

## SUPPLEMENTARY TABLES

**Supplementary Table 1. Baseline characteristics of BHS Longitudinal Study Participants (N=288).**

	Overall (N=288)	Female		Male	
		Black (n=87)	White (n=109)	Black (n=26)	White (n=66)
Age, years, mean (SD)	48.6 (5.2)	48.0 (5.4)	49.0 (4.9)	48.7 (5.6)	49.0 (5.1)
Post-high school education, n (%)	124 (43.1)	25 (28.7)	59 (54.1)	5 (19.2)	35 (53.0)
Smoking, n (%)					
Never	164 (56.9)	52 (59.8)	66 (60.6)	11 (42.3)	35 (53.0)
Former	88 (30.6)	23 (26.4)	33 (30.3)	8 (30.8)	24 (36.4)
Current	36 (12.5)	12 (13.8)	10 (9.2)	7 (26.9)	7 (10.6)
Drinking, n (%)					
Never	56 (19.4)	26 (29.9)	19 (17.4)	5 (19.2)	6 (9.1)
Former	87 (30.2)	26 (29.9)	32 (29.4)	9 (34.6)	20 (30.3)
Current	145 (50.4)	35 (40.2)	58 (53.2)	12 (46.2)	40 (60.6)
BMI, kg/m <sup>2</sup> , mean (SD)	31.0 (7.7)	34.6 (9.8)	29.3 (6.5)	29.8 (7.3)	29.6 (4.3)
SBP, mmHg, mean (SD)	121.7 (16.0)	123.4 (20.5)	116.3 (12.8)	129.0 (13.2)	125.6 (12.2)
Hypertension*, n (%)	172 (59.7)	62 (71.3)	49 (45.0)	21 (80.8)	40 (60.6)
Glucose, mg/dL, mean (SD)	104.9 (33.6)	105.8 (39.9)	103.6 (35.2)	105.7 (24.9)	105.4 (23.8)
Diabetes†, n (%)	49 (17.2)	16 (18.4)	18 (16.8)	8 (30.8)	7 (10.8)
eGFR, mL/min/1.73 m <sup>2</sup> , mean (SD)	95.5 (17.1)	100.6 (19.6)	92.8 (13.7)	100.6 (17.2)	91.4 (16.6)
CKD (GFR‡<60 mL/min/1.73 m <sup>2</sup> ), n (%)	8 (2.8)	2 (2.3)	3 (2.8)	0 (0.0)	3 (4.6)
SPPB score	11.1 (1.4)	10.5 (1.8)	11.4 (1.0)	10.8 (2.0)	11.4 (0.9)
Six-minute walk distance (m)	419.4 (91.1)	369.3 (77.1)	430.5 (91.7)	422.0 (85.7)	464.6 (79.8)
Gait speed (m/s)	1.2 (0.3)	1.0 (0.2)	1.2 (0.3)	1.2 (0.2)	1.3 (0.2)
Grip strength (kg)	32.8 (11.6)	27.1 (6.6)	26.3 (6.1)	42.6 (9.2)	46.8 (9.5)

**Supplementary Table 2. Gait Speed Metabolites from Main Findings in Sensitivity Analysis Additionally Adjusting for Fasting Glucose, Systolic Blood Pressure, and Low-Density Lipoprotein.**

Pathway	Metabolite	Beta (SE)	P
Amino Acid			
Alanine and Aspartate Metabolism	N-acetylalanine	-0.17 (0.03)	4.7×10 <sup>-7</sup>
Alanine and Aspartate Metabolism	N-acetylaspartate (NAA)	-0.13 (0.02)	1.3×10 <sup>-7</sup>
Glutathione Metabolism	2-aminobutyrate	0.09 (0.02)	2.3×10 <sup>-7</sup>
Leucine, Isoleucine and Valine Metabolism	Isovalerate (i5:0)	0.08 (0.02)	1.1×10 <sup>-7</sup>
Methionine, Cysteine, SAM and Taurine Metabolism	N-formylmethionine	-0.14 (0.03)	2.7×10 <sup>-7</sup>
Methionine, Cysteine, SAM and Taurine Metabolism	S-adenosylhomocysteine (SAH)	-0.02 (0.01)	9.7×10 <sup>-5</sup>
Phenylalanine Metabolism	1-carboxyethylphenylalanine	-0.04 (0.01)	2.0×10 <sup>-6</sup>
Polyamine Metabolism	N-acetyl-isoputrescine*	-0.05 (0.01)	5.00E-06
Tryptophan Metabolism	C-glycosyltryptophan	-0.05 (0.01)	4.90E-05
Carbohydrate			

Aminosugar Metabolism	N-acetylneuraminate	-0.06 (0.01)	7.6×10 <sup>-7</sup>
Cofactors and Vitamins			
Ascorbate and Aldarate Metabolism	Oxalate	0.06 (0.01)	6.9×10 <sup>-9</sup>
Lipid			
Fatty Acid Metabolism(Acyl Carnitine)	Suberoylcarnitine (C8-DC)	-0.02 (0.00)	1.0×10 <sup>-7</sup>
Lysophospholipid	1-linoleoyl-GPC (18:2)	0.17 (0.03)	5.1×10 <sup>-8</sup>
Plasmalogen	1-(1-enyl-palmitoyl)-2-arachidonoyl-GPE (P-16:0/20:4)*	0.07 (0.02)	4.4×10 <sup>-6</sup>
Sphingolipid Metabolism	Behenoyl sphingomyelin (d18:1/22:0)*	0.21 (0.04)	4.2×10 <sup>-9</sup>
Sphingolipid Metabolism	Sphingomyelin (40:2)*	0.18 (0.04)	2.2×10 <sup>-6</sup>
Sphingolipid Metabolism	Sphingomyelin (43:1)*	0.08 (0.01)	1.1×10 <sup>-9</sup>
Nucleotide			
Purine Metabolism, Adenine containing	N1-methyladenosine	-0.29 (0.04)	2.9×10 <sup>-11</sup>
Purine Metabolism, Adenine containing	N6-carbamoylthreonyladenosine	-0.05 (0.01)	1.0×10 <sup>-4</sup>
Purine Metabolism, Guanine containing	7-methylguanine	-0.18 (0.03)	2.6×10 <sup>-8</sup>
Purine Metabolism, Guanine containing	N2,N2-dimethylguanosine	-0.08 (0.02)	8.1×10 <sup>-7</sup>
Pyrimidine Metabolism, Cytidine containing	N4-acetylcytidine	-0.06 (0.01)	7.9×10 <sup>-10</sup>
Pyrimidine Metabolism, Uracil containing	5,6-dihydrouridine	-0.13 (0.02)	1.9×10 <sup>-10</sup>
Pyrimidine Metabolism, Uracil containing	Pseudouridine	-0.09 (0.02)	4.3×10 <sup>-8</sup>
Pyrimidine Metabolism, Uracil containing	Uridine	0.14 (0.03)	2.4×10 <sup>-6</sup>
Peptide			
Gamma-glutamyl Amino Acid	Gamma-glutamyl-2-aminobutyrate	0.06 (0.01)	1.9×10 <sup>-7</sup>
Gamma-glutamyl Amino Acid	Gamma-glutamylphenylalanine	-0.11 (0.02)	8.8×10 <sup>-6</sup>
Xenobiotics			
Bacterial/Fungal	Tartronate	0.07 (0.01)	1.7×10 <sup>-9</sup>
Chemical	4-hydroxychlorothalonil	0.06 (0.01)	2.9×10 <sup>-7</sup>
Food Component/Plant	Ergothioneine	0.06 (0.01)	1.5×10 <sup>-7</sup>
Food Component/Plant	Phytanate	0.04 (0.01)	1.5×10 <sup>-7</sup>
Unnamed			
	X - 11315 (m/z=128.07154, RI=1157)	0.09 (0.01)	6.8×10 <sup>-10</sup>
	X - 18914 (m/z=266.88894, RI=4503)	0.08 (0.02)	1.4×10 <sup>-7</sup>
	X - 21471 (m/z=295.11196, RI=4039)	-0.03 (0.01)	1.3×10 <sup>-5</sup>
	X - 24337 (m/z=239.07856, RI=1980)	-0.04 (0.01)	2.0×10 <sup>-6</sup>
	X - 24513 (m/z=149.05558, RI=1148)	-0.05 (0.01)	6.4×10 <sup>-5</sup>

SE=standard error. \* Indicates compounds with Metabolomics Standards Initiative confidence level 2.

**Supplementary Table 3. Grip Strength Metabolites from Main Findings in Sensitivity Analysis Additionally Adjusting for Fasting Glucose, Systolic Blood Pressure, and Low-Density Lipoprotein.**

Pathway	Metabolite	Beta (SE)	P
Amino Acid			
Polyamine Metabolism	5-methylthioadenosine (MTA)	-3.79 (0.75)	5.7×10 <sup>-7</sup>
Tryptophan Metabolism	C-glycosyltryptophan	-2.08 (0.46)	6.5×10 <sup>-6</sup>
Carbohydrate			
Aminosugar Metabolism	N-acetylneuraminate	-2.09 (0.47)	9.5×10 <sup>-6</sup>
Nucleotide			
Purine Metabolism, Adenine containing	N1-methyladenosine	-10.05 (1.53)	8.3×10 <sup>-11</sup>
Pyrimidine Metabolism, Cytidine containing	N4-acetylcytidine	-1.2 (0.32)	2.0×10 <sup>-4</sup>
Pyrimidine Metabolism, Uracil containing	5,6-dihydrouridine	-4.08 (0.73)	3.1×10 <sup>-8</sup>
Pyrimidine Metabolism, Uracil containing	Pseudouridine	-3.05 (0.57)	1.1×10 <sup>-7</sup>

**Supplementary Table 4. All associations with longitudinal change in gait speed between baseline and follow up.**

Pathway	Metabolite	Beta (SE)	P-Value
<u>Positive in Cross-Sectional Analysis</u>			
Amino Acid			
Glutathione Metabolism	2-aminobutyrate	0.04 (0.03)	0.20
Leucine, Isoleucine and Valine Metabolism	Isovalerate (i5:0)	-0.01 (0.03)	0.75
Cofactors and Vitamins			
Ascorbate and Aldarate Metabolism	Oxalate	0.03 (0.02)	0.13
Lipid			
Lysophospholipid	1-linoleoyl-GPC (18:2)	0.06 (0.06)	0.36
Plasmalogen	1-(1-enyl-palmitoyl)-2-arachidonoyl-GPE (P-16:0/20:4) <sub>a</sub>	-0.02 (0.04)	0.55
Sphingolipid Metabolism	Behenoyl sphingomyelin (d18:1/22:0) <sub>a</sub>	0.15 (0.06)	0.02 *
	Sphingomyelin (40:2) <sub>a</sub>	0.26 (0.07)	2.6×10 <sup>-4</sup> **
	Sphingomyelin (43:1) <sub>a</sub>	0.05 (0.03)	0.07
Nucleotide			
Pyrimidine Metabolism, Uracil containing	Uridine	0.07 (0.06)	0.28
Xenobiotics			
Bacterial/Fungal	Tartronate	0.05 (0.03)	0.08
Chemical	4-hydroxychlorothalonil	-0.02 (0.02)	0.38
Food Component/Plant	Ergothioneine	-0.05 (0.02)	9.6×10 <sup>-3</sup>
	Phytanate	0.02 (0.02)	0.33
Unnamed			
	X - 11315 (m/z=128.07154, RI=1157)	0.01 (0.03)	0.70
	X - 18914 (m/z=266.88894, RI=4503)	0.05 (0.03)	0.16
<u>Negative in Cross-Sectional Analysis</u>			
Amino Acid			
Alanine and Aspartate Metabolism	N-acetylalanine	-0.12 (0.07)	0.08
	N-acetylaspartate (NAA)	-0.13 (0.06)	0.04 *
Methionine, Cysteine, SAM and Taurine	N-formylmethionine	-0.12 (0.05)	0.01 *

Metabolism	S-adenosylhomocysteine (SAH)	-0.03 (0.01)	0.02 *
Phenylalanine Metabolism	l-carboxyethylphenylalanine	-0.09 (0.02)	8.8×10 <sup>-5</sup> **
Polyamine Metabolism	N-acetyl-isoputrescine	-0.03 (0.02)	0.15
Tryptophan Metabolism	C-glycosyltryptophan	-0.04 (0.02)	0.09
Carbohydrate			
Aminosugar Metabolism	N-acetylneuraminic acid	-0.05 (0.03)	0.04 *
Lipid			
Fatty Acid Metabolism(Acyl Carnitine)	Suberoylcarnitine (C8-DC)	-0.01 (0.01)	0.21
Nucleotide			
Purine Metabolism, Adenine containing	N1-methyladenosine	-0.08 (0.11)	0.44
Purine Metabolism, Adenine containing	N6-carbamoylthreonyladenosine	-0.04 (0.02)	0.06
Purine Metabolism, Guanine containing	7-methylguanine	-0.06 (0.08)	0.48
Purine Metabolism, Guanine containing	N2,N2-dimethylguanosine	-0.05 (0.03)	0.05 *
Pyrimidine Metabolism, Cytidine containing	N4-acetylcytidine	-0.02 (0.02)	0.21
Pyrimidine Metabolism, Uracil containing	5,6-dihydrouridine	-0.08 (0.04)	0.05
Pyrimidine Metabolism, Uracil containing	Pseudouridine	-0.06 (0.04)	0.09
Peptide			
Gamma-glutamyl Amino Acid	Gamma-glutamylphenylalanine	-0.12 (0.05)	0.03 *
Unnamed			
	X - 21471 (m/z=295.11196, RI=4039)	-0.03 (0.02)	0.10
	X - 24337 (m/z=239.07856, RI=1980)	-0.06 (0.02)	1.70E-03
	X - 24513 (m/z=149.05558, RI=1148)	-0.05 (0.02)	0.04

<sup>a</sup> Indicates compounds that have not been officially confirmed based on a standard.

\* P<0.05.

\*\* Significant at a Bonferroni corrected level for 33 tests (P<1.5×10<sup>-3</sup>).

