< 0.001
ATCA	103.26 [54.88, 194.64]	66.50 [38.46, 116.10]	171.31 [94.60, 258.61]	< 0.001
BMA	6.45 [4.04, 11.26]	5.58 [3.54, 9.22]	7.41 [4.83, 13.75]	< 0.001
BPMA	4.47 [1.76, 10.48]	4.72 [1.74, 10.35]	4.25 [1.77, 10.62]	0.963
CEMA	92.62 [56.99, 153.69]	90.75 [57.41, 149.38]	93.49 [56.67, 156.30]	0.858
CYMA	1.48 [0.88, 9.67]	1.46 [0.86, 17.02]	1.53 [0.91, 4.43]	0.932
DHBMA	314.43 [243.02, 403.76]	294.11 [232.73, 393.86]	325.00 [254.50, 412.87]	0.001
2HPMA	30.14 [18.99, 53.15]	29.74 [19.00, 51.89]	30.54 [18.90, 56.37]	0.854
3HPMA	197.52 [127.36, 348.79]	209.18 [141.63, 371.25]	174.61 [112.43, 302.84]	< 0.001
MA	128.65 [93.48, 185.18]	119.13 [87.56, 173.27]	138.74 [98.33, 195.32]	0.002
MHBMA3	3.67 [2.55, 6.90]	3.71 [2.56, 7.30]	3.67 [2.55, 6.23]	0.885
PGA	217.96 [162.27, 303.17]	199.81 [151.00, 270.59]	241.30 [179.18, 336.40]	< 0.001
HMPMA	179.82 [140.70, 274.60]	175.39 [136.30, 284.67]	183.29 [145.27, 274.34]	0.149

**Table S5. Weighted median [IQR] concentrations of mVOCs in urine grouped by age.**

<b>mVOCs</b>	<b>&lt; 60 years (<i>n</i> = 1338)</b>	<b>≥ 60 years (<i>n</i> = 677)</b>	<b><i>p</i>-Value</b>
2MHA	32.95 [13.43, 82.42]	28.65 [11.94, 75.50]	0.234
3-4MHA	242.76 [80.97, 588.44]	221.01 [91.90, 607.74]	0.710
AAMA	55.96 [34.35, 106.76]	48.97 [32.90, 80.10]	0.023
AMCC	165.82 [95.76, 292.67]	181.89 [119.29, 310.77]	0.050
ATCA	100.00 [53.50, 185.24]	118.97 [58.74, 220.50]	0.081

BMA	6.19 [3.85, 10.60]	6.95 [4.40, 12.90]	0.011
BPMA	4.61 [1.77, 10.48]	4.13 [1.73, 10.44]	0.539
CEMA	87.44 [56.04, 152.59]	99.00 [63.05, 162.14]	0.008
CYMA	1.62 [0.89, 33.42]	1.23 [0.85, 2.08]	< 0.001
DHBMA	293.80 [231.53, 378.09]	372.84 [277.42, 448.11]	< 0.001
2HPMA	29.78 [18.98, 52.74]	30.89 [18.97, 56.29]	0.519
3HPMA	202.89 [128.19, 379.53]	186.50 [124.14, 293.99]	0.025
MA	126.64 [93.08, 187.45]	132.04 [93.94, 178.07]	0.907
MHBMA3	3.54 [2.40, 8.09]	3.99 [2.98, 5.69]	0.087
PGA	206.48 [157.10, 296.10]	238.13 [185.15, 306.02]	0.002
HMPMA	170.48 [132.23, 274.46]	200.74 [161.12, 280.06]	< 0.001

**Table S6. Weighted median [IQR] concentrations of mVOCs in urine grouped by obesity status.**

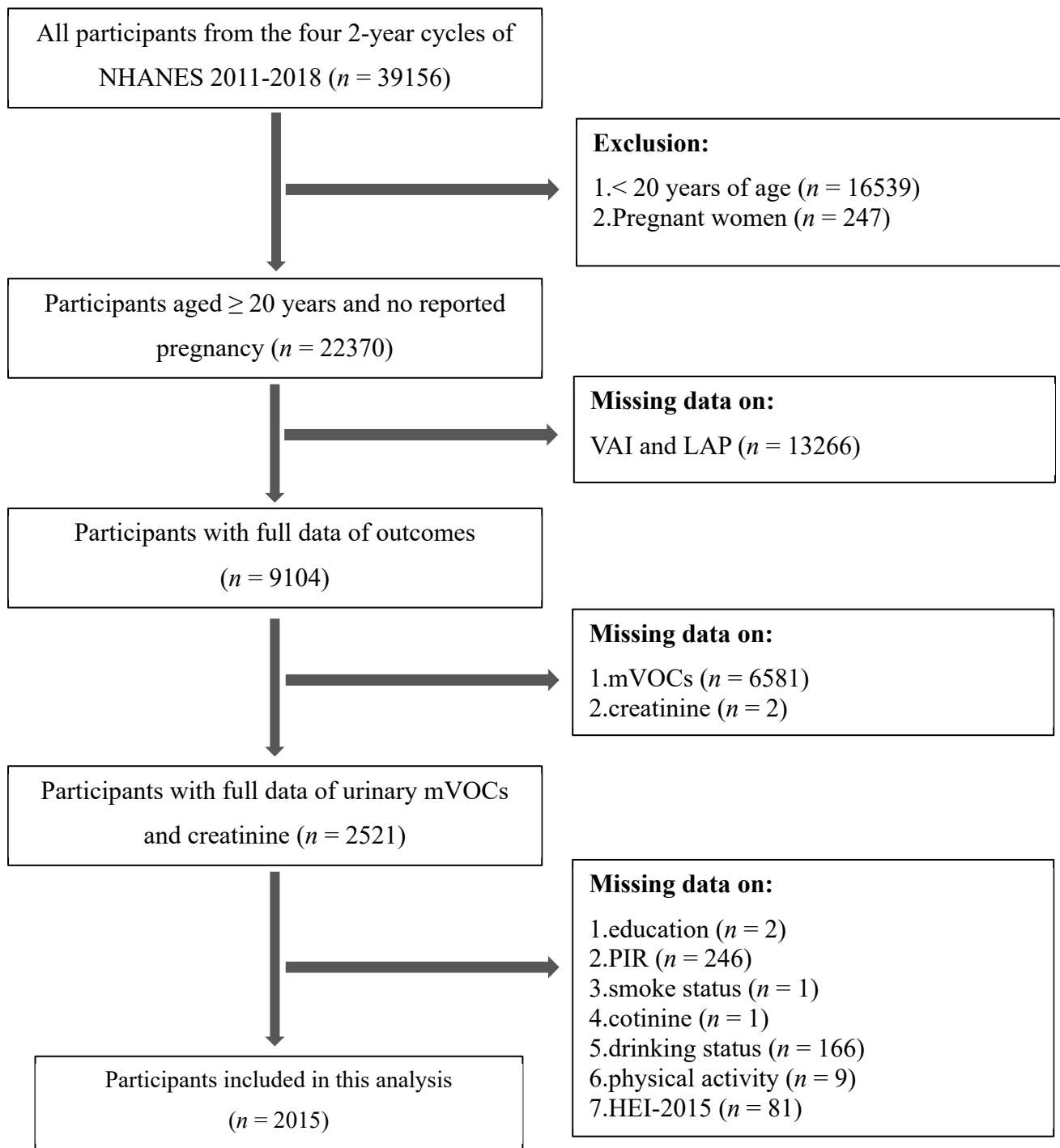
mVOCs	Non-obesity ( <i>n</i> = 1225)	Obesity ( <i>n</i> = 790)	<i>p</i> -Value
2MHA	37.49 [14.11, 93.29]	26.36 [11.72, 64.01]	< 0.001
3-4MHA	285.90 [88.40, 672.26]	167.95 [80.55, 494.71]	< 0.001
AAMA	57.86 [34.07, 107.01]	48.73 [33.59, 85.43]	0.007
AMCC	174.73 [100.29, 306.04]	163.77 [104.08, 290.48]	0.518
ATCA	103.42 [55.63, 194.36]	103.12 [52.52, 195.57]	0.972
BMA	6.97 [4.20, 12.73]	5.75 [3.75, 9.50]	0.003
BPMA	4.95 [1.93, 10.79]	3.88 [1.59, 9.54]	0.050
CEMA	87.59 [54.86, 150.91]	97.19 [65.74, 156.84]	0.015
CYMA	1.54 [0.93, 12.93]	1.41 [0.82, 7.58]	0.020
DHBMA	315.88 [244.75, 403.73]	306.46 [242.43, 402.61]	0.703
2HPMA	32.55 [20.17, 58.41]	26.84 [17.69, 47.62]	0.005
3HPMA	196.74 [125.84, 376.76]	201.51 [130.85, 308.40]	0.469
MA	131.08 [95.10, 190.80]	120.91 [89.76, 178.12]	0.032
MHBMA3	3.74 [2.56, 7.03]	3.54 [2.53, 6.41]	0.358
PGA	226.53 [166.12, 306.13]	202.60 [154.70, 296.03]	0.011
HMPMA	180.00 [139.60, 282.40]	179.63 [142.43, 269.35]	0.618

Notes: The obesity status of participants was determined by their BMI, with a BMI  $\geq 30$  kg/m<sup>2</sup> identified as obesity.

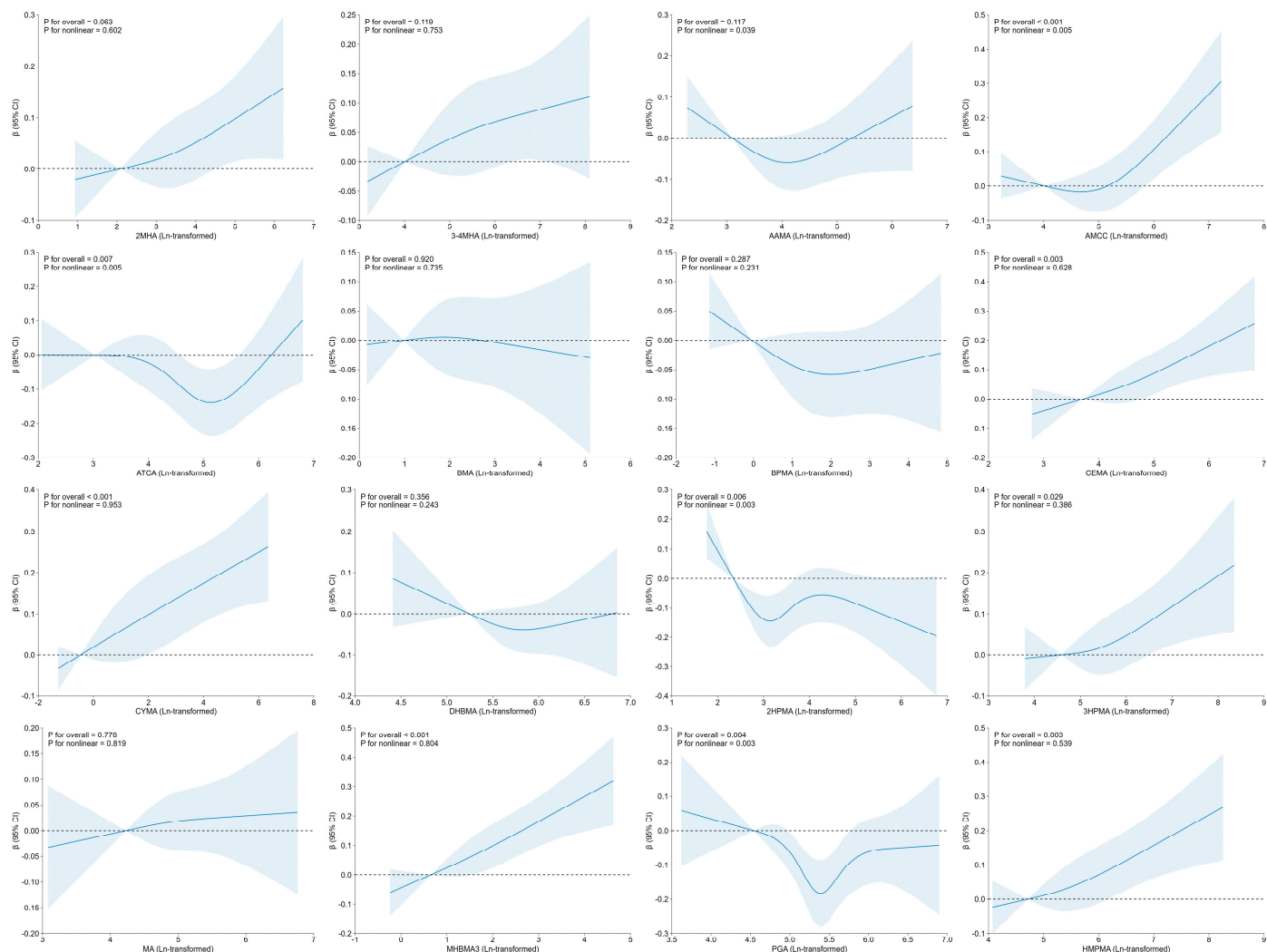


**Table S7. Posterior inclusion probability (PIP) of VOC metabolites derived from BKMR modeling.**

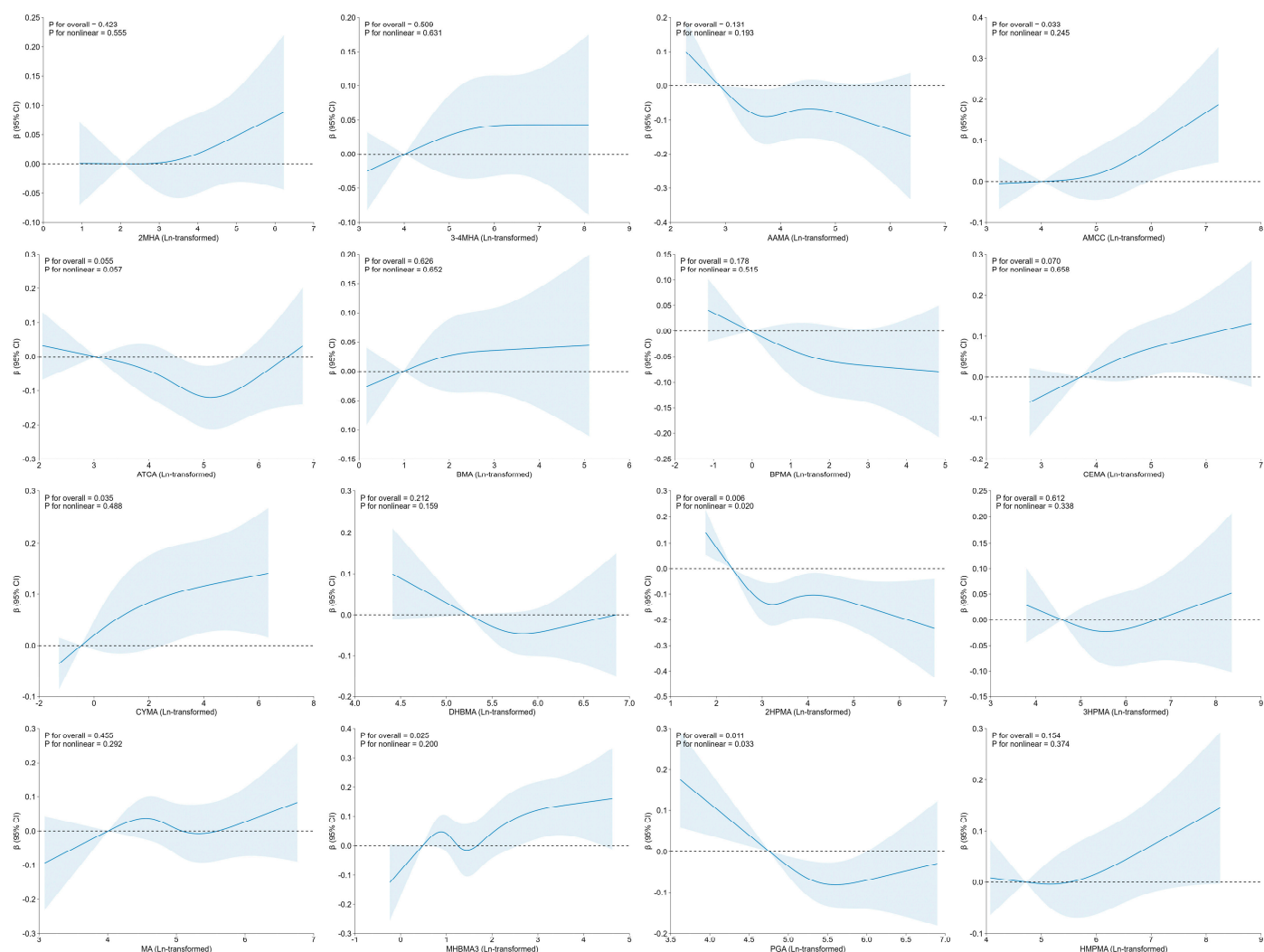
<b>Variable</b>	<b>VAI</b>	<b>LAP</b>
2MHA	0.1838	0
3-4MHA	0.2120	0.0336
AAMA	0.6414	0.2040
AMCC	0.9914	0.8938
ATCA	0.4250	0
BMA	0.2066	0
BPMA	0.1072	0
CEMA	0.0904	0.0114
CYMA	0.4770	0.4698
DHBMA	0.0876	0
2HPMA	0.2714	0.1018
3HPMA	0.2758	0
MA	0.2724	0
MHBMA3	0.5330	0.0124
PGA	0.9128	0.1234
HMPMA	0.5058	0.0028



**Figure S1. Flowchart of the participant screening process for inclusion in the analysis.**



**Figure S2. RCS results of the relationships between urinary mVOCs and VAI. The models were adjusted by sex, age, race, education, PIR, BMI, physical activity, HEI-2015, self-reported smoking status, average daily alcohol consumption, diabetes, hypertension, and CVD.**



**Figure S3. RCS results of the relationships between urinary mVOCs and LAP. The models were adjusted by sex, age, race, education, PIR, BMI, physical activity, HEI-2015, self-reported smoking status, average daily alcohol consumption, diabetes, hypertension, and CVD.**

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