Supplementary Materials

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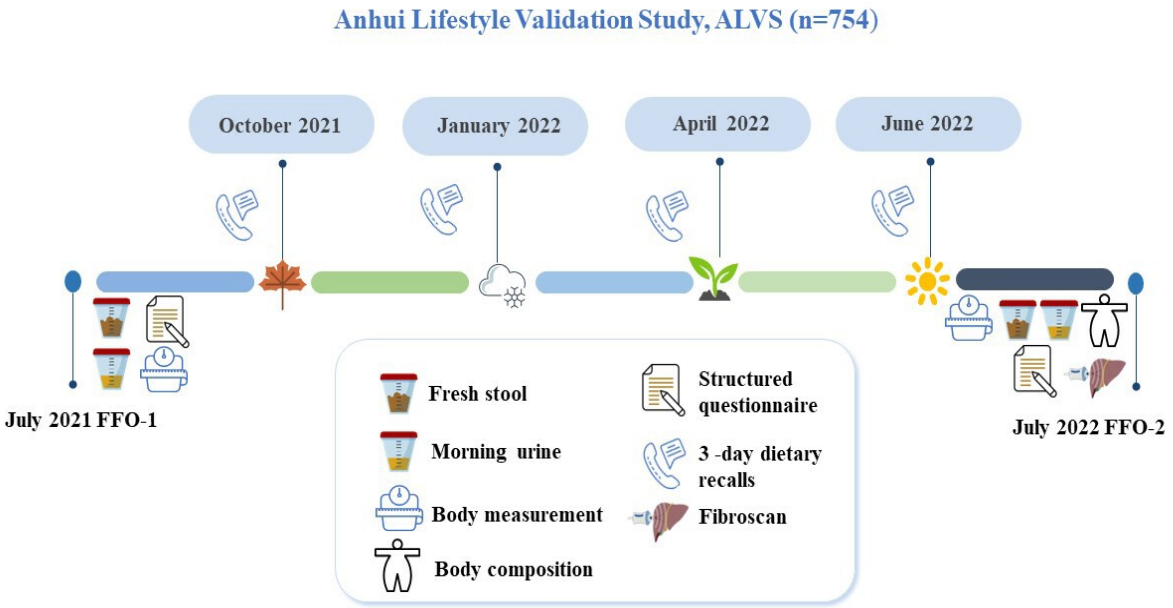
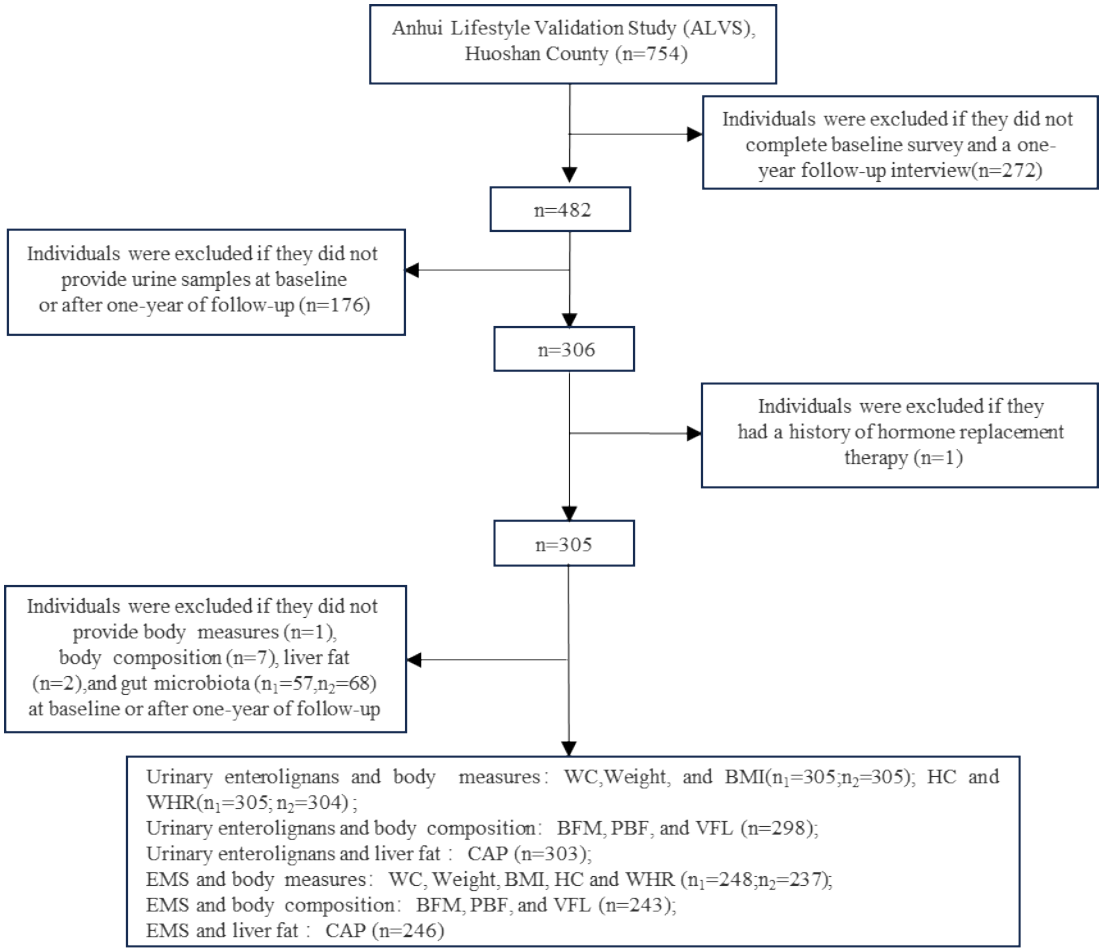


Supplementary Figure 1 The study design of the Anhui Lifestyle Validation Study. FFQ, food frequency questionnaire.



Supplementary Figure 2 Flowchart of the participants selection in the analysis.

n_1, sample size at baseline for repeated measures; n_2, sample size after 1-year of follow-up for repeated measures.

BFM, body fat mass; BMI, body mass index; CAP, controlled attenuation parameter; EMS, enterolignan-predicting microbial score; HC, hip circumference; PBF, percent body fat; VFL, visceral fat level; WC, waist circumference; WHR, waist-to-hip ratio.

Supplementary Table 1 The characteristics of participants according to urinary enterolignans concentration at baseline and after one-year of follow-up in Huoshan, China [a]

Characteristics	Enterolactone at baseline			Enterodiol at baseline			Enterolactone after one-year of follow-up			Enterodiol after one-year of follow-up		
	Tertile 1	Tertile 2	Tertile 3	Tertile 1	Tertile 2	Tertile 3	Tertile 1	Tertile 2	Tertile 3	Tertile 1	Tertile 2	Tertile 3
No. of participants [b]	101	102	102	101	102	102	101	102	102	101	102	102
Age, years	49.0 (37.0-58.0)	53.0 (39.0-60.0)	48.5 (34.0-59.0)	48.0 (37.0-58.0)	50.5 (34.0-58.0)	51.5 (38.0-62.0)	50.0 (37.0-59.0)	50.5 (37.0-60.0)	52.0 (40.0-64.0)	49.0 (35.0-58.0)	50.5 (37.0-60.0)	54.0 (42.0-64.0)
Female**‡, %	43.6	54.9	65.7	44.6	57.8	61.8	49.5	51.0	62.8	44.6	62.8	55.9
Married, %	83.2	76.2	88.2	80.2	81.4	86.1	84.0	79.2	82.4	83.8	78.4	83.3
Household per capita income, %												
<5000 Yuan	11.1	21.7	11.2	13.1	11.6	19.0	7.1	8.3	12.9	6.1	14.1	8.2
5000-10,000 Yuan	24.2	18.6	22.5	26.3	17.9	21.0	13.3	18.6	12.9	14.1	13.1	17.4
10,000-20,000 Yuan	27.3	19.6	30.6	21.2	29.5	27.0	25.5	25.8	26.7	28.3	24.2	25.5
> 20,000 Yuan	37.4	40.2	35.7	39.4	41.1	33.0	54.1	47.4	47.5	51.5	48.5	49.0
Education level, %												
Informal education,	11.9	16.7	13.7	10.9	15.7	15.7	5.9	14.7	17.7	5.9	15.7	16.7
Primary school or below	29.7	26.5	25.5	25.7	26.5	29.4	26.7	27.5	23.5	24.8	26.5	26.5
Junior high school	25.7	23.5	31.4	27.7	24.5	28.4	35.6	25.5	27.5	29.7	28.4	30.4
Senior high school or above	32.7	33.3	29.4	35.6	33.3	26.5	31.7	32.4	31.4	39.6	29.4	26.5
Never smokers, %	65.4	70.6	80.2	64.4	74.3	77.5	63.4	66.7	75.5	62.4	73.5	69.6
Never drinkers*, %	73.2	84.7	86.9	77.9	80.2	86.7	79.0	80.2	88.1	80.8	84.3	82.2
BMI, kg/m^2												
<18.5 kg/m^2	2.0	3.9	2.9	1.0	3.9	3.9	6.9	5.9	4.9	4.0	8.8	4.9
18.5-24.0 kg/m^2	36.6	45.1	53.9	42.6	43.1	50.0	39.6	45.1	52.0	42.6	41.2	52.9
24.0-28.0 kg/m^2	38.6	37.3	27.5	40.6	31.4	31.4	40.6	32.4	33.3	35.6	35.3	35.3
≥28.0 kg/m^2	22.8	13.7	15.7	15.8	21.6	14.7	12.9	16.7	9.8	17.8	14.7	6.9
Total energy intake, kcal/d	2180 (1701-3051)	2235 (1676-2696)	2002 (1665-2660)	2180 (1690-2954)	2081 (1590-2569)	2169 (1684-2822)	1905 (1557-2528)	2016 (1463-2746)	1888 (1550-2329)	1920 (1489-2528)	1789 (1453-2376)	1970 (1680-2509)
Physical activities, METS-h/week	146.1 (112.1-205.6)	162.5 (109.8-223.2)	145.5 (101.5-218.3)	156.1 (112.1-235.7)	148.3 (93.9-206.1)	158.7 (112.2-218.3)	156.6 (113.5-220.6)	155.1 (101.5-237.7)	170.2 (106.6 - 257.5)	139.8 (104.2-207.9)	156.8 (110.7-239.5)	181.5 (109.0-257.5)
Hypertension*, %	59.4	46.1	40.2	52.5	52.9	40.2	51.5	53.9	40.2	48.5	51.0	45.1
Type 2 diabetes, %	12.9	12.8	7.8	11.9	10.8	10.8	13.9	20.6	8.8	16.8	16.7	9.8
DASH score‡	24 (22-28)	24 (22-26)	24 (22-27)	24 (22-27)	24 (22-26)	24 (22-27)	24 (21-26)	24 (21-26)	24 (22-27)	24 (21-26)	23 (21-25)	25 (22-27)

Abbreviations: BMI, body mass index; DASH, dietary approaches to stop hypertension; METS, metabolic equivalent tasks.

[a] Continuous variables are expressed as the median (interquartile range) or mean (SD) according to the distribution of the variables, while categorical variables are presented as percentage. *P* values were calculated from the one-way ANOVA or Kruskal-Wallis test for continuous variables and chi-square test or Fisher's exact test for categorical variables.

[b] Numbers of participants vary due to missing values for outcome variables or covariates or to outliers.

Urinary enterolactone at baseline: **P* value < 0.05, ***P* value < 0.01; Urinary enterodiol at baseline: [|]*P* value <0.05; Urinary enterodiol after one-year of follow-up: [‡]*P* value <0.05.

P <0.05 indicates significant difference.

Supplementary Table 2 One-year longitudinal repeated-measures associations between relative abundances of bacterial genera and urinary enterolactone among 485 participants in Huoshan, China

Phylum; class; order; family; genus	Prevalence (%)1	Average abundance (%) 1	Prevalence (%)2	Average abundance (%)2	β (SE)	*P* value	P_{FDR} value
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Intestinimonas*	41.94	0.02	··	··	96.90 (17.33)	<0.001	<0.001
Proteobacteria; Betaproteobacteria; Burkholderiales; Oxalobacteraceae; *Oxalobacter*	··	··	30.80	0.01	68.14 (15.89)	<0.001	<0.001
Actinobacteria; Actinobacteria; Coriobacteriales; Coriobacteriaceae; *Adlercreutzia*	55.24	0.02	50.63	0.02	66.20 (11.50)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Peptostreptococcaceae; *Mogibacterium*	··	··	29.54	0.02	62.68 (14.60)	<0.001	<0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Porphyromonadaceae; *Odoribacter*	70.97	0.08	64.14	0.04	44.05 (7.39)	<0.001	<0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Porphyromonadaceae; *Butyricimonas*	57.66	0.08	49.37	0.03	42.93 (7.10)	<0.001	<0.001
Actinobacteria; Coriobacteriia; Eggerthellales; Coriobacteriaceae; *Gordonibacter*	··	··	34.60	0.03	26.74 (10.00)	0.008	0.025
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; *Eisenbergiella*	··	··	49.79	0.05	20.97 (8.97)	0.020	0.048
Bacteroidetes; Bacteroidia; Bacteroidales; Porphyromonadaceae; *Coprobacter*	16.53	0.02	12.24	0.03	20.45 (8.31)	0.015	0.037
Bacteroidetes; Bacteroidia; Bacteroidales; Porphyromonadaceae; *Barnesiella*	45.56	0.21	42.19	0.11	20.25 (3.77)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; *Coprococcus*	75.81	0.19	83.97	0.26	19.26 (3.54)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Sporobacter*	61.29	0.16	63.29	0.49	19.05 (3.03)	<0.001	<0.001
Proteobacteria; Deltaproteobacteria; Desulfovibrionales; Desulfovibrionaceae; *Bilophila*	78.63	0.18	80.17	0.19	15.14 (4.16)	<0.001	0.002
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Subdoligranulum*	90.32	0.14	91.56	0.47	14.89 (2.82)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; *Dorea*	89.52	0.20	86.08	0.13	15.02 (5.57)	0.008	0.025
Proteobacteria; Deltaproteobacteria; Desulfovibrionales; Desulfovibrionaceae; *Desulfovibrio*	39.11	0.14	44.73	0.32	12.01 (2.95)	<0.001	<0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Rikenellaceae; *Alistipes*	85.48	0.98	84.81	0.54	11.90 (1.94)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Oscillibacter*	90.73	0.36	91.14	0.71	11.26 (2.04)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Clostridium_IV*	90.32	0.07	92.83	0.17	10.88 (4.66)	0.020	0.048
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Ruminococcus*	84.68	1.23	84.39	1.28	9.21 (1.47)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Eubacteriaceae; *Eubacterium*	62.50	0.25	67.09	0.90	8.86 (1.79)	<0.001	<0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Prevotellaceae; *Paraprevotella*	37.50	0.30	35.44	0.25	8.93 (2.79)	0.002	0.006
Actinobacteria; Actinobacteria; Coriobacteriales; Coriobacteriaceae; *Collinsella*	63.31	0.21	68.78	0.43	7.20 (2.51)	0.005	0.016
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Faecalibacterium*	100.00	7.71	98.73	8.98	4.13 (0.75)	<0.001	0.001
Firmicutes; Negativicutes; Selenomonadales; Acidaminococcaceae; *Phascolarctobacterium*	84.68	2.62	91.56	2.49	3.11 (1.12)	0.006	0.020
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Gemmiger*	83.06	0.82	87.34	3.05	2.73 (1.03)	0.009	0.026

Abbreviations: FDR, false discovery rate.

P values were estimated from a linear mixed-effects model with repeated measures after adjustment for age (18-29, 30-39, 40-49, 50-59, and ≥60 years), sex (women, men), education level (informal education, primary school or below, junior high school, and senior high school or above), household per capita income (<5000, 5000-10,000, 10,000-20,000, and >20,000 yuan), total energy intake (kcal/day, continuous), physical activity (metabolic equivalent tasks-h/week, continuous), current or past smoking (yes, no), current or past alcohol drinking (yes, no), batch effect. All taxa with false discovery rate-adjusted P_{FDR} <0.05 are included in the table.

Supplementary Table 3 One-year longitudinal repeated-measures associations between relative abundances of bacterial genera and urinary enterodiol among 485 participants in Huoshan, China

Phylum; class; order; family; genus	Prevalence (%)1	Average abundance (%)1	Prevalence (%)2	Average abundance (%)2	β (SE)	*P* value	P_{FDR} value
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Intestinimonas*	41.94	0.02	··	··	80.32 (17.67)	<0.001	<0.001
Actinobacteria; Actinobacteria; Coriobacteriales; Coriobacteriaceae; *Adlercreutzia*	55.24	0.02	50.63	0.02	60.35 (12.58)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Peptostreptococcaceae; *Mogibacterium*	··	··	29.54	0.02	47.83 (15.17)	0.002	0.009
Bacteroidetes; Bacteroidia; Bacteroidales; Porphyromonadaceae; *Odoribacter*	70.97	0.08	64.14	0.04	41.27 (7.93)	<0.001	<0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Porphyromonadaceae; *Butyricimonas*	57.66	0.08	49.37	0.03	39.07 (7.51)	<0.001	<0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Porphyromonadaceae; *Barnesiella*	45.56	0.21	42.19	0.11	19.55 (4.06)	<0.001	<0.001
Proteobacteria; Deltaproteobacteria; Desulfovibrionales; Desulfovibrionaceae; *Bilophila*	78.63	0.18	80.17	0.19	18.71 (4.52)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; *Dorea*	89.52	0.20	86.08	0.13	17.64 (6.09)	0.004	0.017
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Sporobacter*	61.29	0.16	63.29	0.49	16.70 (3.35)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; *Coprococcus*	75.81	0.19	83.97	0.26	14.43 (3.91)	<0.001	0.002
Actinobacteria; Actinobacteria; Coriobacteriales; Coriobacteriaceae; *Collinsella*	63.31	0.21	68.78	0.43	10.80 (2.76)	<0.001	0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Rikenellaceae; *Alistipes*	85.48	0.98	84.81	0.54	12.34 (2.10)	<0.001	<0.001
Proteobacteria; Deltaproteobacteria; Desulfovibrionales; Desulfovibrionaceae; *Desulfovibrio*	39.11	0.14	44.73	0.32	10.62 (3.21)	0.001	0.006
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Oscillibacter*	90.73	0.36	91.14	0.71	10.30 (2.31)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Subdoligranulum*	90.32	0.14	91.56	0.47	9.52 (3.24)	0.004	0.016
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; *Ruminococcus2*	98.39	0.65	95.78	0.68	7.96 (2.80)	0.005	0.019
Bacteroidetes; Bacteroidia; Bacteroidales;Prevotellaceae; *Paraprevotella*	37.50	0.30	35.44	0.25	7.84 (3.00)	0.009	0.034
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Ruminococcus*	84.68	1.23	84.39	1.28	7.87 (1.64)	<0.001	<0.001
Firmicutes; Clostridia; Clostridiales; Eubacteriaceae; *Eubacterium*	62.50	0.25	67.09	0.90	6.14 (2.06)	0.003	0.014
Firmicutes; Clostridia; Clostridiales; Lachnospiraceae; *Roseburia*	99.19	4.83	99.16	3.05	3.61 (1.13)	0.002	0.009
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; *Faecalibacterium*	100.00	7.71	98.73	8.98	3.24 (0.84)	<0.001	0.001
Bacteroidetes; Bacteroidia; Bacteroidales; Prevotellaceae; *Prevotella*	89.52	13.99	81.01	10.64	1.23 (0.43)	0.004	0.017

Abbreviations: FDR, false discovery rate.

P values were estimated from a linear mixed-effects model with repeated measures after adjustment for age (18-29, 30-39, 40-49, 50-59, and ≥60 years), sex (women, men), education level (informal education, primary school or below, junior high school, and senior high school or above), household per capita income (<5000, 5000-10,000, 10,000-20,000, and >20,000 yuan), total energy intake (kcal/day, continuous), physical activity (metabolic equivalent tasks-h/week, continuous), current or past smoking (yes, no), current or past alcohol drinking (yes, no), batch effect. All taxa with false discovery rate-adjusted P_{FDR} <0.05 are included in the table.

Supplementary Table 4 Cross-sectional associations between urinary enterolignans and body fat measures at baseline and after 1-year among community-dwelling adults in Huoshan, China [a, b]

Body fat measures	Urinary enterolignans at baseline		Urinary enterolignans after 1-year	
	β (SE)	*P*	β (SE)	*P*
WC (N_1=305; N_2=305)	-0.0093(0.0027)	0.001	-0.0080(0.0036)	0.026
HC (N_1=305; N_2=304)	-0.0027(0.0020)	0.173	-0.0064(0.0025)	0.011
WHR (N_1=305; N_2=304)	-0.0065(0.0019)	0.001	-0.0014(0.0025)	0.561
Weight (N_1=305; N_2=305)	-0.0101(0.0037)	0.007	-0.0122(0.0048)	0.011
BMI (N_1=305; N_2=305)	-0.0102(0.0034)	0.003	-0.0112(0.0043)	0.010
BFM (N_1=298; N_2=298)	-0.0241(0.0092)	0.009	-0.0332(0.0113)	0.004
PBF (N_1=298; N_2=298)	-0.0132(0.0062)	0.035	-0.0193(0.0076)	0.011
VFL (N_1=298; N_2=298)	-0.0275(0.0113)	0.016	-0.0381(0.0137)	0.006
CAP (N_1=303; N_2=303)	-0.0161(0.0046)	0.001	-0.0194(0.0056)	0.001

Abbreviations: BFM, body fat mass; BMI, body mass index; CAP, controlled attenuation parameter; DASH, dietary approaches to stop hypertension; HC, hip circumference; PBF, percent body fat; VFL, visceral fat level; WC, waist circumference; WHR, waist-to-hip ratio.

[a] Linear regression models were adjusted for age (18-29, 30-39, 40-49, 50-59, and ≥60 years), sex (women, men), education level (informal education, primary school or below, junior high school, and senior high school or above), household per capita income (<5000, 5000-10,000, 10,000-20,000, and >20,000 yuan), total energy intake (kcal/day, continuous), physical activity (metabolic equivalent tasks-h/week, continuous), menopausal status (yes, no), current or past smoking (yes, no), current or past

alcohol drinking (yes, no), and DASH diet index (continuous).

[b] The sample size depended on the availability of data on urinary enterolignans and obesity markers. N_1, sample size at baseline, N_2, sample size after 1-year.

$P<0.05$ indicates significant difference.

Supplementary Table 5 Cross-sectional associations between enterolignan-predicting microbial score and body fat measures at baseline and after 1-year among community-dwelling adults in Huoshan, China [a, b]

Body fat measures	Enterolignan-predicting microbial score at baseline		Enterolignan-predicting microbial score after 1-year	
	β (SE)	*P*	β (SE)	*P*
WC (N_1=248; N_2=237)	0.0216(0.0146)	0.141	0.0223(0.0153)	0.146
HC (N_1=248; N_2=237)	0.0116(0.0111)	0.300	0.0078(0.0097)	0.424
WHR (N_1=248; N_2=237)	0.0100(0.0106)	0.345	0.0141(0.0091)	0.123
Weight (N_1=248; N_2=237)	0.0251(0.0197)	0.204	0.0036(0.0212)	0.863
BMI (N_1=248; N_2=237)	0.0281(0.0187)	0.134	0.0181(0.0193)	0.349
BFM (N_1=243; N_2=232)	-0.0749(0.0502)	0.137	-0.0265(0.0511)	0.605
PBF (N_1=243; N_2=232)	-0.0373(0.0349)	0.286	-0.0166(0.0347)	0.633
VFL (N_1=243; N_2=232)	-0.0847(0.0619)	0.173	-0.0416(0.0618)	0.501
CAP (N_1=246; N_2=235)	-0.0776(0.0241)	0.001	-0.0535(0.0237)	0.025

Abbreviations: BFM, body fat mass; BMI, body mass index; CAP, controlled attenuation parameter; PBF, percent body fat; VFL, visceral fat level; WHR, waist-to-hip ratio.

[a] Linear regression models were adjusted for age (18-29, 30-39, 40-49, 50-59, and ≥60 years), sex (women, men), education level (informal education, primary school or below, junior high school, and senior high school or above), household per capita income (<5000, 5000-10,000, 10,000-20,000, and >20,000 yuan), total energy intake (kcal/day, continuous), physical activity (metabolic equivalent tasks-h/week, continuous), current or past smoking (yes, no), and current or past alcohol drinking (yes, no).

[b] The sample size depended on the availability of data on urinary enterolignans, gut microbiota, and obesity markers. N_1, sample size at baseline, N_2, sample size after 1-year.

$P<0.05$ indicates significant difference.