Supplementary Information for

Metabolic effects of a 13-weeks lifestyle intervention in older adults: The Growing Old Together Study

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Suplementary Tables

Supplementary Table 1A. Baseline characteristics of parameters of body composition, health and functioning, and diagnostic measurements.

Characteristic		*n*	Longevity family members	*n*	Controls	*P*-value[a]
Women, n (%)			39 (43.3)		42 (56.8)	
Age, mean (SD) [range], years		90	63.4 (5.4) [49.1-75.1]	74	62.4 (6.1) [46.7-73.5]	0.24
Body composition, mean (SD) [range]						
Weight, kg		89	79.8 (9.6) [62.5-105.7]	73	79.0 (10.2) [60.5-102.4]	0.74
	Men	50	84.3 (8.0) [67.2-105.7]	31	85.4 (8.1) [70.1-102.4]	0.39
	Women	39	74.1 (8.4) [62.5-95.4]	42	74.1 (8.9) [60.5-100.4]	0.73
BMI, kg/m^2		89	27.0 (2.6) [22.9-34.2]	73	26.9 (2.4) [22.9-33.5]	0.77
Waist circumference, cm		90	96.2 (7.9) [74-122]	74	96.1 (8.2) [77-112]	0.47
	Men	51	98.1 (7.4) [80-122]	32	100.1 (6.4) [89-112]	0.26
	Women	39	93.6 (7.9) [74-112]	42	93.0 (8.1) [77-111]	0.63
Body fat, %		89	29.6 (8.8) [11.6-48.3]	73	30.9 (7.0) [17.1-51.0]	0.98
	Men	50	23.7 (5.7) [11.6-38.7]	31	25.5 (4.7) [17.1-35.0]	0.17
	Women	39	37.1 (5.8) [22.9-48.3]	42	34.9 (5.6) [21.0-51.0]	0.13
Fat free mass, kg^2		89	56.3 (10.1) [38.5-78.6]	74	54.6 (10.1) [37.0-81.6]	0.58
	Men	50	64.1 (5.6) [49.5-78.6]	31	63.6 (7.5) [46.9-81.6]	0.98
	Women	39	46.3 (3.9) [38.5-54.7]	42	48.0 (5.9) [37.0-65.5]	0.30
Health and functioning, mean (SD) [range]						
Systolic blood pressure, mmHg[b]		65	135.4 (15.9) [111-196]	48	137.8 (17.1) [101-173]	0.99
Diastolic blood pressure, mmHg[b]		65	83.5 (7.4) [64-101]	48	84.7 (9.2) [65-108]	0.28
REE, kcal/day		68	1,186 (178) [890-1,680]	58	1,189 (163) [871-1,680]	0.42
	Men	38	1,294 (150) [940-1,680]	27	1,282 (160) [1,083-1,680]	0.93
	Women	30	1,048 (96) [890-1,300]	31	1,108 (117) [872-1,349]	**0.04**
Handgrip strength, kg		89	43.2 (12.1) [21-67]	71	40.8 (10.3) [21-78]	0.82

Characteristic		*n*	Longevity family members	*n*	Controls	*P*-value[a]
	Men	50	52.3 (7.5) [36-67]	30	49.5 (7.5) [39-78]	0.20
	Women	39	31.6 (4.8) [21-42]	41	34.4 (6.6) [21-54]	0.18
Physical functioning		90	11.5 (0.6) [10-12]	73	11.6 (0.7) [10-12]	0.31
Physical quality of life		88	52.4 (5.9) [26.7-62.8]	72	52.9 (6.2) [26.8-63.0]	0.61
	Men	51	52.7 (4.8) [39.0-58.9]	31	53.0 (4.2) [37.5-56.8]	0.72
	Women	37	51.9 (7.2) [26.7-62.9]	41	52.7 (7.5) [26.8-63.0]	0.78
Mental quality of life		88	54.5 (6.7) [27.6-63.7]	72	53.6 (8.2) [19.4-67.0]	0.71
	Men	51	56.2 (4.9) [41.5-63.7]	31	55.6 (5.7) [29.0-62.9]	0.56
	Women	37	52.3 (8.1) [27.6-60.8]	41	52.1 (9.4) [19.4-67.0]	0.65
FRS, %		90	8.3 (5.0) [1-20]	74	8.9 (7.3) [1-25]	**<0.001**
	Men	51	11.4 (3.6) [6-20]	32	16.2 (4.6) [10-25]	**<0.001**
	Women	39	4.3 (3.4) [1-17]	42	3.3 (2.2) [1-11]	0.67
Medication use, *n* (%)						
Lipid-lowering agent		90	11 (12.2)	74	18 (24.3)	**0.03**
Antihypertensive agent		90	23 (25.6)	74	26 (35.1)	0.22
Diagnostic measurements, mean (SD) [range]						
Fasting glucose, mmol/L		90	5.0 (0.5) [3.6-6.5]	74	5.0 (0.6) [4.0-7.6]	0.88
Fasting insulin, mU/L[c]		90	9.4 (5.1) [2.0-29.6]	74	9.0 (3.9) [2.0-22.6]	0.84
HOMA-IR		88	1.2 (0.6) [0.4-3.8]	72	1.2 (0.5) [0.4-2.7]	0.72
Total cholesterol, mmol/L[d]		79	5.5 (1.0) [3.3-8.6]	56	5.5 (1.0) [3.2-8.0]	0.58
HDL cholesterol, mmol/L[d]		79	1.6 (0.4) [0.6-3.1]	56	1.4 (0.4) [0.6-2.3]	**0.001**
	Men	43	1.4 (0.3) [1.0-2.0]	23	1.1 (0.2) [0.6-1.6]	**<0.001**
	Women	36	1.7 (0.5) [0.6-3.1]	33	1.6 (0.3) [1.2-2.3]	0.39
LDL cholesterol, mmol/L[d]		79	3.5 (0.8) [1.8-6.4]	56	3.4 (0.9) [1.6-6.0]	0.51
Triglycerides, mmol/L[c,d]		79	1.3 (0.5) [0.6-3.0]	56	1.2 (0.6) [0.5-4.1]	0.13
fT3, pmol/L		90	4.5 (0.4) [3.3-5.5]	74	4.6 (0.4) [3.5-6.2]	0.54

Characteristic		*n*	Longevity family members	*n*	Controls	*P*-value[a]
fT4, pmol/L		90	15.0 (1.8) [10.5-20.3]	74	14.7 (1.6) [10.5-19.3]	0.21
TSH, mU/L[c]		90	2.6 (1.6) [0.3-9.8]	74	3.1 (3.0) [0.2-25.0]	0.32
DHEAS, nmol/L[c]		90	2.9 (1.8) [0.5-8.6]	74	3.3 (1.6) [0.7-6.8]	**0.006**
	Men	51	3.6 (2.0) [0.6-8.6]	32	3.8 (1.4) [1.5-6.8]	0.12
	Women	39	2.0 (1.2) [0.5-5.2]	42	2.8 (1.6) [0.7-6.7]	**0.03**
Leptin, µg/L[c]		90	13.5 (11.5) [1.2-61.7]	74	14.4 (9.2) [2.3-50.3]	0.52
	Men	51	6.7 (3.8) [1.2-17.2]	32	7.6 (3.5) [2.3-18.1]	0.15
	Women	39	22.5 (12.2) [4.5-61.7]	42	19.7 (8.9) [6.5-50.3]	0.35
Adiponectin, mg/L[c]		90	10.6 (5.2) [2.2-28.1]	74	10.1 (5.5) [2.7-25.6]	**0.04**
	Men	51	8.1 (3.5) [2.2-19.3]	32	6.8 (3.0) [2.8-15.2]	0.08
	Women	39	13.9 (5.2) [5.6-28.1]	42	12.7 (5.6) [2.7-25.6]	0.30
IGF-1, nmol/L		90	20.0 (4.8) [7.8-31.9]	74	20.0 (4.8) [8.4-43.0]	0.57
	Men	51	20.8 (4.7) [7.8-31.9]	32	21.6 (5.1) [10.7-31.7]	0.41
	Women	39	19.0 (4.6) [11.4-30.9]	42	19.3 (6.4) [8.4-43.0]	0.88
IGFBP-3, mg/L		90	4.0 (0.9) [1.7-7.7]	74	4.0 (0.9) [2.2-6.7]	0.34
IGF-1:IGFBP-3		90	0.14 (0.03) [0.06-0.26]	74	0.14 (0.03) [0.07-0.23]	0.23
	Men	51	0.15 (0.03) [0.07-0.26]	32	0.15 (0.04) [0.10-0.23]	0.68
	Women	39	0.12 (0.02) [0.06-0.17]	42	0.13 (0.03) [0.07-0.20]	0.33
CRP (high-sensitivity), mg/L[c]		90	1.9 (2.8) [0.2-18.8]	74	2.3 (3.6) [0.2-20.0]	0.23

[a] P value refers to difference between longevity family members and controls. [b] Individuals using antihypertensive agents were removed before analysis. [c] Natural log transformed parameter was used for analysis. [d] Individuals using lipid-lowering agents were removed before analysis. Parameters were analysed separately in men and women if there was a significant gender-difference at baseline. BMI, body mass index; REE, resting energy expenditure; FRS, Framingham risk score; HOMA-IR, homeostatic model assessment - insulin resistance; HDL, high density lipoprotein; LDL, low density lipoprotein; fT3, free triiodothyronine; fT4, free thyroxine; TSH, thyroid stimulating hormone; DHEAS, dehydroepiandrosterone-sulfate; IGF-1, insuline-like growth factor 1; IGFBP-3, insulin-like growth factor binding protein 3; CRP, C-reactive protein..

Supplementary Table 1B. Baseline characteristics of ^{1}H-NMR metabolites.

Characteristic, mean (SD) [range]		*n*	Longevity family members	*n*	Controls	*P*-value[a]
Amino acids						
Alanine, mmol/L		90	0.45 (0.05) [0.34-0.62]	72	0.46 (0.06) [0.33-0.63]	0.64
	Men	51	0.44 (0.05) [0.35-0.58]	30	0.43 (0.05) [0.33-0.56]	0.52
	Women	39	0.46 (0.06) [0.34-0.62]	42	0.47 (0.06) [0.36-0.63]	0.33
Glutamine, mmol/L		90	0.52 (0.06) [0.39-0.74]	73	0.49 (0.05) [0.36-0.62]	**0.01**
Glycine, mmol/L		90	0.29 (0.06) [0.20-0.56]	73	0.29 (0.06) [0.16-0.54]	0.30
	Men	51	0.27 (0.04) [0.20-0.40]	31	0.26 (0.04) [0.16-0.39]	0.15
	Women	39	0.32 (0.07) [0.24-0.56]	42	0.32 (0.07) [0.21-0.54]	0.94
Histidine, mmol/L		90	0.06 (0.01) [0.04-0.09]	73	0.06 (0.01) [0.03-0.08]	0.06
Branched-chain amino acids						
Isoleucine, mmol/L		90	0.06 (0.02) [0.04-0.14]	72	0.06 (0.02) [0.03-0.11]	0.40
	Men	51	0.06 (0.01) [0.04-0.10]	30	0.07 (0.01) [0.05-0.11]	0.09
	Women	39	0.06 (0.02) [0.04-0.14]	42	0.06 (0.01) [0.03-0.11]	0.63
Leucine, mmol/L		90	0.09 (0.01) [0.05-0.13]	72	0.09 (0.01) [0.06-0.14]	0.64
	Men	51	0.09 (0.01) [0.07-0.12]	30	0.09 (0.01) [0.07-0.12]	0.46
	Women	39	0.08 (0.01) [0.05-0.13]	42	0.08 (0.01) [0.06-0.14]	0.78
Valine, mmol/L		89	0.20 (0.03) [0.12-0.28]	72	0.20 (0.03) [0.15-0.34]	0.44
Aromatic amino acids						
Phenylalanine, mmol/L		90	0.08 (0.01) [0.06-0.11]	73	0.08 (0.01) [0.04-0.10]	0.72
Tyrosine, mmol/L		90	0.06 (0.01) [0.04-0.08]	73	0.06 (0.01) [0.02-0.09]	0.48
Glycolysis-related metabolites						
Glucose, mmol/L		90	4.26 (0.48) [3.02-6.51]	73	4.22 (0.50) [2.73-6.56]	0.87
Lactate, mmol/L		90	1.84 (0.33) [1.22-3.02]	73	1.84 (0.37) [0.71-2.78]	0.89

Characteristic, mean (SD) [range]		*n*	Longevity family members	*n*	Controls	*P*-value[a]
Pyruvate, mmol/L		89	0.08 (0.03) [0.04-0.17]	73	0.09 (0.02) [0.04-0.17]	0.46
Citrate, mmol/L		90	0.10 (0.02) [0.06-0.15]	73	0.10 (0.02) [0.04-0.18]	0.12
Glycerol, mmol/L		88	0.08 (0.03) [0.04-0.20]	73	0.08 (0.02) [0.03-0.14]	0.41
	Men	49	0.07 (0.03) [0.04-0.20]	31	0.07 (0.02) [0.04-0.12]	0.62
	Women	39	0.09 (0.03) [0.04-0.15]	42	0.08 (0.02) [0.03-0.14]	0.09
Ketone bodies						
Acetate, mmol/L		90	0.05 (0.09) [0.03-0.77]	73	0.04 (0.01) [0.02-0.07]	0.11
Acetoacetate, mmol/L		90	0.04 (0.02) [0.01-0.15]	73	0.03 (0.01) [0.00-0.10]	0.59
	Men	51	0.04 (0.02) [0.02-0.15]	31	0.04 (0.02) [0.00-0.10]	0.50
	Women	39	0.03 (0.01) [0.01-0.07]	42	0.03 (0.01) [0.01-0.07]	0.87
3-hydroxybutyrate, mmol/L		88	0.09 (0.02) [0.04-0.16]	73	0.09 (0.03) [0.03-0.19]	0.88
Fatty acids[b]						
Total fatty acids, mmol/L		76	12.11 (2.46) [8.55-23.03]	55	12.42 (2.02) [8.70-17.64]	0.48
Omega-3 fatty acids, mmol/L		76	0.44 (0.11) [0.20-0.72]	55	0.46 (0.11) [0.28-0.69]	0.64
Docosahexaenoic acid (DHA), mmol/L		76	0.16 (0.05) [0.06-0.27]	55	0.16 (0.04) [0.10-0.26]	0.77
Omega-6 fatty acids, mmol/L		76	4.18 (0.72) [3.09-6.21]	55	4.25 (0.65) [3.02-6.34]	0.74
Linoleic acid, mmol/L		76	3.37 (0.58) [2.49-5.20]	55	3.44 (0.55) [2.36-5.13]	0.66
Polyunsaturated fatty acids, mmol/L		76	4.62 (0.79) [3.49-6.83]	55	4.71 (0.71) [3.42-7.03]	0.72
Monounsaturated fatty acids, mmol/L		76	2.76 (0.83) [1.54-6.49]	55	2.85 (0.68) [1.80-5.35]	0.35
Saturated fatty acids, mmol/L		76	4.73 (0.99) [3.28-9.71]	55	4.87 (0.84) [3.35-6.93]	0.46
Fatty acid chain length		76	17.32 (0.34) [16.74-18.50]	55	17.38 (0.31) [16.66-18.20]	0.46
Fatty acid ratios, relative to total fatty acids[b]						
Omega-3 fatty acids, %		76	3.68 (0.64) [2.28-5.47]	55	3.71 (0.77) [2.15-5.77]	0.65
Docosahexaenoic acid (DHA), %		76	1.29 (0.31) [0.73-2.33]	55	1.30 (0.32) [0.62-2.03]	0.57
Omega-6 fatty acids, %		76	34.75 (2.86) [26.55-41.19]	55	34.38 (2.36) [28.29-39.22]	0.36

Characteristic, mean (SD) [range]		*n*	Longevity family members	*n*	Controls	*P*-value[a]
Linoleic acid, %		76	28.08 (2.69) [20.56-35.62]	55	27.84 (2.40) [21.81-34.00]	0.57
Polyunsaturated fatty acids, %		76	38.43 (2.88) [29.65-43.47]	55	38.08 (2.59) [30.43-43.80]	0.33
Monounsaturated fatty acids, %		76	22.48 (2.60) [17.82-30.75]	55	22.77 (2.78) [18.89-30.91]	0.25
Saturated fatty acids, %		76	39.09 (1.75) [35.45-43.55]	55	39.15 (1.82) [35.19-43.52]	0.97
Unsaturation degree, double bonds per fatty acids		76	1.19 (0.05) [1.03-1.29]	55	1.19 (0.05) [1.02-1.31]	0.57
Fluid balance						
Creatinine, mmol/L		90	0.06 (0.01) [0.03-0.09]	73	0.06 (0.01) [0.04-0.12]	0.18
	Men	51	0.07 (0.01) [0.03-0.09]	31	0.07 (0.01) [0.04-0.12]	0.09
	Women	39	0.05 (0.01) [0.04-0.07]	42	0.05 (0.01) [0.04-0.07]	0.90
Albumin, signal area		90	0.09 (0.00) [0.08-0.10]	73	0.09 (0.00) [0.08-0.10]	0.91
Inflammation						
Glycoprotein acetyls, mainly a1-acid glycoprotein, mmol/L		90	1.21 (0.20) [0.91-2.15]	73	1.25 (0.18) [0.88-1.90]	0.11
	Men	51	1.17 (0.15) [0.91-1.54]	31	1.31 (0.18) [0.99-1.90]	**<0.001**
	Women	39	1.26 (0.24) [0.97-2.15]	42	1.20 (0.17) [0.88-1.57]	0.25
Apolipoproteins[b]						
Apolipoprotein B, g/L		79	0.94 (0.23) [0.56-1.94]	55	0.99 (0.18) [0.61-1.51]	0.07
Apolipoprotein A1, g/L		79	1.60 (0.17) [1.21-2.07]	55	1.55 (0.21) [1.08-2.10]	**<0.001**
	Men	43	1.53 (0.15) [1.21-1.87]	22	1.39 (0.13) [1.08-1.57]	**<0.001**
	Women	36	1.68 (0.15) [1.43-2.07]	33	1.66 (0.18) [1.28-2.10]	0.68
Lipids[b]						
Triglycerides, mmol/L		79	1.16 (0.65) [0.41-4.88]	55	1.26 (0.50) [0.63-3.16]	**0.03**
	Men	43	1.13 (0.40) [0.59-2.09]	22	1.55 (0.56) [0.81-3.16]	**<0.001**
	Women	36	1.20 (0.86) [0.41-4.88]	33	1.07 (0.35) [0.63-2.02]	0.88
Phosphoglycerides, mmol/L		76	2.14 (0.32) [1.54-3.01]	55	2.16 (0.37) [1.43-2.92]	0.55
	Men	42	2.06 (0.30) [1.54-2.62]	22	1.97 (0.30) [1.43-2.45]	0.33

Characteristic, mean (SD) [range]		*n*	Longevity family members	*n*	Controls	*P*-value[a]
	Women	34	2.24 (0.32) [1.69-3.01]	33	2.29 (0.36) [1.60-2.92]	0.55
Cholines, mmol/L		76	2.55 (0.33) [1.93-3.30]	55	2.57 (0.40) [1.68-3.42]	0.45
	Men	42	2.45 (0.34) [1.93-3.18]	22	2.35 (0.32) [1.68-2.91]	0.32
	Women	34	2.67 (0.29) [2.07-3.30]	33	2.71 (0.38) [2.00-3.42]	0.61
Sphingomyelins, mmol/L		76	0.51 (0.09) [0.33-0.79]	55	0.51 (0.08) [0.32-0.69]	0.22
	Men	42	0.48 (0.09) [0.33-0.79]	22	0.47 (0.07) [0.32-0.62]	0.55
	Women	34	0.55 (0.07) [0.41-0.71]	33	0.54 (0.08) [0.39-0.69]	0.81
Total lipid concentrations in lipoprotein subclasses[b]						
Extremely large VLDL, mmol/L		73	0.03 (0.02) [0.00-0.14]	52	0.03 (0.02) [0.00-0.11]	0.12
Very large VLDL, mmol/L		68	0.06 (0.07) [0.00-0.41]	49	0.06 (0.06) [0.01-0.31]	0.08
Large VLDL, mmol/L		73	0.22 (0.23) [0.02-1.56]	53	0.23 (0.20) [0.03-1.09]	0.42
Medium VLDL, mmol/L		79	0.48 (0.37) [0.09-2.64]	55	0.52 (0.30) [0.17-1.67]	0.06
Small VLDL, mmol/L		79	0.61 (0.26) [0.16-1.90]	55	0.67 (0.20) [0.31-1.06]	**0.01**
Very small VLDL, mmol/L		79	0.58 (0.16) [0.24-1.06]	55	0.63 (0.14) [0.34-1.01]	**0.03**
IDL, mmol/L		79	1.28 (0.30) [0.76-2.22]	55	1.35 (0.28) [0.77-2.24]	0.14
Large LDL, mmol/L		79	1.47 (0.35) [0.87-2.53]	55	1.55 (0.33) [0.82-2.57]	0.19
Medium LDL, mmol/L		79	0.84 (0.21) [0.46-1.43]	55	0.88 (0.19) [0.44-1.47]	0.20
Small LDL, mmol/L		79	0.54 (0.13) [0.31-0.89]	55	0.56 (0.12) [0.30-0.93]	0.30
Very large HDL, mmol/L		79	0.48 (0.21) [0.10-1.14]	55	0.42 (0.21) [0.11-0.96]	**0.001**
	Men	43	0.41 (0.16) [0.10-0.92]	22	0.26 (0.10) [0.11-0.56]	**<0.001**
	Women	36	0.55 (0.23) [0.13-1.14]	33	0.53 (0.20) [0.18-0.96]	0.95
Large HDL, mmol/L		75	0.80 (0.29) [0.25-1.73]	51	0.73 (0.34) [0.23-1.55]	**<0.001**
	Men	41	0.68 (0.24) [0.25-1.15]	18	0.45 (0.16) [0.23-0.83]	**<0.001**
	Women	34	0.95 (0.29) [0.54-1.73]	33	0.89 (0.31) [0.34-1.55]	0.29
Medium HDL, mmol/L		79	0.95 (0.16) [0.66-1.44]	55	0.93 (0.20) [0.51-1.38]	**0.005**
	Men	43	0.91 (0.15) [0.66-1.44]	22	0.79 (0.15) [0.51-1.10]	**0.003**

Characteristic, mean (SD) [range]		*n*	Longevity family members	*n*	Controls	*P*-value[a]
	Women	36	1.01 (0.15) [0.70-1.30]	33	1.02 (0.17) [0.72-1.38]	0.88
Small HDL, mmol/L		79	1.15 (0.11) [0.92-1.42]	55	1.15 (0.10) [0.95-1.38]	0.70
	Men	43	1.15 (0.10) [0.92-1.41]	22	1.12 (0.09) [0.95-1.31]	0.30
	Women	36	1.15 (0.13) [0.95-1.42]	33	1.16 (0.10) [0.97-1.38]	0.48
Lipoprotein particle size[b]						
VLDL diameter, nm		79	35.76 (1.11) [33.87-39.22]	55	35.87 (1.26) [34.26-39.69]	0.28
LDL diameter, nm		79	23.58 (0.11) [23.33-23.83]	55	23.60 (0.10) [23.43-23.81]	0.30
HDL diameter, nm		79	9.97 (0.24) [9.46-10.61]	55	9.90 (0.27) [9.39-10.47]	**0.001**
	Men	43	9.90 (0.20) [9.46-10.41]	22	9.67 (0.17) [9.39-10.08]	**<0.001**
	Women	36	10.07 (0.25) [9.48-10.61]	33	10.04 (0.22) [9.64-10.47]	0.62
Cholesterol[b]						
Total cholesterol, mmol/L		79	5.05 (0.90) [3.64-7.70]	55	5.16 (0.91) [2.98-7.95]	0.77
VLDL cholesterol, mmol/L		79	0.76 (0.33) [0.22-2.27]	55	0.83 (0.24) [0.36-1.38]	**0.02**
IDL cholesterol, mmol/L		79	0.82 (0.20) [0.48-1.47]	55	0.86 (0.19) [0.45-1.48]	0.23
LDL cholesterol, mmol/L		79	1.93 (0.51) [1.04-3.45]	55	2.02 (0.47) [0.98-3.52]	0.22
HDL cholesterol, mmol/L		79	1.55 (0.32) [0.79-2.49]	55	1.45 (0.38) [0.68-2.35]	**<0.001**
	Men	43	1.44 (0.25) [0.96-1.96]	22	1.14 (0.22) [0.68-1.51]	**<0.001**
	Women	36	1.68 (0.35) [0.79-2.49]	33	1.66 (0.31) [1.08-2.35]	0.97
HDL2 cholesterol, mmol/L		79	1.04 (0.30) [0.28-1.94]	55	0.94 (0.34) [0.25-1.77]	**<0.001**
	Men	43	0.94 (0.24) [0.48-1.44]	22	0.66 (0.20) [0.25-0.98]	**<0.001**
	Women	36	1.16 (0.32) [0.28-1.94]	33	1.13 (0.28) [0.61-1.77]	0.99
HDL3 cholesterol, mmol/L		79	0.51 (0.03) [0.42-0.60]	55	0.51 (0.04) [0.42-0.59]	**0.03**
	Men	43	0.51 (0.03) [0.43-0.60]	22	0.48 (0.03) [0.42-0.55]	**0.001**
	Women	36	0.52 (0.04) [0.42-0.60]	33	0.53 (0.03) [0.47-0.59]	0.33

[a] P value refers to difference between longevity family members and controls. [b] Individuals using lipid-lowering agents were removed before analysis. All metabolite concentrations were natural log-transformed and scaled to standard deviation units before analysis. Parameters were analysed separately in men and women if there was a significant gender-difference at baseline. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

Supplementary Table 2A. Effects of the intervention on parameters of body composition, health and functioning, and diagnostic measurements.

			Unadjusted		Weight loss adjusted	
Characteristic, mean (SE)		***n***	**Difference**	***P*-value[a]**	**Difference**	***P*-value[b]**
Body composition						
Weight, kg		161	-3.34 (0.18)	**<0.001**		
	Men	80	-3.42 (0.27)	**<0.001**		
	Women	81	-3.25 (0.23)	**<0.001**		
BMI, kg/m^2		161	-1.13 (0.06)	**<0.001**		
Waist circumference, cm		163	-4.3 (0.4)	**<0.001**		
	Men	82	-4.4 (0.6)	**<0.001**		
	Women	81	-4.2 (0.6)	**<0.001**		
Body fat, %		161	-2.26 (0.16)	**<0.001**		
	Men	80	-2.22 (0.23)	**<0.001**		
	Women	81	-2.29 (0.21)	**<0.001**		
Fat free mass, kg^2		161	-0.67 (0.10)	**<0.001**		
	Men	80	-0.83 (0.16)	**<0.001**		
	Women	81	-0.51 (0.13)	**<0.001**		
Health and functioning						
Systolic blood pressure, mmHg[c]		113	-4.33 (0.98)	**<0.001**	-2.74 (1.12)	**0.01**
Diastolic blood pressure, mmHg[c]		113	-1.66 (0.61)	**0.007**	-0.52 (0.68)	0.44
REE, kcal/day		126	-49.2 (8.0)	**<0.001**	-20.2 (8.3)	**0.02**
	Men	65	-46.59 (11.76)	**<0.001**	-8.09 (12.41)	0.51
	Women	61	-51.94 (10.79)	**<0.001**	-28.42 (11.28)	**0.01**
Handgrip strength, kg		153	0.38 (0.32)	0.25		

Characteristic, mean (SE)		*n*	Unadjusted Difference	Unadjusted *P*-value[a]	Weight loss adjusted Difference	Weight loss adjusted *P*-value[b]
	Men	76	0.24 (0.53)	0.65		
	Women	77	0.51 (0.38)	0.18		
Physical functioning		159	0.14 (0.05)	**0.01**	0.11 (0.06)	**0.04**
Physical quality of life		157	-0.18 (0.61)	0.77		
	Men	82	-0.72 (0.83)	0.39		
	Women	75	0.42 (0.92)	0.65		
Mental quality of life		157	0.9 (0.70)	0.19		
	Men	82	-1.13 (0.84)	0.18		
	Women	75	3.13 (1.12)	**0.01**	3.13 (1.16)	**0.007**
FRS, %		163	-0.51 (0.23)	**0.03**	-0.09 (0.24)	0.73
	Men	82	-0.65 (0.43)	0.13		
	Women	81	-0.37 (0.15)	**0.01**	-0.15 (0.17)	0.38
Diagnostic measurements						
Fasting glucose, mmol/L		163	-0.06 (0.04)	0.16		
Fasting insulin, mU/L[d]		163	-0.05 (0.03)	**0.04**	0.04 (0.03)	0.21
HOMA-IR		153	-0.03 (0.03)	0.33		
Total cholesterol, mmol/L[e]		135	-0.29 (0.06)	**<0.001**	-0.28 (0.06)	**<0.001**
HDL cholesterol, mmol/L[e]		135	-0.01 (0.02)	0.49		
	Men	66	0.04 (0.02)	0.11		
	Women	69	-0.06 (0.03)	**0.02**	-0.08 (0.03)	**0.02**
LDL cholesterol, mmol/L[e]		135	-0.26 (0.05)	**<0.001**	-0.23 (0.05)	**<0.001**
Triglycerides, mmol/L[d,e]		135	-0.04 (0.03)	0.11		
fT3, pmol/L		163	-0.14 (0.03)	**<0.001**	-0.12 (0.03)	**<0.001**
fT4, pmol/L		163	-0.07 (0.09)	0.44		
TSH, mU/L[e]		163	-0.04 (0.03)	0.17		

Characteristic, mean (SE)		*n*	Unadjusted Difference	Unadjusted *P*-value[a]	Weight loss adjusted Difference	Weight loss adjusted *P*-value[b]
DHEAS, nmol/L[d]		163	-0.02 (0.01)	0.20		
	Men	82	-0.01 (0.02)	0.47		
	Women	81	-0.02 (0.02)	0.28		
Leptin, µg/L[d]		163	-0.26 (0.03)	**<0.001**	-0.11 (0.03)	**<0.001**
	Men	82	-0.29 (0.04)	**<0.001**	-0.14 (0.05)	**0.002**
	Women	81	-0.23 (0.03)	**<0.001**	-0.09 (0.03)	**0.009**
Adiponectin, mg/L[d]		163	0.04 (0.01)	**0.005**	0.01 (0.02)	0.78
	Men	82	0.09 (0.02)	**<0.001**	0.04 (0.03)	0.11
	Women	81	-0.01 (0.02)	0.76		
IGF-1, nmol/L		163	0.10 (0.24)	0.67		
	Men	82	0.36 (0.31)	0.24		
	Women	81	-0.17 (0.35)	0.64		
IGFBP-3, mg/L		163	-0.05 (0.05)	0.37		
IGF-1:IGFBP-3		163	0.004 (0.003)	0.21		
	Men	82	0.009 (0.006)	0.14		
	Women	81	-0.001 (0.003)	0.82		
CRP (high-sensitivity), mg/L[d]		163	-0.11 (0.07)	0.09		

[a] P value refers to difference between baseline and end. [b] P value refers to difference between baseline and end after adjustement for weight loss. [c] Individuals using antihypertensive agents were removed before analysis. [d] Natural log transformed parameter was used for analysis. [e] Individuals using lipid-lowering agents were removed before analysis. Parameters were analysed separately in men and women if there was a significant gender-difference at baseline. BMI, body mass index; REE, resting energy expenditure; FRS, Framingham risk score; HOMA-IR, homeostatic model assessment - insulin resistance; HDL, high density lipoprotein; LDL, low density lipoprotein; fT3, free triiodothyronine; fT4, free thyroxine; TSH, thyroid stimulating hormone; DHEAS, dehydroepiandrosterone-sulfate; IGF-1, insuline-like growth factor 1; IGFBP-3, insulin-like growth factor binding protein 3; CRP, C-reactive protein.

Supplementary Table 2B. Effects of the intervention on ^{1}H-NMR metabolites.

			Unadjusted		Weight loss adjusted	
Characteristic, mean (SE)		***n***	**Difference**	***P*-value[a]**	**Difference**	***P*-value[b]**
Amino acids						
Alanine, mmol/L		161	0.011 (0.070)	0.87		
	Men	80	0.011 (0.101)	0.92		
	Women	81	0.012 (0.097)	0.90		
Glutamine, mmol/L		162	0.194 (0.068)	**0.005**	0.184 (0.074)	**0.01**
Glycine, mmol/L		161	0.204 (0.042)	**<0.001**		
	Men	81	0.253 (0.058)	**<0.001**	0.234 (0.067)	**0.001**
	Women	80	0.153 (0.061)	**0.01**	0.113 (0.073)	0.12
Histidine, mmol/L		162	-0.524 (0.095)	**<0.001**	-0.517 (0.099)	**<0.001**
Branched-chain amino acids						
Isoleucine, mmol/L		161	-0.119 (0.062)	0.05		
	Men	80	-0.085 (0.088)	0.33		
	Women	81	-0.152 (0.086)	0.08		
Leucine, mmol/L		161	-0.178 (0.068)	**0.008**		
	Men	80	-0.145 (0.089)	0.10		
	Women	81	-0.210 (0.102)	**0.04**	-0.121 (0.107)	0.26
Valine, mmol/L		160	-0.117 (0.073)	0.11		
Aromatic amino acids						
Phenylalanine, mmol/L		162	-0.015 (0.079)	0.85		
Tyrosine, mmol/L		162	-0.242 (0.087)	**0.005**	-0.163 (0.090)	**0.07**
Glycolysis-related metabolites						
Glucose, mmol/L		162	-0.241 (0.069)	**0.001**	-0.185 (0.075)	**0.01**
Lactate, mmol/L		162	-0.049 (0.094)	0.60		
Pyruvate, mmol/L		161	-0.261 (0.086)	**0.002**	-0.260 (0.090)	**0.004**
Citrate, mmol/L		162	0.199 (0.078)	**0.01**	0.220 (0.082)	**0.007**

Characteristic, mean (SE)		*n*	Unadjusted Difference	Unadjusted *P*-value[a]	Weight loss adjusted Difference	Weight loss adjusted *P*-value[b]
Glycerol, mmol/L		157	-0.172 (0.068)	**0.01**		
	Men	77	-0.178 (0.084)	**0.03**	-0.107 (0.094)	0.25
	Women	80	-0.167 (0.106)	0.12		
Ketone bodies						
Acetate, mmol/L		162	-0.012 (0.061)	0.85		
Acetoacetate, mmol/L		162	-0.097 (0.083)	0.24		
	Men	81	-0.016 (0.122)	0.90		
	Women	81	-0.179 (0.113)	0.11		
3-hydroxybutyrate, mmol/L		158	-0.152 (0.073)	**0.04**	-0.089 (0.078)	0.26
Fatty acids[c]						
Total fatty acids, mmol/L		130	-0.217 (0.061)	**<0.001**	-0.159 (0.069)	**0.02**
Omega-3 fatty acids, mmol/L		130	-0.173 (0.067)	**0.01**	-0.154 (0.074)	**0.04**
Docosahexaenoic acid (DHA), mmol/L		130	-0.057 (0.060)	0.35		
Omega-6 fatty acids, mmol/L		130	-0.322 (0.062)	**<0.001**	-0.288 (0.070)	**<0.001**
Linoleic acid, mmol/L		130	-0.262 (0.061)	**<0.001**	-0.232 (0.068)	**0.001**
Polyunsaturated fatty acids, mmol/L		130	-0.319 (0.059)	**<0.001**	-0.283 (0.067)	**<0.001**
Monounsaturated fatty acids, mmol/L		130	-0.211 (0.057)	**<0.001**	-0.114 (0.065)	0.08
Saturated fatty acids, mmol/L		130	-0.103 (0.072)	0.15		
Fatty acid chain length		130	0.414 (0.099)	**<0.001**	0.437 (0.104)	**<0.001**
Fatty acid ratios, relative to total fatty acids[c]						
Omega-3 fatty acids, %		130	-0.017 (0.085)	0.84		
Docosahexaenoic acid (DHA), %		130	0.093 (0.073)	0.20		
Omega-6 fatty acids, %		130	-0.170 (0.073)	**0.02**	-0.206 (0.079)	**0.01**
Linoleic acid, %		130	-0.088 (0.060)	0.14		
Polyunsaturated fatty acids, %		130	-0.166 (0.073)	**0.02**	-0.207 (0.080)	**0.01**
Monounsaturated fatty acids, %		130	-0.131 (0.060)	**0.03**	-0.027 (0.066)	0.68

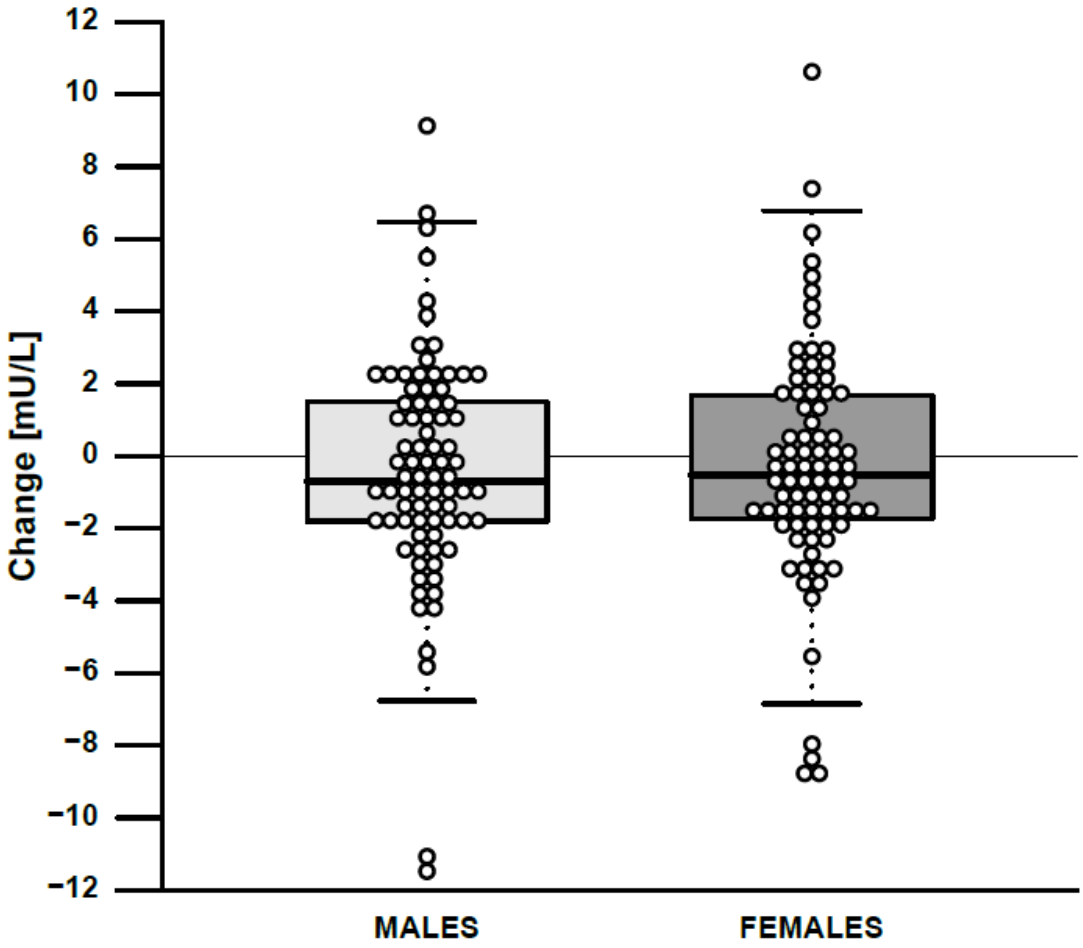
Characteristic, mean (SE)		*n*	Unadjusted Difference	Unadjusted *P*-value[a]	Weight loss adjusted Difference	Weight loss adjusted *P*-value[b]
Saturated fatty acids, %		130	0.378 (0.096)	**<0.001**	0.305 (0.100)	**0.002**
Unsaturation degree, double bonds per fatty acids		130	-0.125 (0.078)	0.11	-0.137 (0.085)	0.11
Fluid balance						
Creatinine, mmol/L		162	-0.090 (0.050)	0.07		
	Men	81	-0.033 (0.069)	0.63		
	Women	81	-0.146 (0.072)	**0.04**	-0.110 (0.078)	0.16
Albumin, signal area		162	-0.069 (0.076)	0.37		
Inflammation						
Glycoprotein acetyls, mainly a1-acid glycoprotein, mmol/L		162	-0.155 (0.058)	**0.008**		
	Men	81	-0.221 (0.082)	**0.007**	-0.126 (0.092)	0.16
	Women	81	-0.089 (0.083)	0.28		
Apolipoproteins[c]						
Apolipoprotein B, g/L		134	-0.311 (0.048)	**<0.001**	-0.225 (0.056)	**<0.001**
Apolipoprotein A1, g/L		134	-0.147 (0.052)	**0.004**	-0.210 (0.059)	**<0.001**
	Men	65	-0.009 (0.071)	0.90		
	Women	69	-0.278 (0.072)	**<0.001**	-0.308 (0.081)	**<0.001**
Lipids[c]						
Triglycerides, mmol/L		134	-0.179 (0.058)	**0.002**		
	Men	65	-0.290 (0.086)	**0.001**	-0.200 (0.097)	**0.04**
	Women	69	-0.075 (0.075)	0.32		
Phosphoglycerides, mmol/L		130	-0.258 (0.068)	**<0.001**	-0.276 (0.075)	**<0.001**
	Men	63	-0.246 (0.094)	**0.009**	-0.323 (0.107)	**0.003**
	Women	67	-0.269 (0.097)	**0.006**	-0.248 (0.105)	**0.02**
Cholines, mmol/L		130	-0.189 (0.064)	**0.003**	-0.218 (0.071)	**0.002**
	Men	63	-0.171 (0.090)	0.06		
	Women	67	-0.205 (0.091)	**0.02**	-0.183 (0.098)	0.06

			Unadjusted		Weight loss adjusted	
Characteristic, mean (SE)		***n***	**Difference**	***P*-value[a]**	**Difference**	***P*-value[b]**
Sphingomyelins, mmol/L		130	-0.258 (0.051)	**<0.001**	-0.286 (0.059)	**<0.001**
	Men	63	-0.182 (0.067)	**0.006**	-0.281 (0.083)	**0.001**
	Women	67	-0.329 (0.076)	**<0.001**	-0.313 (0.083)	**<0.001**
Total lipid concentrations in lipoprotein subclasses[c]						
Extremely large VLDL, mmol/L		115	-0.244 (0.079)	**0.002**	-0.235 (0.085)	**0.006**
Very large VLDL, mmol/L		103	-0.306 (0.084)	**<0.001**	-0.277 (0.091)	**0.002**
Large VLDL, mmol/L		119	-0.288 (0.066)	**<0.001**	-0.195 (0.072)	**0.007**
Medium VLDL, mmol/L		134	-0.232 (0.056)	**<0.001**	-0.114 (0.063)	0.07
Small VLDL, mmol/L		134	-0.284 (0.055)	**<0.001**	-0.176 (0.062)	**0.005**
Very small VLDL, mmol/L		134	-0.283 (0.059)	**<0.001**	-0.239 (0.067)	**<0.001**
IDL, mmol/L		134	-0.245 (0.051)	**<0.001**	-0.222 (0.059)	**<0.001**
Large LDL, mmol/L		134	-0.232 (0.052)	**<0.001**	-0.188 (0.060)	**0.002**
Medium LDL, mmol/L		134	-0.240 (0.055)	**<0.001**	-0.179 (0.063)	**0.004**
Small LDL, mmol/L		134	-0.266 (0.054)	**<0.001**	-0.205 (0.061)	**0.001**
Very large HDL, mmol/L		133	0.069 (0.061)	0.26		
	Men	64	0.217 (0.094)	**0.02**	0.025 (0.096)	0.80
	Women	69	-0.068 (0.075)	0.36		
Large HDL, mmol/L		126	0.091 (0.046)	0.05		
	Men	59	0.241 (0.079)	**0.002**	0.077 (0.087)	0.38
	Women	67	-0.042 (0.048)	0.38		
Medium HDL, mmol/L		134	-0.115 (0.068)	0.09		
	Men	65	0.025 (0.091)	0.79		
	Women	69	-0.247 (0.098)	**0.01**	-0.246 (0.105)	**0.02**
Small HDL, mmol/L		134	-0.200 (0.088)	**0.02**	-0.111 (0.092)	0.228
	Men	65	-0.215 (0.120)	0.07		
	Women	69	-0.185 (0.129)	0.15		

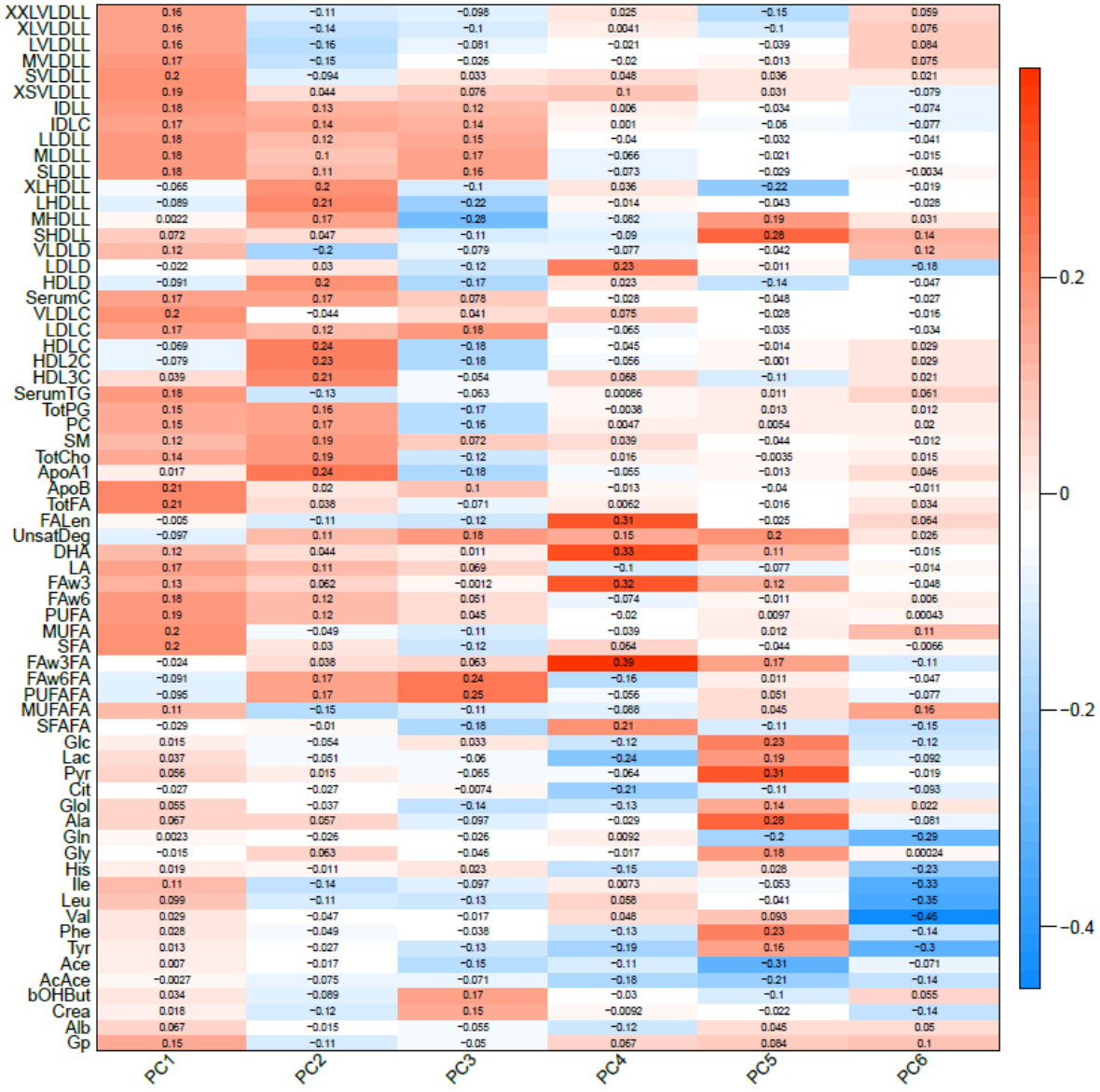
Characteristic, mean (SE)		*n*	Unadjusted Difference	Unadjusted *P*-value[a]	Weight loss adjusted Difference	Weight loss adjusted *P*-value[b]
Lipoprotein particle size[c]						
VLDL diameter, nm		134	-0.136 (0.067)	**0.04**	-0.032 (0.073)	0.66
LDL diameter, nm		134	0.115 (0.095)	0.23		
HDL diameter, nm		134	0.108 (0.050)	**0.03**	-0.051 (0.054)	0.35
	Men	65	0.258 (0.077)	**0.001**	0.081 (0.081)	0.32
	Women	69	-0.032 (0.060)	0.59		
Cholesterol[c]						
Total cholesterol, mmol/L		134	-0.296 (0.051)	**<0.001**	-0.279 (0.059)	**<0.001**
VLDL cholesterol, mmol/L		134	-0.301 (0.059)	**<0.001**	-0.223 (0.067)	**0.001**
IDL cholesterol, mmol/L		134	-0.265 (0.051)	**<0.001**	-0.249 (0.059)	**<0.001**
LDL cholesterol, mmol/L		134	-0.246 (0.054)	**<0.001**	-0.197 (0.061)	**0.001**
HDL cholesterol, mmol/L		134	0.005 (0.043)	0.90		
	Men	65	0.140 (0.062)	**0.02**	0.015 (0.072)	0.83
	Women	69	-0.122 (0.055)	**0.03**	-0.174 (0.066)	**0.008**
HDL2 cholesterol, mmol/L		134	0.023 (0.042)	0.58		
	Men	65	0.163 (0.061)	**0.008**	0.036 (0.073)	0.62
	Women	69	-0.108 (0.055)	**0.05**	-0.160 (0.066)	**0.02**
HDL3 cholesterol, mmol/L		134	-0.023 (0.074)	0.75		
	Men	65	-0.005 (0.104)	0.96		
	Women	69	-0.041 (0.107)	0.70		

[a] P value refers to difference between baseline and end. [b] P value refers to difference between baseline and end after adjustment for weight loss. [c] Individuals using lipid-lowering agents were removed before analysis. All metabolite concentrations were natural log-transformed and scaled to standard deviation units before analysis. Parameters were analysed separately in men and women if there was a significant gender-difference at baseline. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

Suplementary Figures



Supplementary Figure 1. Effect of the intervention on insulin levels.



Supplementary Figure 2. Association of ^{1}H-NMR metabolites with PC's identified using PCA analysis. The colour of the cells represents the magnitude of the effect.