SUPPLEMENTAL METHODS

Microbiome Data Collection and Sequencing

Fecal samples were collected using the Genotek OMR-200 Gut Microbiome DNA Collection Kit. Metagenomic shotgun sequencing was employed to determine the composition of the gut microbiome in the fecal samples. For DNA sample preparations, 1 μg of DNA per sample was used as input material. Sequencing libraries were generated using NEBNext® Ultra DNA Library Prep Kit for Illumina (NEB, USA) following the manufacturer's recommendations, and index codes were added to attribute sequences to each sample. The DNA samples were fragmented by sonication to a size of 350 bp. Subsequently, DNA fragments were end-polished, A-tailed, and ligated with the full-length adaptor for Illumina sequencing with further PCR amplification. PCR products were purified using the AMPure XP system, and library size distribution was assessed using the Agilent2100 Bioanalyzer. Quantification of libraries was performed using real-time PCR. The library preparations were sequenced on an Illumina HiSeq platform, and paired-end reads were generated.

Quality control of the metagenomic data was carried out on a per-sample basis. Reads containing more than 40bp of low-quality bases, more than 10 bp of N bases, and more than 15bp overlap with adapters were excluded using Readfq software. Considering the possibility of host contamination may exist in samples, contamination with human sequences was also filtered by mapping the metagenomic reads to human (hg38) genome using bowtie2. After that, clean data was assembled by SOAPdenovo software. The ORFs of Scaftigs (≥ 500 bp) were all predicted by MetaGeneMark software, and any length information shorter than 100 nt has been filtered from the predicted result. CD-HIT software was used to remove redundancy and obtain the unique initial gene catalogue. DIAMOND software was used to blast the unigenes to the sequences from the NR database of NCBI. LCA algorithm from MEGAN software was used to align results of each sequence, and the number of genes and microbial abundance information for each sample in each taxonomy hierarchy were obtained. All metagenomics profiling processes were performed at Novogene Bioinformatics Technology Co., Ltd. (Beijing, China). Microbes detected in at least 10% of the samples were included in this analysis.

Targeted Metabolomics Profiling

Plasma targeted metabolomics profiling was performed for participants using ultra-performance liquid chromatography coupled with tandem mass spectrometry (UPLC-MS/MS) system (ACQUITY UPLCXevo TQ-S, Waters Corp., Milford, MA, 570 USA). We used two metabolomics kits provided by Metabo-Profile Corp. (Shanghai, China) for profiling. 1) The Q300 Kit, containing 310 metabolites from 12 classes, including bile acids, amino acids, fatty acids, indoles, etc. 2) The trimethylamine N-oxide (TMAO) Kits, containing seven TMAO-related metabolites. All metabolomics profiling processes were performed at Metabo-Profile Corp. (Shanghai, China). The raw data generated by UPLC-MS/MS were processed using TMBQ software (v1.0; Metabo-Profile, Shanghai, China) to perform peak integration, calibration, and quantitation for each metabolite. The plasma concentration of metabolite in the study samples was obtained by comparing the sample with unknown metabolite concentration to a set of standard samples with known metabolite concentration.

Supplementary Table S1. Main diet-related factors of the MetaSalt study

Main diet-related factors	All participants (*n* = 523)
Rice, g/d	450.00 (250.00, 550.00)
Red meat, g/d	14.28 (5.00, 35.71)
White meat, g/d	3.33 (0.55, 14.28)
Vegetable, g/d	250.00 (125.00, 500.00)
Fruits, g/d	71.43 (16.67, 150.00)
Egg, g/d	50.00 (14.29, 100.00)
Bean products, g/d	171.43 (57.14, 248.30)
Dietary score, point	2.00 (1.00, 3.00)
24-hour UNa, mmol	204.86 (50.22)
24-hour UK, mmol	36.98 (8.93)

Note. Normal distributed variables are presented as mean (standard deviation); skewed distributed variables are presented as median (inter-quartile range).

Supplementary Table S2. Characteristics of the prospective cohort

Characteristics	Overall (*n* = 2,169)	Male (*n* = 1,030)	Female (*n* = 1,139)
Age, y	55.52 (6.79)	55.58 (6.99)	55.47 (6.61)
BMI, kg/m^2	25.02 (3.67)	24.60 (3.51)	25.39 (3.78)
Drinking alcohol, *n* (%)	696 (32.09)	601 (58.35)	95 (8.34)
Smoking, *n* (%)	683 (31.49)	645 (62.62)	38 (3.34)
Work related Physical Activity, *n* (%)			
No job or retirement	1,072 (49.42)	370 (35.92)	702 (61.63)
Light or sedentary activity	533 (24.57)	292 (28.35)	241 (21.16)
Vigorous or moderate activity	564 (26.00)	368 (35.73)	196 (17.21)
Urban, *n* (%)	659 (30.38)	331 (32.14)	328 (28.80)
Education, *n* (%)	608 (28.03)	316 (30.68)	292 (25.64)
SBP, mmHg	134.97 (20.19)	136.25 (20.07)	133.81 (20.25)
DBP, mmHg	82.82 (11.64)	84.31 (11.71)	81.46 (11.42)
Hypertension, *n* (%)	1,103 (50.85)	562 (54.56)	541 (47.50)
Diabetes, *n* (%)	258 (11.89)	122 (11.84)	136 (11.94)
Dyslipidemia, *n* (%)	1,199 (55.28)	621 (60.29)	578 (50.75)

Note. Characteristics of the study population are described as *n* (%) for categorical variables and mean (standard deviation) for continuous variables. BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure. Education was classified as high school or above.

Supplementary Table S3. Sensitivity analyses of the association between α-diversity and ambulatory BP indices

α-diversity	24-hour		Daytime		Nighttime	
	β (95% *CI*)	*P* value	β (95% *CI*)	*P* value	β (95% *CI*)	*P* value
SBP						
Chao1	-0.92 (-1.83, -0.01)	0.04	-1.16 (-2.09, -0.23)	0.01	-0.45 (-1.53, 0.63)	0.41
Shannon	-0.44 (-1.37, 0.48)	0.35	-0.71 (-1.65, 0.23)	0.14	0.09 (-1.00, 1.18)	0.87
DBP						
Chao1	-0.56 (-1.27, 0.15)	0.12	-0.76 (-1.51, -0.01)	0.05	-0.25 (-1.04, 0.53)	0.53
Shannon	-0.25 (-0.97, 0.47)	0.49	-0.44 (-1.21, 0.32)	0.25	0.10 (-0.69, 0.89)	0.81
SBPV						
Chao1	-0.32 (-0.61, -0.03)	0.03	-0.15 (-0.43, 0.13)	0.30	-0.31 (-0.64, 0.03)	0.07
Shannon	-0.21 (-0.50, 0.09)	0.17	0.01 (-0.28, 0.29)	0.96	-0.24 (-0.57, 0.09)	0.16
DBPV						
Chao1	-0.05 (-0.28,0.18)	0.69	0.04 (-0.19,0.28)	0.71	0.07 (-0.18,0.32)	0.58
Shannon	-0.08 (-0.32, 0.15)	0.50	0.05 (-0.19, 0.29)	0.69	0.00 (-0.25, 0.25)	0.98

Note. Sensitivity analysis of further adjusting for several baseline covariates including dietary score, 24-hour UNa, and 24-hour UK.

Supplementary Table S4. Associations between α-diversity indices and office BP

Office BP	β	SE	*P* value
Office SBP			
Chao1	-1.71	0.52	0.01
Shannon	-1.16	0.53	0.03
Office DBP			
Chao1	-0.76	0.37	0.04
Shannon	-0.57	0.38	0.13

Note. LMMs adjusted for age, sex, BMI, study sites, and the random effect of families were used. DBP, diastolic blood pressure; SBP, systolic blood pressure; SE, standard error.

Supplementary Table S5. Plasma metabolites that were associated with gut microbial richness

Metabolites	β	SE	Bonferroni *P*
2-Phenylpropionate	0.58	0.04	7.78×10^{-47}
Hippuric acid	0.53	0.03	4.49×10^{-41}
Hydrocinnamic acid	0.47	0.04	1.20×10^{-32}
GLCA-3S	0.46	0.04	1.35×10^{-26}
Phenylacetylglutamine	0.41	0.04	2.53×10^{-19}
1-Methylnicotinamide	0.38	0.04	5.06×10^{-17}
GDCA-3S	0.37	0.04	2.12×10^{-15}
IsoLCA	0.36	0.04	2.13×10^{-15}
Indole-3-propionic acid	0.36	0.04	7.32×10^{-15}
GDCA	0.36	0.04	2.44×10^{-14}
TMAO	0.34	0.04	2.70×10^{-13}
DCA	0.30	0.04	1.78×10^{-9}
GLCA	0.29	0.04	1.37×10^{-8}
Imidazole propionate	-0.26	0.04	2.29×10^{-7}
3-(3-Hydroxyphenyl)-3-hydroxypropanoic acid	0.27	0.04	2.67×10^{-7}
GCDCA-3S	-0.22	0.04	7.56×10^{-6}
Alanine	-0.24	0.04	1.00×10^{-5}
LCA	0.24	0.04	1.12×10^{-5}
CDCA	-0.21	0.04	2.39×10^{-4}
TDCA	0.20	0.04	7.41×10^{-4}
GUDCA	-0.19	0.04	4.99×10^{-3}
GCDCA	-0.18	0.04	5.96×10^{-3}
Homovanillic acid	-0.16	0.04	9.55×10^{-3}
2-Hydroxy-3-methylbutyric acid	-0.14	0.04	0.038
Citramalic acid	-0.16	0.04	0.038
Hydroxyphenyllactic acid	-0.15	0.04	0.039

Note. LMMs adjusted for age, sex, BMI, study sites, and the random effect of families were used. The β-coefficient, and *P* value after multiple testing correction for each metabolite in the LMM are provided. SE, standard error.

Supplementary Table S6. Origin of gut microbial richness-related metabolites annotated by MetOrigin

Metabolites	Origins annotated by MetOrigin
2-Phenylpropionate	Microbiota; Food related
Hippuric acid	Microbiota; Food related; Drug related; Environment
Hydrocinnamic acid	Microbiota; Food related; Drug related
GLCA-3S	Microbiota; Food related
Phenylacetylglutamine	Microbiota; Food related
1-Methylnicotinamide	Host; Microbiota; Food related; Drug related
GDCA-3S	Unknown
IsoLCA	Food related
Indole-3-propionic acid	Microbiota; Food related; Drug related
GDCA	Microbiota; Food related
TMAO	Microbiota; Food related; Environment
DCA	Food related; Drug related
GLCA	Microbiota; Food related
Imidazole propionate	Microbiota; Food related
3-(3-Hydroxyphenyl)-3-hydroxypropanoic acid	Microbiota; Food related
GCDCA-3S	Food related
Alanine	Host; Microbiota; Food related; Drug related; Environment
LCA	Food related
CDCA	Host; Microbiota; Food related; Drug related
TDCA	Microbiota; Food related
GUDCA	Microbiota; Food related
GCDCA	Host; Microbiota; Food related; Drug related
Homovanillic acid	Host; Microbiota; Food related
Hydroxyphenyllactic acid	Microbiota; Food related
2-Hydroxy-3-methylbutyric acid	Food related
Citramalic acid	Microbiota; Food related

Supplementary Table S7. Associations between richness-related metabolites and ambulatory SBP indices

Metabolites	24-hour SBP		Daytime SBP		Nighttime SBP	
	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR
Imidazole propionate	1.79 (0.86, 2.71)	0.01	1.72 (0.79, 2.66)	0.01	2.05 (0.95, 3.15)	0.01
Homovanillic acid	1.36 (0.33, 2.39)	0.13	1.59 (0.55, 2.63)	0.02	0.70 (-0.53, 1.93)	0.64
2-Hydroxy-3-methylbutyric acid	1.28 (0.20, 2.36)	0.18	1.72 (0.63, 2.81)	0.02	0.59 (-0.71, 1.89)	0.70
2-Phenylpropionate	-1.02 (-1.93, -0.11)	0.19	-1.07 (-1.99, -0.14)	0.10	-0.88 (-1.97, 0.21)	0.64
Hydrocinnamic acid	-0.84 (-1.76, 0.07)	0.27	-1.24 (-2.16, -0.31)	0.06	0.10 (-0.99, 1.19)	0.98
Hydroxyphenyllactic acid	0.94 (-0.08, 1.96)	0.27	1.27 (0.24, 2.31)	0.08	0.13 (-1.10, 1.35)	0.98
GLCA	-0.85 (-1.74, 0.03)	0.27	-1.02 (-1.91, -0.12)	0.10	-0.90 (-1.94, 0.15)	0.64
Citramalic acid	0.77 (-0.15, 1.68)	0.33	0.87 (-0.05, 1.79)	0.21	0.66 (-0.43, 1.74)	0.64
GUDCA	0.70 (-0.19, 1.59)	0.33	0.76 (-0.14, 1.66)	0.28	0.48 (-0.58, 1.53)	0.70
GCDCA-3S	0.77 (-0.20, 1.74)	0.33	0.74 (-0.24, 1.72)	0.36	0.66 (-0.49, 1.82)	0.64
Hippuric acid	-0.68 (-1.62, 0.26)	0.37	-0.61 (-1.56, 0.34)	0.45	-0.74 (-1.87, 0.38)	0.64
1-Methylnicotinamide	-0.59 (-1.49, 0.30)	0.39	-0.66 (-1.56, 0.25)	0.37	-0.30 (-1.37, 0.76)	0.88
GDCA	0.59 (-0.29, 1.47)	0.39	0.50 (-0.40, 1.39)	0.48	0.57 (-0.47, 1.62)	0.64
isoLCA	-0.40 (-1.30, 0.50)	0.66	-0.51 (-1.42, 0.40)	0.48	-0.15 (-1.24, 0.93)	0.98
GDCA-3S	0.42 (-0.48, 1.32)	0.66	0.36 (-0.55, 1.26)	0.64	0.34 (-0.73, 1.42)	0.86
GCDCA	0.37 (-0.55, 1.28)	0.70	0.51 (-0.41, 1.44)	0.48	0.12 (-0.98, 1.22)	0.98
Alanine	0.34 (-0.57, 1.25)	0.70	0.33 (-0.59, 1.25)	0.66	0.69 (-0.39, 1.77)	0.64
LCA	-0.32 (-1.21, 0.57)	0.70	-0.21 (-1.12, 0.69)	0.84	-0.60 (-1.65, 0.45)	0.64
Phenylacetylglutamine	-0.29 (-1.19, 0.60)	0.71	-0.38 (-1.29, 0.53)	0.64	-0.03 (-1.10, 1.04)	0.98
GLCA-3S	-0.21 (-1.11, 0.68)	0.79	-0.39 (-1.30, 0.51)	0.64	-0.18 (-1.24, 0.88)	0.98
TDCA	0.19 (-0.70, 1.09)	0.79	0.06 (-0.85, 0.96)	0.95	0.57 (-0.50, 1.63)	0.64
DCA	-0.23 (-1.12, 0.67)	0.79	-0.14 (-1.05, 0.77)	0.95	-0.63 (-1.70, 0.45)	0.64
3-(3-Hydroxyphenyl)-3-hydroxy propanoic acid	-0.16 (-1.06, 0.73)	0.82	-0.04 (-0.95, 0.87)	0.95	-0.39 (-1.47, 0.68)	0.82
CDCA	-0.12 (-1.03, 0.79)	0.86	-0.07 (-0.99, 0.85)	0.95	-0.03 (-1.11, 1.05)	0.98
Indole-3-propionic acid	0.06 (-0.85, 0.96)	0.90	-0.03 (-0.95, 0.88)	0.95	-0.01 (-1.11, 1.08)	0.98
TMAO	0.06 (-0.85, 0.98)	0.90	0.07 (-0.85, 0.99)	0.95	0.01 (-1.07, 1.10)	0.98

Note. LMMs adjusted for age, sex, BMI, study sites, and the random effect of families were used. FDR was obtained by Benjamini-Hochberg method at a 5% false discovery rate.

Supplementary Table S8. Associations between richness-related metabolites and ambulatory DBP indices

Metabolites	24-hour DBP		Daytime DBP		Nighttime DBP	
	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR
2-Hydroxy-3-methylbutyric acid	1.04 (0.20, 1.88)	0.25	1.37 (0.49, 2.26)	0.05	0.47 (-0.47, 1.40)	0.89
Homovanillic acid	0.92 (0.12, 1.72)	0.25	1.09 (0.25, 1.94)	0.10	0.33 (-0.56, 1.21)	0.89
2-Phenylpropionate	-0.78 (-1.49, -0.08)	0.25	-0.81 (-1.55, -0.06)	0.15	-0.80 (-1.59, -0.02)	0.58
Citramalic acid	0.75 (0.04, 1.45)	0.25	0.88 (0.14, 1.62)	0.12	0.58 (-0.20, 1.36)	0.74
Hydrocinnamic acid	-0.69 (-1.40, 0.01)	0.28	-0.96 (-1.71, -0.21)	0.10	-0.13 (-0.91, 0.66)	0.92
Imidazole propionate	0.68 (-0.04, 1.40)	0.28	0.69 (-0.08, 1.46)	0.25	0.75 (-0.05, 1.55)	0.58
Hydroxyphenyllactic acid	0.69 (-0.10, 1.49)	0.32	0.98 (0.14, 1.81)	0.12	0.04 (-0.84, 0.93)	0.92
1-Methylnicotinamide	-0.56 (-1.25, 0.14)	0.38	-0.56 (-1.29, 0.18)	0.33	-0.49 (-1.25, 0.28)	0.80
GLCA	-0.51 (-1.20, 0.17)	0.42	-0.66 (-1.39, 0.06)	0.25	-0.51 (-1.26, 0.24)	0.80
GUDCA	0.46 (-0.22, 1.15)	0.47	0.56 (-0.17, 1.29)	0.33	0.28 (-0.48, 1.04)	0.89
isoLCA	-0.46 (-1.16, 0.24)	0.47	-0.56 (-1.29, 0.18)	0.33	-0.21 (-0.99, 0.57)	0.92
DCA	-0.43 (-1.13, 0.26)	0.49	-0.38 (-1.12, 0.36)	0.57	-0.75 (-1.52, 0.02)	0.58
Alanine	0.38 (-0.33, 1.08)	0.53	0.36 (-0.39, 1.10)	0.57	0.66 (-0.12, 1.44)	0.63
Phenylacetylglutamine	-0.38 (-1.08, 0.31)	0.53	-0.39 (-1.13, 0.35)	0.57	-0.33 (-1.10, 0.43)	0.89
GCDCA-3S	0.39 (-0.36, 1.14)	0.53	0.45 (-0.35, 1.24)	0.57	0.21 (-0.62, 1.04)	0.92
Indole-3-propionic acid	-0.30 (-1.00, 0.40)	0.64	-0.37 (-1.11, 0.37)	0.57	-0.35 (-1.13, 0.44)	0.89
GDCA-3S	0.29 (-0.41, 0.98)	0.64	0.29 (-0.44, 1.02)	0.67	0.04 (-0.73, 0.81)	0.92
Hippuric acid	-0.19 (-0.92, 0.54)	0.84	-0.12 (-0.90, 0.65)	0.89	-0.37 (-1.18, 0.44)	0.89
GDCA	0.19 (-0.50, 0.88)	0.84	0.12 (-0.61, 0.85)	0.89	0.16 (-0.60, 0.91)	0.92
3-(3-Hydroxyphenyl)-3-hydroxy propanoic acid	0.09 (-0.60, 0.79)	0.95	0.22 (-0.51, 0.96)	0.75	-0.22 (-0.99, 0.55)	0.92
GCDCA	0.09 (-0.62, 0.80)	0.95	0.21 (-0.54, 0.97)	0.75	0.06 (-0.73, 0.85)	0.92
LCA	-0.07 (-0.76, 0.62)	0.95	-0.08 (-0.82, 0.65)	0.94	-0.17 (-0.93, 0.59)	0.92
GLCA-3S	-0.09 (-0.78, 0.60)	0.95	-0.24 (-0.97, 0.50)	0.75	-0.06 (-0.82, 0.70)	0.92
TDCA	0.05 (-0.65, 0.74)	0.97	-0.03 (-0.76, 0.71)	0.94	0.31 (-0.46, 1.08)	0.89
CDCA	-0.02 (-0.73, 0.68)	0.99	0.05 (-0.69, 0.80)	0.94	-0.05 (-0.82, 0.73)	0.92
TMAO	0.00 (-0.70, 0.71)	1.00	0.05 (-0.70, 0.79)	0.94	-0.08 (-0.87, 0.70)	0.92

Note. LMMs adjusted for age, sex, BMI, study sites, and the random effect of families were used. FDR was obtained by Benjamini-Hochberg method at a 5% false discovery rate.

Supplementary Table S9. Associations between richness-related metabolites and ambulatory SBPV indices

Metabolites	24-hour SBPV		Daytime SBPV		Nighttime SBPV	
	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR
Hydrocinnamic acid	-0.53 (-0.81, -0.24)	0.01	-0.29 (-0.57, -0.01)	0.40	0.07 (-0.26, 0.40)	0.87
Hydroxyphenyllactic acid	0.37 (0.05, 0.69)	0.22	0.17 (-0.15, 0.48)	0.81	-0.18 (-0.55, 0.20)	0.87
GUDCA	0.32 (0.04, 0.60)	0.22	0.34 (0.06, 0.61)	0.22	0.24 (-0.08, 0.57)	0.70
Alanine	-0.14 (-0.43, 0.14)	0.58	-0.14 (-0.42, 0.14)	0.81	0.06 (-0.27, 0.39)	0.87
2-Hydroxy-3-methylbutyric acid	0.29 (-0.05, 0.63)	0.58	0.03 (-0.31, 0.37)	0.97	0.20 (-0.19, 0.60)	0.87
Homovanillic acid	0.18 (-0.14, 0.51)	0.58	0.02 (-0.30, 0.34)	0.97	-0.03 (-0.40, 0.35)	0.89
TDCA	-0.16 (-0.44, 0.12)	0.58	-0.10 (-0.37, 0.18)	0.81	-0.06 (-0.39, 0.26)	0.87
GCDCA	0.15 (-0.13, 0.44)	0.58	0.14 (-0.14, 0.42)	0.81	-0.09 (-0.42, 0.24)	0.87
LCA	0.14 (-0.14, 0.42)	0.58	-0.05 (-0.32, 0.23)	0.91	0.03 (-0.29, 0.35)	0.89
DCA	0.15 (-0.14, 0.43)	0.58	0.15 (-0.12, 0.43)	0.81	-0.11 (-0.43, 0.22)	0.87
GLCA	-0.22 (-0.50, 0.06)	0.58	-0.11 (-0.38, 0.17)	0.81	-0.35 (-0.67, -0.04)	0.38
GLCA-3S	-0.17 (-0.45, 0.11)	0.58	-0.05 (-0.32, 0.23)	0.91	-0.40 (-0.72, -0.08)	0.38
GCDCA-3S	0.17 (-0.14, 0.47)	0.58	0.23 (-0.07, 0.53)	0.70	0.05 (-0.30, 0.41)	0.87
Imidazole propionate	0.19 (-0.10, 0.48)	0.58	0.37 (0.08, 0.65)	0.22	0.32 (-0.02, 0.66)	0.53
isoLCA	-0.20 (-0.48, 0.09)	0.58	-0.11 (-0.38, 0.17)	0.81	-0.10 (-0.43, 0.23)	0.87
Hippuric acid	0.13 (-0.17, 0.43)	0.62	0.09 (-0.20, 0.38)	0.81	0.08 (-0.26, 0.42)	0.87
Indole-3-propionic acid	0.11 (-0.17, 0.40)	0.66	0.23 (-0.05, 0.50)	0.70	-0.07 (-0.41, 0.26)	0.87
Phenylacetylglutamine	-0.09 (-0.37, 0.19)	0.78	-0.01 (-0.29, 0.27)	0.97	0.03 (-0.30, 0.35)	0.89
2-Phenylpropionate	-0.06 (-0.35, 0.23)	0.80	-0.05 (-0.33, 0.23)	0.91	-0.05 (-0.38, 0.28)	0.87
1-Methylnicotinamide	-0.06 (-0.34, 0.22)	0.80	-0.01 (-0.28, 0.27)	0.97	0.18 (-0.15, 0.50)	0.87
GDCA	0.06 (-0.21, 0.34)	0.80	0.09 (-0.18, 0.36)	0.81	0.07 (-0.25, 0.39)	0.87
Citramalic acid	0.07 (-0.21, 0.36)	0.80	-0.08 (-0.36, 0.20)	0.84	0.24 (-0.09, 0.56)	0.70
TMAO	0.05 (-0.24, 0.34)	0.83	0.01 (-0.28, 0.29)	0.97	0.07 (-0.26, 0.40)	0.87
3-(3-Hydroxyphenyl)-3-hydroxy propanoic acid	0.00 (-0.28, 0.28)	0.99	-0.09 (-0.36, 0.19)	0.81	-0.15 (-0.47, 0.18)	0.87
CDCA	0.00 (-0.28, 0.29)	0.99	-0.15 (-0.43, 0.13)	0.81	0.29 (-0.04, 0.62)	0.53
GDCA-3S	0.00 (-0.28, 0.28)	0.99	0.09 (-0.18, 0.37)	0.81	-0.11 (-0.43, 0.22)	0.87

Note. LMMs adjusted for age, sex, BMI, study sites, and the random effect of families were used. FDR was obtained by Benjamini-Hochberg method at a 5% false discovery rate.

Supplementary Table S10. Associations between richness-related metabolites and ambulatory DBPV indices

Metabolites	24-hour DBPV		Daytime DBPV		Nighttime DBPV	
	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR	Effect Size (95% *CI*)	FDR
Hydrocinnamic acid	-0.30 (-0.53, -0.07)	0.13	-0.21 (-0.44, 0.03)	0.96	0.15 (-0.09, 0.40)	0.81
GUDCA	0.32 (0.10, 0.54)	0.13	0.27 (0.04, 0.49)	0.59	0.15 (-0.09, 0.38)	0.81
Hydroxyphenyllactic acid	0.23 (-0.02, 0.49)	0.49	-0.01 (-0.28, 0.25)	0.99	-0.10 (-0.37, 0.18)	0.90
isoLCA	-0.22 (-0.44, 0.01)	0.49	-0.17 (-0.40, 0.06)	0.96	-0.14 (-0.39, 0.10)	0.81
2-Hydroxy-3-methylbutyric acid	0.21 (-0.06, 0.49)	0.52	0.02 (-0.26, 0.30)	0.99	0.10 (-0.19, 0.39)	0.90
GCDCA	0.17 (-0.06, 0.40)	0.52	0.13 (-0.11, 0.36)	0.96	0.03 (-0.21, 0.28)	0.96
GCDCA-3S	0.19 (-0.05, 0.43)	0.52	0.12 (-0.12, 0.37)	0.96	0.06 (-0.20, 0.32)	0.91
Homovanillic acid	0.16 (-0.10, 0.42)	0.74	0.00 (-0.27, 0.26)	0.99	-0.08 (-0.35, 0.20)	0.90
Alanine	-0.10 (-0.33, 0.13)	0.86	-0.07 (-0.30, 0.16)	0.99	-0.01 (-0.26, 0.23)	0.98
Hippuric acid	0.11 (-0.13, 0.34)	0.86	-0.03 (-0.27, 0.22)	0.99	0.17 (-0.08, 0.43)	0.81
Indole-3-propionic acid	0.09 (-0.14, 0.31)	0.86	0.10 (-0.13, 0.33)	0.96	0.07 (-0.17, 0.32)	0.90
TDCA	-0.11 (-0.34, 0.11)	0.86	-0.13 (-0.36, 0.10)	0.96	-0.07 (-0.31, 0.17)	0.90
DCA	0.07 (-0.15, 0.30)	0.86	0.03 (-0.20, 0.26)	0.99	0.01 (-0.24, 0.25)	0.98
GLCA	-0.08 (-0.30, 0.15)	0.86	-0.03 (-0.26, 0.20)	0.99	-0.16 (-0.39, 0.08)	0.81
Citramalic acid	0.10 (-0.13, 0.33)	0.86	-0.01 (-0.24, 0.23)	0.99	0.05 (-0.20, 0.29)	0.92
Imidazole propionate	0.07 (-0.16, 0.31)	0.86	0.10 (-0.14, 0.34)	0.96	0.07 (-0.18, 0.32)	0.90
Phenylacetylglutamine	-0.06 (-0.29, 0.16)	0.87	-0.11 (-0.34, 0.11)	0.96	0.01 (-0.23, 0.25)	0.98
GDCA-3S	0.06 (-0.16, 0.29)	0.87	0.04 (-0.19, 0.27)	0.99	-0.03 (-0.27, 0.21)	0.96
2-Phenylpropionate	0.04 (-0.19, 0.27)	0.88	-0.06 (-0.30, 0.17)	0.99	0.19 (-0.06, 0.43)	0.81
3-(3-Hydroxyphenyl)-3-hydroxy propanoic acid	0.05 (-0.18, 0.27)	0.88	-0.02 (-0.25, 0.21)	0.99	-0.18 (-0.42, 0.07)	0.81
1-Methylnicotinamide	-0.02 (-0.24, 0.21)	0.88	-0.10 (-0.33, 0.12)	0.96	0.10 (-0.14, 0.34)	0.90
CDCA	0.04 (-0.19, 0.27)	0.88	-0.08 (-0.31, 0.15)	0.99	0.25 (0.00, 0.49)	0.81
GDCA	0.02 (-0.20, 0.24)	0.88	0.03 (-0.20, 0.25)	0.99	0.08 (-0.16, 0.32)	0.90
LCA	0.03 (-0.19, 0.25)	0.88	-0.04 (-0.27, 0.19)	0.99	0.00 (-0.24, 0.24)	0.98
GLCA-3S	-0.02 (-0.25, 0.20)	0.88	0.02 (-0.21, 0.25)	0.99	-0.05 (-0.28, 0.19)	0.92
TMAO	0.03 (-0.20, 0.26)	0.88	-0.16 (-0.39, 0.07)	0.96	0.09 (-0.15, 0.34)	0.90

Note. LMMs adjusted for age, sex, BMI, study sites, and the random effect of families were used. FDR was obtained by Benjamini-Hochberg method at a 5% false discovery rate.

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Supplementary Table S11. Effect sizes of identified metabolic mediators on BP indices after adjusting for richness

Metabolites	24-hour	Daytime	Nighttime
	Effect Size (95% *CI*)	Effect Size (95% *CI*)	Effect Size (95% *CI*)
SBP			
Imidazole propionate	1.62 (0.67, 2.58)	1.50 (0.53, 2.46)	2.03 (0.89, 3.17)
2-Hydroxy-3-methylbutyric acid	1.10 (0.01, 2.20)	1.51 (0.41, 2.62)	0.48 (-0.83, 1.80)
Homovanillic acid	1.18 (0.14, 2.23)	1.39 (0.33, 2.44)	0.59 (-0.66, 1.85)
Hydrocinnamic acid	-0.44 (-1.49, 0.62)	-0.83 (-1.89, 0.23)	0.55 (-0.71, 1.81)
DBP			
Imidazole propionate	0.55 (-0.20, 1.30)	0.51 (-0.28, 1.30)	0.70 (-0.13, 1.53)
2-Hydroxy-3-methylbutyric acid	0.94 (0.09, 1.79)	1.25 (0.35, 2.14)	0.40 (-0.54, 1.35)
Homovanillic acid	0.82 (0.01, 1.63)	0.96 (0.10, 1.82)	0.26 (-0.64, 1.16)
Hydrocinnamic acid	-0.50 (-1.32, 0.32)	-0.75 (-1.61, 0.11)	0.08 (-0.83, 0.98)
SBPV			
Imidazole propionate	0.11 (-0.20, 0.41)	0.34 (0.05, 0.63)	0.24 (-0.11, 0.59)
2-Hydroxy-3-methylbutyric acid	0.23 (-0.12, 0.57)	-0.01 (-0.35, 0.33)	0.13 (-0.26, 0.53)
Homovanillic acid	0.12 (-0.22, 0.45)	-0.02 (-0.33, 0.31)	-0.10 (-0.48, 0.28)
Hydrocinnamic acid	-0.48 (-0.81, -0.15)	-0.26 (-0.58, 0.07)	0.34 (-0.04, 0.72)
DBPV			
Imidazole propionate	0.07 (-0.18, 0.31)	0.12 (-0.13, 0.37)	0.09 (-0.17, 0.35)
2-Hydroxy-3-methylbutyric acid	0.21 (-0.07, 0.48)	0.03 (-0.25, 0.31)	0.12 (-0.18, 0.41)
Homovanillic acid	0.16 (-0.11, 0.42)	0.01 (-0.26, 0.27)	-0.07 (-0.35, 0.21)
Hydrocinnamic acid	-0.37 (-0.64, -0.11)	-0.30 (-0.57, -0.03)	0.17 (-0.12, 0.45)

Note. LMMs were used to estimate the effects of the four discovered metabolites on ambulatory BP indices adjusting for gut microbial richness (Chao1), age, sex, BMI, study sites, and the random effect of families. *CI*, confidence interval; DBP, diastolic blood pressure; DBPV, diastolic blood pressure variability; SBP, systolic blood pressure; SBPV, systolic blood pressure variability.

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Supplementary Table S12. Multivariable-Adjusted *ORs* (95% *CIs*) of prevalent hypertension by quartiles of identified metabolites in the cohort

Metabolites	***OR* (95% *CI*)**				P_{trend}
	Q1	Q2	Q3	Q4	
Imidazole propionate	[Reference]	0.86 (0.66, 1.11)	1.02 (0.78, 1.32)	1.34 (1.02, 1.74)	0.02
2-Hydroxy-3-methylbutyric acid	[Reference]	1.21 (0.93, 1.58)	1.26 (0.96, 1.66)	1.57 (1.17, 2.11)	3.40×10^{-3}
Homovanillic acid	[Reference]	1.21 (0.93, 1.57)	1.06 (0.80, 1.39)	1.40 (1.05, 1.88)	0.06
Hydrocinnamic acid	[Reference]	1.07 (0.82, 1.39)	0.77 (0.59, 1.00)	0.76 (0.58, 0.99)	0.01

Note. Each identified metabolite was categorized into quartile groups. Covariates included age, sex, BMI, work-related physical activity, urbanization, smoking status, alcohol drinking, education level, dyslipidemia, and diabetes mellitus. *CI*, confidence interval. *OR*, odds ratio.

Supplementary Table S13. Multivariable-Adjusted *HRs* (95% *CIs*) of incident hypertension by quartiles of identified metabolites in the cohort

Metabolites	***HR* (95% *CI*)**				P_{trend}
	Q1	Q2	Q3	Q4	
Imidazole propionate	[Reference]	1.23 (0.82, 1.83)	1.31 (0.84, 2.02)	1.59 (1.04, 2.45)	0.03
2-Hydroxy-3-methylbutyric acid	[Reference]	0.73 (0.48, 1.11)	0.92 (0.61, 1.40)	0.59 (0.37, 0.95)	0.10
Homovanillic acid	[Reference]	0.74 (0.48, 1.15)	1.24 (0.83, 1.87)	1.24 (0.78, 1.98)	0.12
Hydrocinnamic acid	[Reference]	0.87 (0.57, 1.33)	0.78 (0.51, 1.18)	0.63 (0.41, 0.97)	0.03

Note. Each identified metabolite was categorized into quartile groups. Covariates included age, sex, BMI, work-related physical activity, urbanization, smoking status, alcohol drinking, education level, dyslipidemia, and diabetes mellitus. *CI*, confidence interval. *HR*, hazard ratio.