Table S1. Parameters of the single-ion monitoring (SIM) mode acquisition and performance of the short-chain fatty acid (SCFA) quantification method using gas chromatography–mass spectrometry (GC/MS).

Descriptor	SCFAs			
	Acetic	**Propionic**	**Butyric**	**Isobutyric**
SIM Ions m/z (m/z)/Dwell time (mS)				
SIM target	43.1/30	74.1/25	60.1/30	43.1/30
SIM qualifier	60.1/15; 45.2/15	73.1/10; 45.1/15	88.2/15; 73.2/10	88.2/10; 73.1/15
Regression equation n=9				
(Y=mX+b) range=25-750 ng/mL	y=6E+07x+4E+06	y=7E+07x+1E+07	y=3E+08x+5E+07	y=2E+08x+5E+07
Regression adjustment (r)	0.992	0.996	0.998	0.993
Response factor n=9				
(RF+%RSD)	1.09E-08 ≤ 2.0	7.40E-09 ≤ 2.0	1.75E-09 ≤ 2.0	1.90E-09 ≤ 2.0
Linearity test				
Homoscedasticity value ($G_{exp}<G_{table}$)	0.4924	0.0947	0.0942	0.1478
G_{table} (a=0.05; k=6; n=3)=0.616)				
Precision (n=27)				
Instrument (Repeatability, %RSD <3)	1.72	0.99	1.12	1.09
Method (%RSD <2)	1.32	1.04	1.11	1.08
Recovery (n=9)				
% ± SD	99.45 ± 1.22	100.45 ± 1.04	99.92 ± 0.99	99.84 ± 1.02
Cochran test value ($G_{exp}<G_{table}$)	0.637	0.211	0.206	0.198
G_{table} (a=0.05; k=3; n=3)=0.871				

Table S2. Characteristics of the study population overall and according to tertiles (1: low, 2: intermediate, 3: high) of unadjusted fecal SCFA levels (total SCFAs, acetate, propionate and isobutyrate). Data presented as mean ± SEM. P-values from ANOVA to the exception of sex (chi-squared test). FDR-adjusted p-values are highlighted (*=q<0.05).

Variables	Total fecal SCFAs (μmol/g)				Fecal acetate (μmol/g)			
	Tertile 1	**Tertile 2**	**Tertile 3**	**P-value**	**Tertile 1**	**Tertile 2**	**Tertile 3**	**P-value**
n	147	147	147		147	147	147	
Age (years)	40 ± 1	41 ± 1	42 ± 1	0.40	39 ± 1	41 ± 1	42 ± 1	0.06*
Sex (%males:%females)	40/60	50/50	54/46	0.05*	41/59	51/49	52/48	0.10
Diet								
Calorie intake (kcal/day)	1873 ± 32	1941 ± 40	1977 ± 37	0.14	1887 ± 34	1928 ± 38	1976 ± 38	0.10
Fiber intake (g/day)	16.7 ± 0.4	18.4 ± 0.4	17.9 ± 0.4	0.009*	16.9 ± 0.4	18.0 ± 0.4	18.2 ± 0.4	0.02*
Physical activity								
MET/min/week	4308 ± 376	5456 ± 534	5550 ± 440	0.25	4349 ± 376	5507 ± 543	5457 ± 430	0.19
Adiposity								
BMI (kg/m²)	26.7 ± 0.3	27.5 ± 0.4	29.6 ± 0.5	<0.0001*	26.8 ± 0.3	27.2 ± 0.4	29.7 ± 0.5	<0.0001*
Body fat (%)	36.3 ± 0.4	37.1 ± 0.5	38.1 ± 0.5	0.02*	36.4 ± 0.4	36.8 ± 0.5	38.3 ± 0.5	0.006*
Waist circumference (cm)	89.4 ± 0.9	92.0 ± 1.1	96.9 ± 1.2	<0.0001*	89.7 ± 0.9	91.7 ± 1.0	96.8 ± 1.2	<0.0001*
Blood chemistry								
HDL (mg/dL)	46 ± 1	46 ± 1	46 ± 1	0.98	46 ± 1	46 ± 1	47 ± 1	0.69
LDL (mg/dL)	117 ± 2	115 ± 2	113 ± 2	0.53	116 ± 2	116 ± 2	113 ± 2	0.47
VLDL (mg/dL)	27.3 ± 1.8	28.3 ± 1.4	30.6 ± 1.7	0.10	27.4 ± 1.8	29.0 ± 1.4	29.8 ± 1.6	0.08*
Triglycerides (mg/dL)	136 ± 9	142 ± 7	152 ± 8	0.11	137 ± 9	144 ± 7	149 ± 8	0.08*
hs-CRP (mg/L)	2.64 ± 0.32	3.41 ± 0.44	3.4 ± 0.36	0.03*	2.72 ± 0.32	3.22 ± 0.43	3.50 ± 0.36	0.02*
Glucose (mg/dL)	87 ± 2	90 ± 2	92 ± 2	0.02*	86 ± 2	90 ± 2	92 ± 2	0.005*
HbA1c (%)	5.46 ± 0.04	5.57 ± 0.06	5.63 ± 0.06	0.05*	5.44 ± 0.04	5.58 ± 0.05	5.64 ± 0.06	0.006*
Insulin (μU/mL)	12.0 ± 0.6	12.8 ± 0.7	15.0 ± 0.8	0.01*	11.7 ± 0.5	13.2 ± 0.7	14.9 ± 0.8	0.005*
HOMA-IR	3.07 ± 0.34	3.20 ± 0.23	3.10 ± 0.17	0.43	3.17 ± 0.35	3.17 ± 0.21	3.03 ± 0.17	0.36
Leptin (ng/mL)	6.92 ± 0.56	6.51 ± 0.49	7.98 ± 0.52	0.23	7.05 ± 0.58	6.15 ± 0.44	8.22 ± 0.54	0.17
Adiponectin (μg/mL)	6.4 ± 0.2	7.2 ± 0.4	6.8 ± 0.4	0.44	6.5 ± 0.2	7.0 ± 0.4	6.9 ± 0.4	0.53
LBP (μg/mL)	4.27 ± 0.14	4.66 ± 0.14	4.58 ± 0.12	0.09	4.26 ± 0.14	4.59 ± 0.13	4.66 ± 0.13	0.03*
Blood pressure								
Systolic (mm Hg)	120 ± 1	125 ± 2	128 ± 2	0.0005*	120 ± 1	125 ± 2	128 ± 2	0.001*
Diastolic (mm Hg)	78 ± 1	80 ± 1	83 ± 1	0.001*	78 ± 1	80 ± 1	82 ± 1	0.001*
Mean (mm Hg)	92 ± 1	95 ± 1	98 ± 1	0.0006*	92 ± 1	95 ± 1	97 ± 1	0.001*
OTU richness	157 ± 3	140 ± 3	136 ± 3	<0.0001*	154 ± 3	140 ± 3	140 ± 3	0.002*
Fecal SCFAs								
Total SCFAs (μmol/g)	0.87 ± 0.05	3.70 ± 0.08	12.24 ± 0.81	<0.0001*	0.93 ± 0.06	3.81 ± 0.12	12.06 ± 0.82	<0.0001*
Acetate (μmol/g)	0.60 ± 0.04	2.51 ± 0.07	8.38 ± 0.52	<0.0001*	0.57 ± 0.04	2.47 ± 0.06	8.45 ± 0.51	<0.0001*
Propionate (μmol/g)	0.15 ± 0.01	0.74 ± 0.03	2.66 ± 0.24	<0.0001*	0.21 ± 0.02	0.85 ± 0.07	2.49 ± 0.24	<0.0001*
Butyrate (μmol/g)	0.12 ± 0.01	0.45 ± 0.02	1.19 ± 0.11	<0.0001*	0.16 ± 0.02	0.48 ± 0.03	1.12 ± 0.11	<0.0001*
Isobutyrate (μmol/g)	0.01 ± 0.001	0.03 ± 0.002	0.07 ± 0.02	<0.0001*	0.01 ± 0.001	0.03 ± 0.002	0.07 ± 0.02	<0.0001*

Table S2 (cont.)

Variables	Fecal propionate (μmol/g)				Fecal isobutyrate (μmol/g)			
	Tertile 1	**Tertile 2**	**Tertile 3**	**P-value**	**Tertile 1**	**Tertile 2**	**Tertile 3**	**P-value**
n	147	147	147		147	147	147	
Age (years)	40 ± 1	41 ± 1	41 ± 1	0.34	40 ± 1	41 ± 1	40 ± 1	0.90
Sex (%males:%females)	41/59	48/52	55/45	0.06*	42/58	56/44	46/54	0.06
Diet								
Calorie intake (kcal/day)	1886 ± 32	1931 ± 41	1974 ± 36	0.10*	1897 ± 39	1977 ± 37	1918 ± 33	0.55
Fiber intake (g/day)	16.8 ± 0.4	18.5 ± 0.4	17.9 ± 0.4	0.04*	16.9 ± 0.4	18.7 ± 0.4	17.4 ± 0.4	0.42
Physical activity								
MET/min/week	4059 ± 340	5671 ± 547	5583 ± 449	0.08*	5197 ± 468	4621 ± 412	5494 ± 485	0.62
Adiposity								
BMI (kg/m^2)	26.7 ± 0.3	27.5 ± 0.4	29.5 ± 0.5	<0.0001*	27.2 ± 0.4	27.8 ± 0.4	28.7 ± 0.4	0.01
Body fat (%)	36.0 ± 0.4	37.6 ± 0.4	37.9 ± 0.5	0.006*	36.7 ± 0.5	36.7 ± 0.5	38.2 ± 0.4	0.02
Waist circumference (cm)	89.3 ± 0.9	91.8 ± 1.1	97.1 ± 1.2	<0.0001*	90.6 ± 1.0	93.1 ± 1.1	94.5 ± 1.2	0.02
Blood chemistry								
HDL (mg/dL)	46 ± 1	46 ± 1	46 ± 1	0.66	46 ± 1	45 ± 1	46 ± 1	0.78
LDL (mg/dL)	116 ± 2	114 ± 2	114 ± 2	0.59	115 ± 2	115 ± 2	115 ± 2	0.99
VLDL (mg/dL)	26.9 ± 1.7	28.5 ± 1.4	30.8 ± 1.7	0.02*	28.8 ± 1.8	28.9 ± 1.4	28.5 ± 1.6	0.93
Triglycerides (mg/dL)	134 ± 9	142 ± 7	153 ± 8	0.02*	143 ± 9	144 ± 7	143 ± 8	0.98
hs-CRP (mg/L)	2.62 ± 0.32	3.12 ± 0.35	3.71 ± 0.45	0.005*	2.52 ± 0.21	3.05 ± 0.35	3.88 ± 0.50	0.004
Glucose (mg/dL)	88 ± 2	87 ± 1	93 ± 2	0.002*	88 ± 2	89 ± 1	91 ± 2	0.17
HbA1c (%)	5.50 ± 0.05	5.54 ± 0.04	5.62 ± 0.06	0.09*	5.49 ± 0.04	5.57 ± 0.05	5.60 ± 0.06	0.12
Insulin (μU/mL)	12.0 ± 0.6	12.8 ± 0.7	15.0 ± 0.8	0.003*	12.1 ± 0.5	13.2 ± 0.8	14.5 ± 0.8	0.02
HOMA-IR	2.88 ± 0.17	3.06 ± 0.35	3.43 ± 0.22	0.03*	3.14 ± 0.34	3.02 ± 0.22	3.22 ± 0.19	0.23
Leptin (ng/mL)	6.83 ± 0.56	6.88 ± 0.50	7.71 ± 0.51	0.26	6.68 ± 0.45	6.92 ± 0.60	7.81 ± 0.51	0.16
Adiponectin (μg/mL)	6.5 ± 0.2	7.5 ± 0.4	6.4 ± 0.3	0.22	6.7 ± 0.3	6.6 ± 0.3	7.1 ± 0.4	0.66
LBP (μg/mL)	4.32 ± 0.13	4.56 ± 0.14	4.62 ± 0.12	0.12	4.37 ± 0.13	4.63 ± 0.13	4.51 ± 0.13	0.45
Blood pressure								
Systolic (mm Hg)	121 ± 1	123 ± 2	129 ± 2	<0.0001*	123 ± 2	126 ± 1	124 ± 2	0.41
Diastolic (mm Hg)	78 ± 1	79 ± 1	83 ± 1	0.0004*	80 ± 1	81 ± 1	80 ± 1	0.94
Mean (mm Hg)	92 ± 1	94 ± 1	99 ± 1	0.0001*	94 ± 1	96 ± 1	95 ± 1	0.68
OTU richness	158 ± 3	144 ± 3	131 ± 3	<0.0001*	147 ± 3	141 ± 3	144 ± 3	0.51
Fecal SCFAs								
Total SCFAs (μmol/g)	0.96 ± 0.07	3.90 ± 0.13	11.94 ± 0.82	<0.0001*	3.91 ± 0.51	3.89 ± 0.31	9.00 ± 0.82	<0.0001
Acetate (μmol/g)	0.71 ± 0.06	2.77 ± 0.11	8.02 ± 0.54	<0.0001*	2.72 ± 0.35	2.60 ± 0.21	6.18 ± 0.52	<0.0001
Propionate (μmol/g)	0.14 ± 0.01	0.69 ± 0.02	2.73 ± 0.24	<0.0001*	0.86 ± 0.13	0.82 ± 0.08	1.87 ± 0.23	<0.0001
Butyrate (μmol/g)	0.11 ± 0.01	0.45 ± 0.03	1.20 ± 0.11	<0.0001*	0.33 ± 0.04	0.47 ± 0.04	0.95 ± 0.11	<0.0001
Isobutyrate (μmol/g)	0.01 ± 0.001	0.03 ± 0.002	0.08 ± 0.02	<0.0001*	0.0002 ± 0.0001	0.02 ± 0.001	0.09 ± 0.02	<0.0001

Table S3. Multivariable-adjusted fecal SCFA concentrations according to stool consistency. Models adjusted for participant age, city of residence, physical activity, fiber intake and caloric intake. Stool consistency sorted from rapid to slow intestinal transit time. P-values from ANOVA.

Fecal SCFAs	Rapid transit time → Slow transit time				P-value
	Diarrheic (N=18)	Mushy (N=63)	Normal (N=293)	Hard (N=67)	
Acetate	0.48 ± 0.26	0.09 ± 0.14	0.02 ± 0.07	-0.32 ± 0.18	0.06
Propionate	0.82 ± 0.29	0.06 ± 0.17	0.05 ± 0.07	-0.48 ± 0.15	0.0003
Butyrate	0.78 ± 0.27	0.03 ± 0.18	0.09 ± 0.08	-0.64 ± 0.18	<0.0001
Total SCFAs	0.64 ± 0.29	0.07 ± 0.15	0.04 ± 0.07	-0.43 ± 0.18	0.005
Isobutyrate	-0.16 ± 0.43	0.24 ± 0.21	0.01 ± 0.10	-0.22 ± 0.23	0.50

Table S4. Procrustes analysis correlating the gut microbiota-beta diversity with SCFA concentrations and variables informing about the risk of cardiometabolic disease. P-values obtained from 10,000 permutations. cor = correlation in a symmetric Procrustes rotation; the Y axis was scaled in all cases.

Variable	Unweighted UniFrac			Weighted UniFrac		
	cor	P-value	q-value	cor	P-value	q-value
Total SCFAs	0.14	0.0001	0.0002	0.17	0.0001	0.0002
Acetate	0.12	0.0002	0.0003	0.15	0.0001	0.0002
Propionate	0.16	0.0001	0.0002	0.19	0.0001	0.0002
Butyrate	0.17	0.0001	0.0002	0.19	0.0001	0.0002
Isobutyrate	0.10	0.003	0.004	0.06	0.19	0.19
Body mass index	0.07	0.07	0.08	0.10	0.0007	0.001
Waist circumference	0.08	0.02	0.02	0.11	0.0002	0.0003
Blood pressure	0.09	0.006	0.008	0.12	0.0002	0.0003

Table S5. Prevalence ratios of total fecal SCFAs, acetate and propionate concentrations for obesity, central obesity, and hypertension with robust 95% confidence intervals. Levels of SCFAs were divided by tertiles (tertile 1: low level, tertile 2: intermediate level, tertile 3: high level).

	Total fecal SCFAs		
	Tertile 1	**Tertile 2**	**Tertile 3**
Obesity[1]	N=78	N=81	N=104
Unadjusted model	Referent	1.26 (1.04, 1.48)	1.93 (1.74, 2.13)
Confounder-adjusted model[4]	Referent	1.56 (1.33, 1.78)	2.24 (2.04, 2.44)
Confounder-adjusted[4] + LBP model	Referent	1.33 (1.10, 1.55)	1.87 (1.67, 2.07)
Central obesity[2]	N=144	N=143	N=144
Unadjusted model	Referent	1.27 (1.10, 1.44)	1.88 (1.72, 2.05)
Confounder-adjusted model[4]	Referent	1.15 (0.98, 1.32)	1.80 (1.63, 1.96)
Confounder-adjusted[4] + LBP model	Referent	0.99 (0.82, 1.16)	1.54 (1.37, 1.71)
Hypertension[3]	N=144	N=143	N=144
Unadjusted model	Referent	1.16 (0.99, 1.32)	1.33 (1.16, 1.49)
Confounder-adjusted model[4]	Referent	1.15 (0.99, 1.32)	1.26 (1.10, 1.43)
Confounder-adjusted[4] + LBP model	Referent	1.09 (0.93, 1.26)	1.19 (1.03, 1.36)

[1] Defined as BMI ≥30 kg/m^2; [2] defined waist circumference ≥102 cm (men) and ≥88 cm (women); [3] defined as SBP ≥130 mm Hg or DBP ≥80 mm Hg or previous diagnosis of hypertension or use of antihypertensive medications; [4] model adjusted for participant age, city of residence, physical activity, fiber intake and total caloric intake.

Table S5 (cont.)

	Fecal acetate		
	Tertile 1	**Tertile 2**	**Tertile 3**
Obesity[1]	N=77	N=77	N=109
Unadjusted model	Referent	1.15 (0.92, 1.38)	1.80 (1.61, 2.00)
Confounder-adjusted model[4]	Referent	1.43 (1.20, 1.66)	2.04 (1.85, 2.24)
Confounder-adjusted[4] + LBP model	Referent	1.30 (1.07, 1.53)	1.76 (1.57, 1.96)
Central obesity[2]	N=144	N=143	N=144
Unadjusted model	Referent	1.12 (0.96, 1.29)	1.84 (1.68, 2.01)
Confounder-adjusted model[4]	Referent	0.98 (0.81, 1.15)	1.72 (1.56, 1.89)
Confounder-adjusted[4] + LBP model	Referent	0.86 (0.70, 1.03)	1.48 (1.31, 1.64)
Hypertension[3]	N=144	N=143	N=144
Unadjusted model	Referent	1.06 (0.90, 1.23)	1.33 (1.17, 1.50)
Confounder-adjusted model[4]	Referent	1.06 (0.89, 1.22)	1.27 (1.10, 1.43)
Confounder-adjusted[4] + LBP model	Referent	1.02 (0.86, 1.19)	1.20 (1.04, 1.36)

[1] Defined as BMI ≥30 kg/m^2; [2] defined waist circumference ≥102 cm (men) and ≥88 cm (women); [3] defined as SBP ≥130 mm Hg or DBP ≥80 mm Hg or previous diagnosis of hypertension or use of antihypertensive medications; [4] model adjusted for participant age, city of residence, physical activity, fiber intake and total caloric intake.

Table S5 (cont.)

	Fecal propionate		
	Tertile 1	**Tertile 2**	**Tertile 3**
Obesity[1]	N=83	N=84	N=96
Unadjusted model	Referent	1.23 (1.01, 1.45)	1.85 (1.64, 2.05)
Confounder-adjusted model[4]	Referent	1.38 (1.16, 1.60)	2.22 (2.01, 2.42)
Confounder-adjusted[4] + LBP model	Referent	1.25 (1.03, 1.47)	1.96 (1.76, 2.17)
Central obesity[2]	N=144	N=143	N=144
Unadjusted model	Referent	1.29 (1.12, 1.46)	1.77 (1.60, 1.93)
Confounder-adjusted model[4]	Referent	1.20 (1.04, 1.37)	1.77 (1.60, 1.94)
Confounder-adjusted[4] + LBP model	Referent	1.06 (0.90, 1.23)	1.55 (1.38, 1.72)
Hypertension[3]	N=144	N=143	N=144
Unadjusted model	Referent	1.05 (0.88, 1.21)	1.35 (1.18, 1.51)
Confounder-adjusted model[4]	Referent	1.01 (0.85, 1.18)	1.32 (1.16, 1.49)
Confounder-adjusted[4] + LBP model	Referent	0.97 (0.81, 1.14)	1.28 (1.11, 1.44)

[1] Defined as BMI ≥30 kg/m^2; [2] defined waist circumference ≥102 cm (men) and ≥88 cm (women); [3] defined as SBP ≥130 mm Hg or DBP ≥80 mm Hg or previous diagnosis of hypertension or use of antihypertensive medications; [4] model adjusted for participant age, city of residence, physical activity, fiber intake and total caloric intake.

Table S6. Prevalence ratios of fecal butyrate and total SCFA concentrations for obesity, central obesity, and hypertension with robust 95% confidence intervals in the subset of participants who did not report smoking or use of pharmacological treatments. Levels of SCFAs were divided by tertiles (tertile 1: low level, tertile 2: intermediate level, tertile 3: high level).

	Fecal butyrate		
	Tertile 1	**Tertile 2**	**Tertile 3**
Obesity[1]	N=40	N=45	N=46
Unadjusted model	Referent	1.07 (0.75, 1.38)	2.26 (1.96, 2.57)
Confounder-adjusted model[4]	Referent	1.00 (0.68, 1.32)	2.69 (2.38, 3.00)
Confounder-adjusted[4] + LBP model	Referent	0.85 (0.53, 1.18)	2.32 (2.00, 2.63)
Central obesity[2]	N=73	N=72	N=72
Unadjusted model	Referent	1.13 (0.89, 1.38)	1.91 (1.67, 2.15)
Confounder-adjusted model[4]	Referent	0.89 (0.64, 1.14)	2.00 (1.76, 2.24)
Confounder-adjusted[4] + LBP model	Referent	0.78 (0.53, 1.02)	1.74 (1.50, 1.98)
Hypertension[3]	N=73	N=72	N=72
Unadjusted model	Referent	1.13 (0.89, 1.38)	1.91 (1.67, 2.15)
Confounder-adjusted model[4]	Referent	0.89 (0.64, 1.14)	2.00 (1.76, 2.24)
Confounder-adjusted[4] + LBP model	Referent	0.78 (0.53, 1.02)	1.74 (1.50, 1.98)

[1] Defined as BMI ≥30 kg/m^2; [2] defined waist circumference ≥102 cm (men) and ≥88 cm (women); [3] defined as SBP ≥130 mm Hg or DBP ≥80 mm Hg or previous diagnosis of hypertension or use of antihypertensive medications; [4] model adjusted for participant age, city of residence, physical activity, fiber intake and total caloric intake.

Table S6 (cont.)

	Total fecal SCFAs		
	Tertile 1	**Tertile 2**	**Tertile 3**
Obesity[1]	N=40	N=38	N=53
Unadjusted model	Referent	0.86 (0.51, 1.21)	1.92 (1.64, 2.20)
Confounder-adjusted model[4]	Referent	0.69 (0.32, 1.06)	2.17 (1.88, 2.45)
Confounder-adjusted[4] + LBP model	Referent	0.66 (0.30, 1.03)	2.05 (1.77, 2.34)
Central obesity[2]	N=73	N=72	N=72
Unadjusted model	Referent	0.96 (0.72, 1.20)	1.65 (1.42, 1.89)
Confounder-adjusted model[4]	Referent	0.74 (0.50, 0.99)	1.62 (1.38, 1.86)
Confounder-adjusted[4] + LBP model	Referent	0.63 (0.38, 0.88)	1.37 (1.13, 1.62)
Hypertension[3]	N=73	N=72	N=72
Unadjusted model	Referent	0.96 (0.72, 1.20)	1.65 (1.42, 1.89)
Confounder-adjusted model[4]	Referent	0.74 (0.50, 0.99)	1.62 (1.38, 1.86)
Confounder-adjusted[4] + LBP model	Referent	0.63 (0.38, 0.88)	1.37 (1.13, 1.62)

[1] Defined as BMI ≥30 kg/m^2; [2] defined waist circumference ≥102 cm (men) and ≥88 cm (women); [3] defined as SBP ≥130 mm Hg or DBP ≥80 mm Hg or previous diagnosis of hypertension or use of antihypertensive medications; [4] model adjusted for participant age, city of residence, physical activity, fiber intake and total caloric intake.

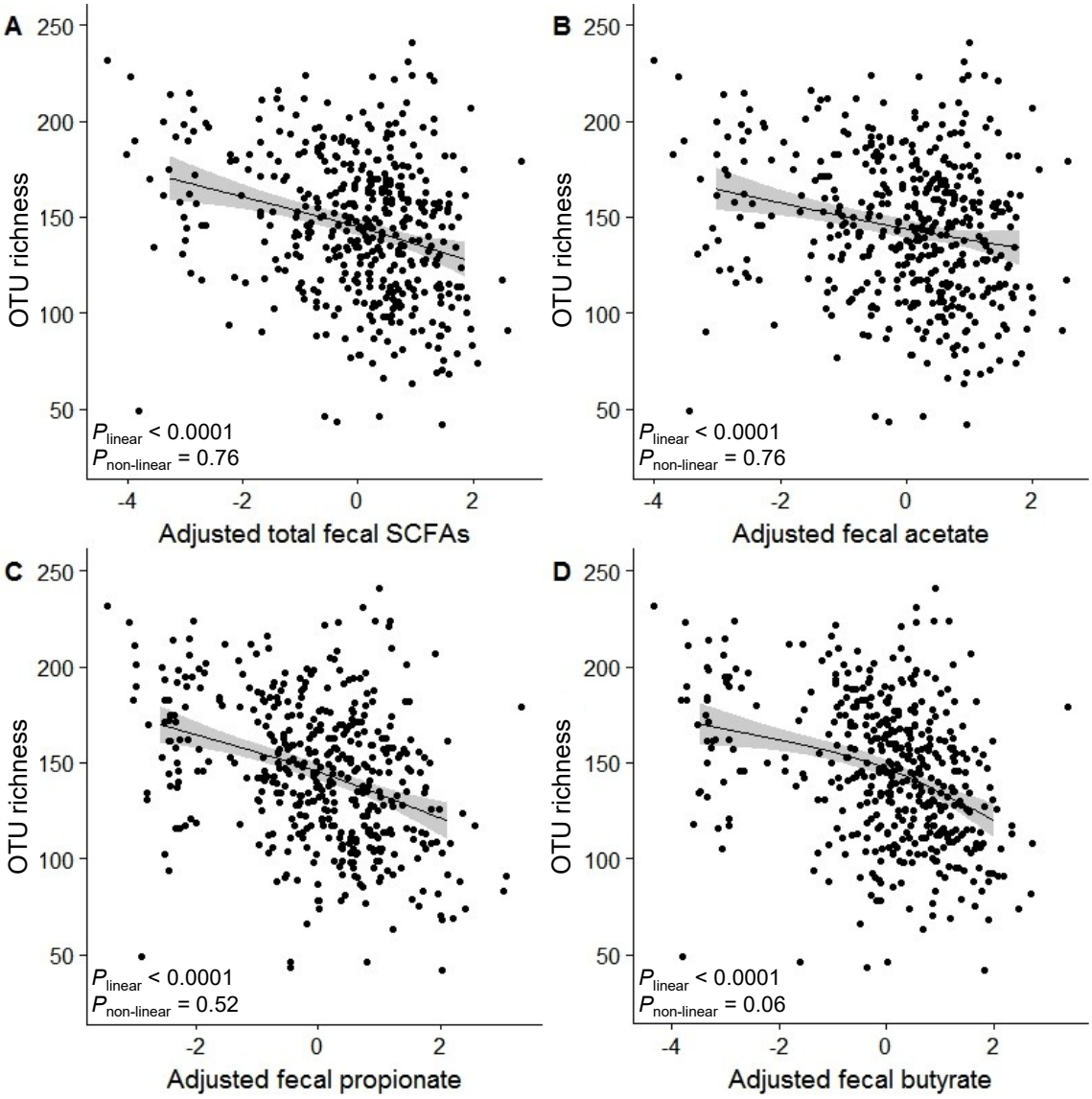

Figure S1. Distribution of the gut microbiota diversity according to multivariable-adjusted fecal SCFA concentrations (**A**: total SCFAs; **B**: acetate; **C**: propionate; **D**: butyrate). SCFA concentrations adjusted for age, city of origin, caloric intake, physical activity and fiber intake. Restricted cubic splines fits with 95% confidence intervals are shown. P-values from ordinary least squares testing the linearity and non-linearity of the regression are also shown.

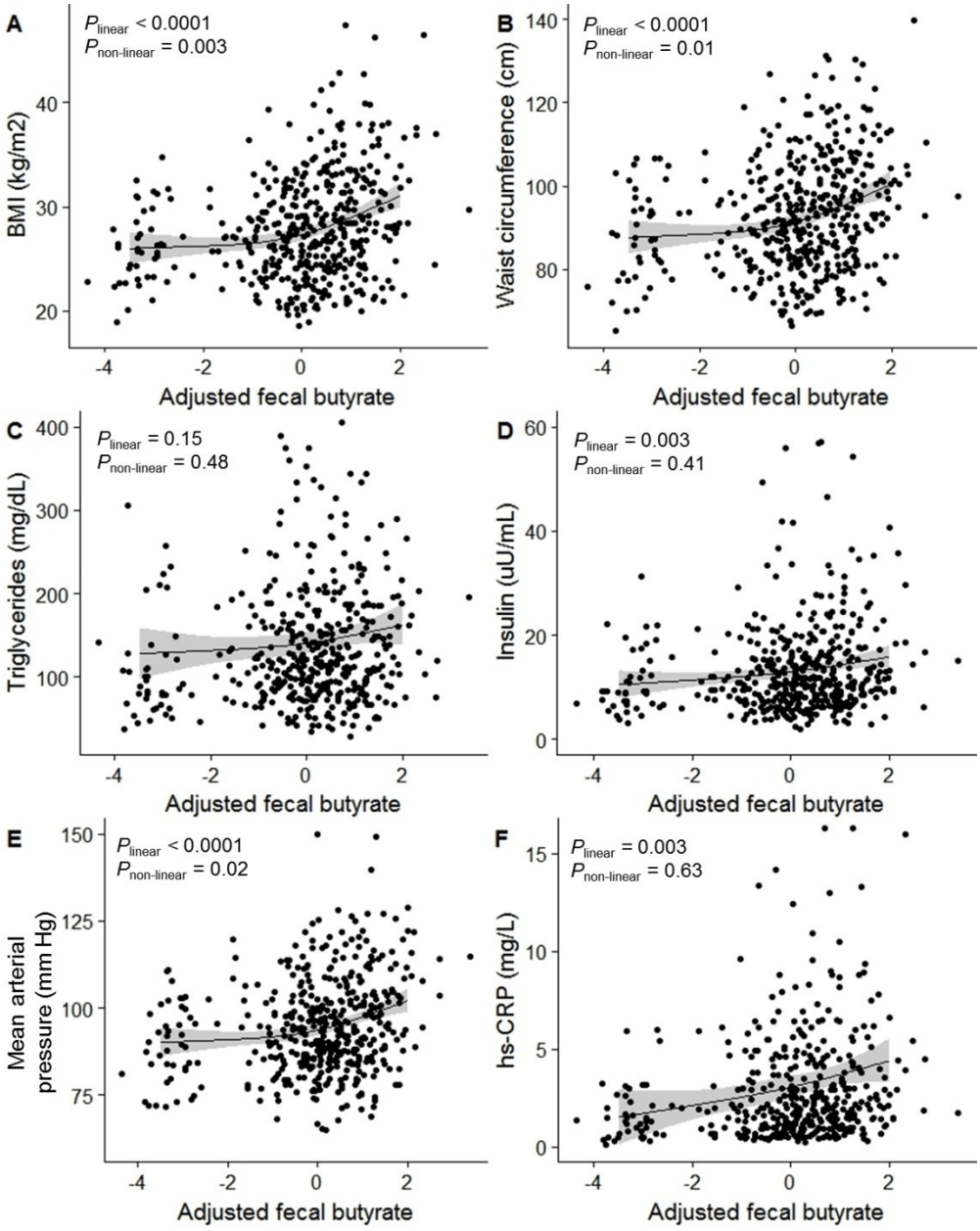

Figure S2. Distribution of cardiometabolic health indicators according to multivariable-adjusted fecal butyrate concentration. Butyrate concentrations adjusted for age, city of origin, caloric intake, physical activity and fiber intake. Restricted cubic splines fits with 95% confidence intervals are shown. P-values from ordinary least squares testing the linearity and non-linearity of the regression are also shown. BMI: body mass index; hs-CRP: high-sensitivity C-reactive protein.

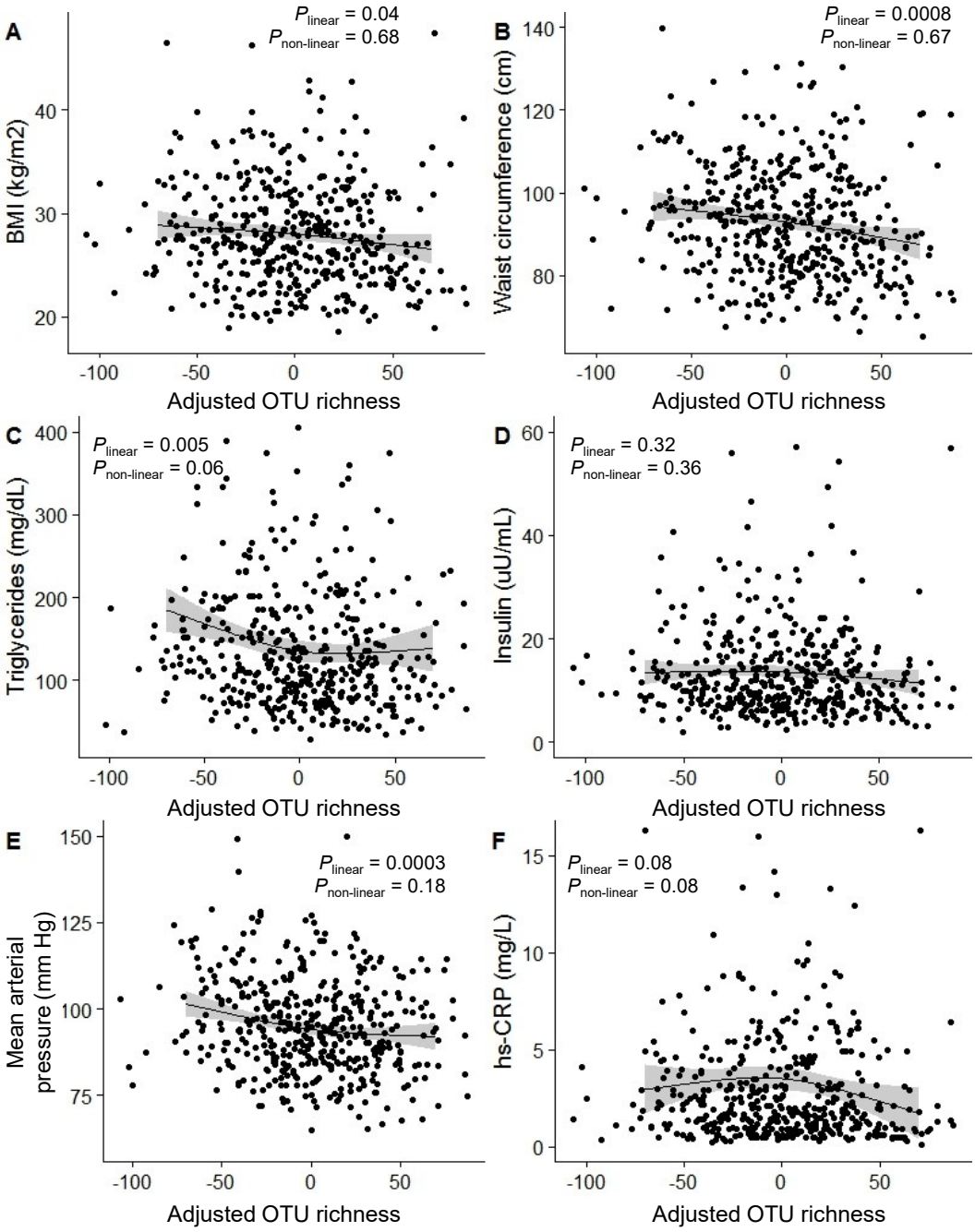

Figure S3. Distribution of cardiometabolic health indicators according to multivariable-adjusted gut microbiota diversity. OTU richness adjusted for age, city of origin, caloric intake, physical activity and fiber intake. Restricted cubic splines fits with 95% confidence intervals are shown. P-values from ordinary least squares testing the linearity and non-linearity of the regression are also shown. BMI: body mass index; hs-CRP: high-sensitivity C-reactive protein.

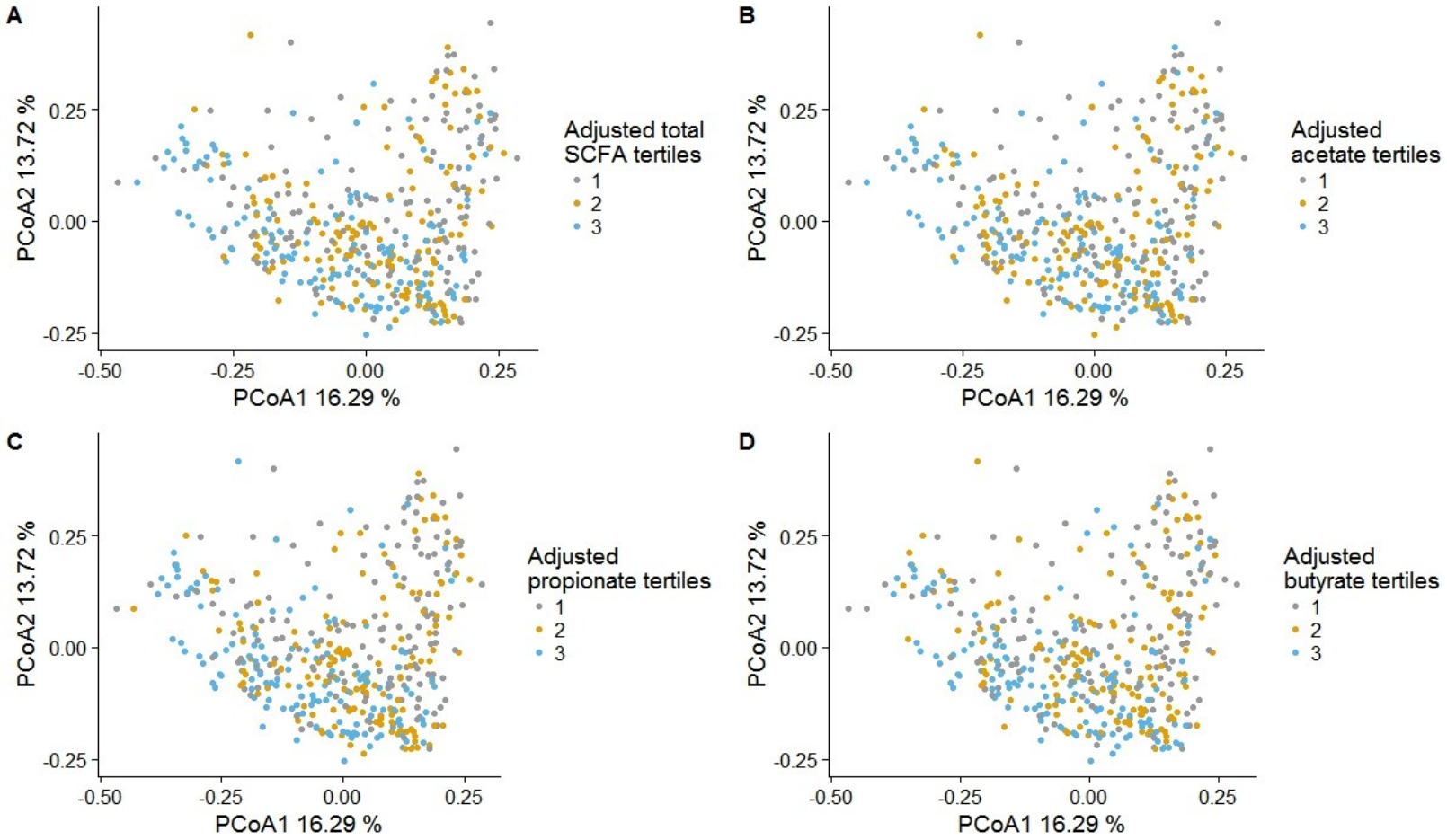

Figure S4. Principal coordinates analysis (PCoA) plot based on weighted UniFrac distances. Samples colored by tertiles (1: low, 2: intermediate, 3: high) of multivariable-adjusted fecal SCFA concentrations. (**A**) Total SCFAs, (**B**) acetate, (**C**) propionate, (**D**) butyrate. Percentages on the axes represent the proportion of the explained variation of each component of the PCoA.

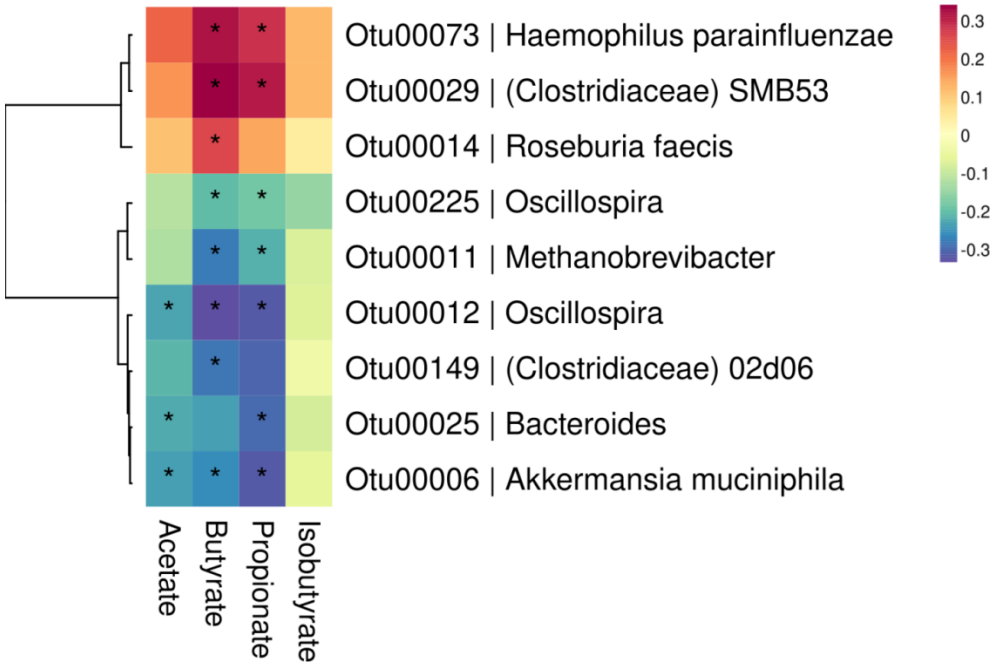

Figure S5. Heatmap showing the correlations between rarefied OTU abundances and multivariable-adjusted fecal SCFA concentrations in the subset of participants who did not report smoking or use of pharmacological treatments (N=217). OTUs with moderate or strong association with at least one of the measured SCFAs are shown (|rho|>0.2). The dendrogram to the left was obtained by hierarchical Ward-linkage clustering based on correlation coefficients of the relative abundances of the OTUs that had median abundances ≥0.001%. Models adjusted for age, city of origin, caloric intake, physical activity and fiber intake. The color scale indicates the Spearman's correlation coefficients. FDR-adjusted p-values from quasi-Poisson generalized linear models are indicated (*=q<0.10).