SUPPLEMENTAL MATERIAL

Supplemental Methods

Additional description of the Look AHEAD study design:

Eligibility criteria included age 45 to 76 years; self-reported type 2 diabetes mellitus (T2DM) with verification of anti-hyperglycemic medication use or medical records; and body mass index ≥25 kg/m^2 or ≥27 kg/m^2 if taking insulin. All participants had to complete a maximal exercise treadmill test at baseline. Participants with a history of bariatric surgery were excluded from enrolling in the trial.

Interventions:

Participants of the Look AHEAD trial were randomly assigned to either the intensive lifestyle intervention (ILI) or diabetes support and education (DSE) treatment groups.[11, 12] The ILI consisted of individual and group counseling sessions and strategies to achieve and maintain ≥7% weight loss, including caloric restriction (1,200-1,800 kcal/day) and increased physical activity (≥175 minutes/week of moderate intensity physical activity). The DSE included less frequent group sessions focused on nutrition, exercise, and social support.

Covariates:

Baseline, 1- and 4-year follow-up dual-energy X-ray absorptiometry (DXA) scans were performed across the following study sites: Baton Rouge, Louisiana; Boston, Massachusetts; Houston, Texas; Los Angeles, California; Seattle, Washington.[14, 15] A Hologic QDR4500A fan beam densitometer was used at all sites except Boston, Massachusetts, which used a Hologic Delphi A densitometer. The regions of interest were the trunk, leg, and arm. Two-compartment models differentiated fat mass (FM) and fat-free mass. Fat-free mass was classified as bone mineral content versus soft tissue. The difference between fat-free mass and bone mineral

content was lean mass (LM). Differences across scanners were assessed using calibration phantoms (whole body, spine, hip, linearity). Regular scans of phantoms were performed for quality control and corrections were applied as previously described.[15, 34] The central DXA reading center (University of California at San Francisco) reviewed all scans. Participants who weighed >300 pounds were excluded from DXA assessment due to weight limits of the equipment. The coefficient of variation for FM and LM was 1.5% and 0.8%, respectively. [15, 35]

Participants underwent a baseline examination that included questionnaires and a clinical examination as previously described.[11, 12, 36] Demographics details (age, sex, race/ethnicity), education level completed, income, smoking history, alcohol use history, diabetes history, and medication use were self-reported. History of cardiovascular disease was defined based on prior myocardial infarction, stroke, transient ischemic attack, heart failure, or cardiovascular procedure, including percutaneous transluminal coronary angioplasty/stent, coronary artery bypass graft, aortic aneurysm repair, carotid endarterectomy, or angioplasty of lower extremity artery.[37] Blood pressure (BP) was measured in a seated position with an automated device in duplicate. History of hypertension was based on use of antihypertensive medication or BP ≥140/90 mm Hg. Glycated hemoglobin (HbA1c) was measured at a core laboratory. Estimated glomerular filtration rate was calculated as previously described.[38] Cardiorespiratory fitness was assessed from a symptom-limited graded treadmill exercise test. At a constant treadmill speed that was selected based on a standardized protocol, study participants started the exercise test at 0% grade that increased incrementally by 1% every minute until voluntary exhaustion or standard stopping criteria were met.[17] During each stage and at the termination of the test protocol, heart rate and rating of perceived exertion were measured. Peak oxygen consumption was estimated based on speed and grade using established American College of Sports Medicine equations.[39]

Supplemental Table I. Baseline characteristics stratified by baseline waist circumference tertiles

	Tertile 1 70.8 to 107.3 cm (n=1,700)	Tertile 2 107.4 to 118.7 cm (n=1,703)	Tertile 3 118.8 to 210.8 cm (n=1,700)	P-value for WC tertiles
Predicted fat mass, kg	33.9 (6.8)	40.4 (8.0)	50.8 (9.8)	<0.001
Predicted lean mass, kg	48.4 (8.7)	56.3 (10.0)	66.3 (13.1)	<0.001
Waist circumference, cm	99.5 (5.8)	112.8 (3.2)	129.4 (9.5)	<0.001
Age, years	58.9 (6.9)	59.2 (6.9)	58.0 (6.7)	<0.001
Female, n (%)	1,278 (75.2)	982 (57.7)	784 (46.1)	<0.001
White, n (%)	901 (53.0)	1,107 (65.0)	1,221 (71.8)	<0.001
Education, n (%)				
<13 years	396 (23.3)	325 (19.1)	290 (17.1)	0.001
13-16 years	606 (35.7)	642 (37.7)	655 (38.5)	
>16 years	661 (38.9)	694 (40.8)	720 (42.4)	
Missing	37 (2.2)	42 (2.5)	35 (2.1)	
Income, n (%)				
<$20,000	226 (13.3)	190 (11.2)	166 (9.8)	<0.001
$20,000-$39,999	358 (21.1)	304 (17.9)	317 (18.7)	
$40,000-$59,999	310 (18.2)	303 (17.8)	333 (19.6)	
$60,000-$79,999	208 (12.2)	247 (14.5)	288 (16.9)	
≥$80,000	432 (25.4)	477 (28.0)	443 (26.1)	
Missing	166 (9.8)	182 (10.7)	153 (9.0)	
Weight, kg	84.0 (10.3)	98.7 (10.8)	119.3 (16.2)	<0.001
BMI, kg/m^2	31.4 (3.3)	35.3 (4.0)	41.1 (5.4)	<0.001
Systolic BP, mm Hg	127 (17)	129 (17)	131 (17)	<0.001
Diastolic BP, mm Hg	70 (9)	70 (10)	71 (10)	0.001
History of hypertension, n (%)	1,326 (78.0)	1,415 (83.1)	1,500 (88.2)	<0.001
History of CVD, n (%)	191 (11.2)	231 (13.6)	254 (14.9)	0.006
Diabetes duration, years	6.6 (6.7)	6.9 (6.6)	6.9 (6.2)	0.36
Insulin use, n (%)	195 (11.9)	277 (16.9)	311 (18.9)	<0.001
Smoking, n (%)				<0.001
Never	962 (56.7)	848 (49.9)	749 (44.2)	
Past	678 (40.0)	754 (44.3)	876 (51.7)	
Present	57 (3.4)	99 (5.8)	69 (4.1)	
Alcohol, n (%)				0.09
None/week	1,194 (70.4)	1,127 (66.5)	1,128 (66.6)	
1-3/week	299 (17.6)	343 (20.2)	345 (20.4)	
4+/week	203 (12.0)	226 (13.3)	221 (13.1)	
HbA1c, %	7.2 (1.2)	7.3 (1.1)	7.4 (1.2)	<0.001
GFR, mL/min per 1.73 m^2	90.0 (15.8)	88.8 (15.9)	90.3 (16.3)	0.01
LDL-C, mg/dL	115 (33)	111 (32)	110 (31)	<0.001
Estimated CRF, METs	7.8 (2.1)	7.3 (1.9)	6.5 (1.7)	<0.001
ILI treatment group, n (%)	863 (50.8)	848 (49.8)	835 (49.1)	0.63

Categorical data presented as n (percentage) and continuous data presented as mean (standard deviation). Comparison across groups performed using generalized linear models.

BMI = body mass index; BP = blood pressure; CRF = cardiorespiratory fitness; CVD = cardiovascular disease; FM = fat mass; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; ILI = intensive lifestyle intervention; LDL-C = low-density lipoprotein cholesterol; LM = lean mass; METs = metabolic equivalents; WC = waist circumference

Supplemental Table II. Baseline and follow-up characteristics stratified by year 1 percent change in predicted fat mass and predicted lean mass tertiles

	1-year change in predicted fat mass			1-year change in predicted lean mass				
	Tertile 1 -65.5 to -10% (n=1,608)	Tertile 2 -9.9 to -1.5% (n=1,609)	Tertile 3 -1.4 to 53.7% (n=1,609)	Tertile 1 -39.9 to -4.6% (n=1,608)	Tertile 2 -4.5% to -0.7% (n=1,609)	Tertile 3 -0.6 to 73.3% (n=1,609)	P-value for FM tertiles	P-value for LM tertiles
Baseline variables								
Predicted fat mass, kg	40.8 (10.8)	42.4 (10.8)	41.9 (10.6)	42.0 (10.9)	41.3 (10.6)	41.7 (10.7)	<0.001	0.24
Predicted lean mass, kg	57.6 (12.9)	56.3 (13.0)	57.2 (13.3)	58.6 (13.9)	55.9 (12.7)	56.6 (12.5)	0.02	<0.001
Waist circumference, cm	113.8 (14.6)	113.9 (13.6)	113.8 (13.8)	114.3 (14.1)	112.6 (13.4)	114.7 (14.4)	0.99	<0.001
Age, years	59.3 (6.9)	58.6 (6.7)	58.2 (6.9)	59.0 (6.8)	58.8 (6.8)	58.4 (6.9)	<0.001	0.03
Female, n (%)	848 (52.7)	1,033 (64.2)	988 (61.4)	913 (56.8)	1,022 (63.5)	934 (58.1)	<0.001	<0.001
White, n (%)	1,120 (69.7)	982 (61.0)	966 (60.0)	1,128 (70.2)	954 (59.3)	986 (61.3)	<0.001	<0.001
Education, n (%)								
<13 years	313 (19.5)	311 (19.3)	324 (20.1)	308 (19.2)	321 (20.0)	319 (19.8)	0.008	0.01
13-16 years	539 (33.5)	628 (39.0)	626 (38.9)	549 (34.1)	620 (38.5)	624 (38.8)		
>16 years	720 (44.8)	634 (39.4)	623 (38.7)	720 (44.8)	630 (39.2)	627 (39.0)		
Missing	36 (2.2)	36 (2.2)	36 (2.2)	31 (1.9)	38 (2.4)	39 (2.4)		
Income, n (%)								
<$20,000	169 (10.5)	189 (11.8)	180 (11.2)	162 (10.1)	187 (11.6)	189 (11.8)	0.002	0.05
$20,000-$39,999	290 (18.0)	323 (20.1)	310 (19.3)	286 (17.8)	337 (20.9)	300 (18.7)		
$40,000-$59,999	279 (17.4)	302 (18.8)	316 (19.6)	286 (17.8)	297 (18.5)	314 (19.5)		
$60,000-$79,999	228 (14.2)	248 (15.4)	241 (15.0)	234 (14.6)	239 (14.9)	244 (15.2)		
≥$80,000	481 (29.9)	368 (22.9)	430 (26.7)	473 (29.4)	391 (24.3)	415 (25.8)		
Missing	161 (10.0)	179 (11.1)	132 (8.2)	167 (10.4)	158 (9.8)	147 (9.1)		
Weight, kg	100.2 (19.1)	100.6 (19.4)	101.1 (19.2)	102.4 (20.1)	99.1 (19.0)	100.4 (18.6)	0.41	<0.001
BMI, kg/m^2	35.4 (5.8)	36.1 (5.9)	36.2 (5.9)	36.3 (5.9)	35.6 (5.8)	35.9 (5.9)	<0.001	0.006
Systolic BP, mm Hg	129 (17)	129 (17)	129 (17)	129 (17)	129 (17)	129 (17)	0.82	0.77
Diastolic BP, mm Hg	70 (10)	70 (10)	70 (10)	70 (10)	70 (10)	70 (10)	0.70	0.16
History of hypertension, n (%)	1,359 (84.5)	1,326 (82.4)	1,327 (82.5)	1,368 (85.1)	1,315 (81.7)	1,329 (82.6)	0.19	0.03
History of CVD, n (%)	205 (12.8)	196 (12.2)	227 (14.1)	199 (12.4)	203 (12.6)	226 (14.1)	0.25	0.31
Diabetes duration, years	6.7 (6.5)	6.9 (6.8)	6.7 (6.3)	6.7 (6.6)	6.8 (6.6)	6.8 (6.4)	0.69	0.92
Insulin use, n (%)	202 (12.9)	253 (16.3)	274 (17.7)	212 (13.6)	250 (16.1)	267 (17.3)	<0.001	0.02
Smoking, n (%)								
Never	764 (47.6)	847 (52.8)	832 (51.8)	779 (48.5)	851 (53.1)	813 (50.6)	0.02	0.07
Past	774 (48.2)	683 (42.6)	711 (44.2)	764 (47.6)	684 (42.7)	720 (44.8)		
Present	67 (4.2)	74 (4.6)	64 (4.0)	63 (3.9)	68 (4.2)	74 (4.6)		
Alcohol, n (%)								
None/week	1,053 (65.6)	1,075 (67.1)	1,122 (70.0)	1,074 (66.9)	1,072 (66.9)	1,104 (68.8)	0.03	0.45
1-3/week	320 (19.9)	332 (20.7)	285 (17.8)	309 (19.3)	330 (20.6)	298 (18.6)		
4+/week	233 (14.5)	195 (12.2)	196 (12.2)	222 (13.8)	200 (12.5)	202 (12.6)		
HbA1c, %	7.1 (1.1)	7.4 (1.2)	7.3 (1.2)	7.1 (1.1)	7.4 (1.2)	7.3 (1.3)	<0.001	<0.001
GFR, mL/min per 1.73 m^2	88.4 (16.0)	90.2 (15.8)	90.3 (16.0)	88.9 (16.0)	90.0 (15.9)	90.1 (15.9)	<0.001	0.06
LDL-C, mg/dL	110 (32)	113 (32)	113 (32)	110 (33)	114 (31)	112 (33)	0.04	0.006
Estimated CRF, METs	7.4 (2.0)	7.1 (2.0)	7.2 (2.0)	7.1 (1.8)	6.9 (1.9)	7.6 (2.1)	<0.001	<0.001
ILI treatment group, n (%)	1,392 (86.6)	757 (47.1)	284 (17.7)	1,321 (82.2)	764 (47.5)	348 (21.6)	<0.001	<0.001

	1-year change in predicted fat mass			1-year change in predicted lean mass				
	Tertile 1 -65.5 to -10% (n=1,608)	**Tertile 2 -9.9 to -1.5% (n=1,609)**	**Tertile 3 -1.4 to 53.7% (n=1,609)**	**Tertile 1 -39.9 to -4.6% (n=1,608)**	**Tertile 2 -4.5% to -0.7% (n=1,609)**	**Tertile 3 -0.6 to 73.3% (n=1,609)**	**P-value for FM tertiles**	**P-value for LM tertiles**
Year 1 variables								
Predicted fat mass, kg	32.7 (96.1)	40.1 (10.3)	43.5 (11.0)	34.8 (10.4)	39.3 (10.7)	42.2 (11.4)	<0.001	<0.001
Change in predicted fat mass, %	-20.0 (8.8)	-5.3 (2.5)	4.0 (5.0)	-17.3 (11.0)	-5.1 (6.8)	1.1 (7.7)	<0.001	<0.001
Predicted lean mass, kg	53.3 (11.9)	55.0 (12.6)	57.6 (13.3)	53.6 (12.5)	54.5 (12.4)	57.9 (12.8)	<0.001	<0.001
Change in predicted lean mass, %	-7.2 (5.9)	-2.3 (2.9)	0.8 (3.3)	-8.6 (3.9)	-2.4 (1.1)	2.2 (3.5)	<0.001	<0.001
Waist circumference, cm	102.4 (12.9)	110.8 (13.3)	115.6 (14.0)	104.9 (14.4)	109.9 (13.6)	114.0 (13.9)	<0.001	<0.001
Change in waist circumference, %	-9.8 (5.9)	-2.7 (4.1)	1.6 (5.0)	-8.2 (6.8)	-2.4 (5.3)	-0.4 (6.0)	<0.001	<0.001
Change in systolic BP, mmHg	-8.7 (16.9)	-4.0 (16.5)	-1.7 (17.1)	-8.5 (17.2)	-4.5 (16.8)	-1.4 (16.5)	<0.001	<0.001
Change in systolic BP, %	-6.0 (13.0)	-2.3 (12.6)	-0.5 (13.4)	-5.8 (13.2)	-2.7 (12.9)	-0.3 (12.9)	<0.001	<0.001
Change in HbA1c, %	-9.6 (12.2)	-3.7 (12.0)	-0.4 (12.5)	-9.0 (12.8)	-3.7 (12.3)	-1.0 (12.0)	<0.001	<0.001

Categorical data presented as n (percentage) and continuous data presented as mean (standard deviation). Comparison across groups performed using generalized linear models. Follow-up variables were assessed post-baseline visit.

BMI = body mass index; BP = blood pressure; CRF = cardiorespiratory fitness; CVD = cardiovascular disease; FM = fat mass; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; ILI = intensive lifestyle intervention; LDL-C = low-density lipoprotein cholesterol; LM = lean mass; METs = metabolic equivalents; MI = myocardial infarction; WC = waist circumference

Supplemental Table III. Baseline and follow-up characteristics stratified by year 4 percent change in predicted fat mass and predicted lean mass tertiles

	4-year change in predicted fat mass			4-year change in predicted lean mass				
Variable	Tertile 1 -61.9 to -7.3% (n=1,528)	Tertile 2 -7.2 to 1.8% (n=1,528)	Tertile 3 1.9 to 89.2% (n=1,529)	Tertile 1 -44.7 to -4.6% (n=1,528)	Tertile 2 -4.5 to -0.1% (n=1,528)	Tertile 3 0 to 64.4% (n=1,529)	P-value for FM tertiles	P-value for LM tertiles
Baseline variables								
Predicted fat mass, kg	41.9 (11.4)	42.1 (10.4)	40.9 (10.4)	42.6 (11.2)	40.5 (10.2)	41.9 (10.6)	0.005	<0.001
Predicted lean mass, kg	57.3 (12.8)	56.5 (13.0)	57.0 (13.2)	57.7 (13.6)	56.3 (12.5)	56.8 (12.8)	0.26	0.009
Waist circumference, cm	114.6 (14.6)	113.8 (13.5)	112.8 (13.6)	114.5 (14.0)	112.2 (13.2)	114.6 (14.4)	0.002	<0.001
Age, years	59.4 (6.9)	58.6 (6.8)	58.0 (6.7)	59.1 (6.9)	59.0 (6.7)	57.9 (6.8)	<0.001	<0.001
Female, n (%)	865 (56.6)	973 (63.6)	905 (59.2)	932 (61.0)	919 (60.1)	892 (58.3)	<0.001	0.31
White, n (%)	994 (65.1)	961 (62.9)	967 (63.2)	989 (64.8)	945 (61.8)	988 (64.6)	0.42	<0.001
Education, n (%)								
<13 years	309 (20.2)	296 (19.4)	293 (19.2)	349 (22.8)	278 (18.2)	271 (17.7)	0.11	0.001
13-16 years	519 (34.0)	576 (37.7)	601 (39.3)	525 (34.4)	566 (37.0)	605 (39.6)		
>16 years	666 (43.6)	620 (40.6)	601 (39.3)	624 (40.8)	641 (41.9)	622 (40.7)		
Missing	34 (2.2)	37 (2.4)	34 (2.2)	30 (2.0)	44 (2.9)	31 (2.0)		
Income, n (%)								
<$20,000	168 (11.0)	171 (11.2)	158 (10.3)	190 (12.4)	165 (10.8)	142 (9.3)	0.42	0.04
$20,000-$39,999	304 (19.9)	271 (17.7)	300 (19.6)	308 (20.2)	293 (19.2)	274 (17.9)		
$40,000-$59,999	279 (18.3)	274 (17.9)	302 (19.8)	281 (18.4)	272 (17.8)	302 (19.8)		
$60,000-$79,999	206 (13.5)	251 (16.4)	228 (14.9)	201 (13.2)	231 (15.1)	253 (16.6)		
≥$80,000	413 (27.0)	418 (27.3)	396 (25.9)	390 (25.5)	420 (27.5)	417 (27.3)		
Missing	158 (10.3)	144 (9.4)	145 (9.5)	158 (10.3)	148 (9.7)	141 (9.2)		
Weight, kg	101.1 (19.5)	100.5 (19.0)	100.0 (18.8)	102.2 (20.2)	98.7 (18.1)	100.6 (18.9)	0.29	<0.001
BMI, kg/m^2	35.9 (6.2)	36.0 (5.7)	35.7 (5.7)	36.6 (6.1)	35.2 (5.5)	35.9 (5.9)	0.30	<0.001
Systolic BP, mm Hg	128 (17)	129 (17)	128 (17)	130 (17)	129 (17)	128 (16)	0.61	0.01
Diastolic BP, mm Hg	70 (10)	70 (10)	70 (9)	70 (10)	70 (9)	70 (10)	0.71	0.82
History of hypertension, n (%)	1,268 (83.0)	1,255 (82.1)	1,276 (83.5)	1,292 (84.6)	1,243 (81.3)	1,264 (82.7)	0.59	0.06
History of CVD, n (%)	203 (13.3)	177 (11.6)	203 (13.3)	208 (13.6)	188 (12.3)	187 (12.2)	0.26	0.43
Diabetes duration, years	6.6 (6.3)	6.5 (6.5)	7.1 (6.7)	6.6 (6.4)	6.6 (6.6)	7.0 (6.6)	0.03	0.23
Insulin use, n (%)	209 (14.2)	225 (15.2)	249 (16.9)	216 (14.6)	219 (14.8)	248 (16.9)	0.12	0.17
Smoking, n (%)								
Never	764 (50.2)	784 (51.3)	785 (51.4)	775 (51.0)	782 (51.2)	776 (50.8)	0.85	>0.99
Past	688 (45.2)	684 (44.8)	678 (44.4)	681 (44.8)	680 (44.5)	689 (45.1)		
Present	70 (4.6)	59 (3.9)	63 (4.1)	65 (4.3)	65 (4.3)	62 (4.1)		
Alcohol, n (%)								
None/week	1,037 (68.0)	1,014 (66.6)	1,028 (67.6)	1,084 (71.1)	1,003 (65.8)	992 (65.2)	0.75	0.004
1-3/week	299 (19.6)	295 (19.4)	299 (19.7)	271 (17.8)	305 (20.0)	317 (20.8)		
4+/week	190 (12.5)	214 (14.1)	194 (12.8)	169 (11.1)	216 (14.2)	213 (14.0)		
HbA1c, %	7.2 (1.1)	7.3 (1.2)	7.3 (1.2)	7.2 (1.1)	7.3 (1.1)	7.3 (1.2)	0.26	0.39
GFR, mL/min per 1.73 m^2	89.6 (15.6)	90.0 (16.3)	89.9 (15.7)	89.8 (15.8)	89.7 (15.9)	90.1 (16.0)	0.78	0.74
LDL, mg/dL	110 (31)	113 (32)	113 (34)	112 (32)	112 (32)	113 (33)	0.03	0.61
Estimated CRF, METs	7.2 (2)	7.2 (1.9)	7.3 (2.0)	7.1 (1.9)	7.4 (2.0)	7.3 (2.0)	<0.001	0.06
ILI treatment group, n (%)	973 (63.7)	762 (49.8)	575 (37.6)	953 (62.4)	777 (50.8)	580 (37.9)	<0.001	<0.001

	4-year change in predicted fat mass			4-year change in predicted lean mass				
Variable	**Tertile 1 -61.9 to -7.3% (n=1,528)**	**Tertile 2 -7.2 to 1.8% (n=1,528)**	**Tertile 3 1.9 to 89.2% (n=1,529)**	**Tertile 1 -44.7 to -4.6% (n=1,528)**	**Tertile 2 -4.5 to -0.1% (n=1,528)**	**Tertile 3 0 to 64.4% (n=1,529)**	**P-value for FM tertiles**	**P-value for LM tertiles**
Year 4 variables								
Predicted fat mass, kg	34.8 (9.7)	41.0 (10.2)	44.8 (11.5)	36.7 (10.1)	39.6 (10.3)	44.3 (11.9)	<0.001	<0.001
Change in predicted fat mass, %	-16.5 (8.7)	-2.56 (2.5)	9.6 (7.6)	-13.3 (11.7)	-2.1 (7.4)	5.9 (10.3)	<0.001	<0.001
Predicted lean mass, kg	53.1 (11.9)	55.3 (12.9)	58.1 (13.6)	52.5 (12.2)	55.1 (12.3)	59.0 (13.5)	<0.001	<0.001
Change in predicted lean mass, %	-7.2 (6.4)	-2.1 (3.2)	2.0 (5.1)	-8.9 (4.5)	-2.3 (1.2)	3.7 (4.2)	<0.001	<0.001
Waist circumference, cm	105.1 (12.9)	112.5 (13.3)	117.5 (14.7)	107.3 (14.2)	111.1 (13.3)	116.8 (14.6)	<0.001	<0.001
Change in waist circumference, %	-8.0 (6.3)	-1.0 (4.3)	4.2 (6.2)	-6.1 (7.9)	-0.9 (5.4)	2.2 (6.8)	<0.001	<0.001
Change in systolic BP, mmHg	-7.0 (18.7)	-2.9 (19.4)	-2.1 (18.9)	-7.7 (18.9)	-3.4 (18.8)	-0.9 (19.2)	<0.001	<0.001
Change in systolic BP, %	-4.6 (14.3)	-1.4 (14.9)	-0.6 (15.1)	-5.1 (14.4)	-1.7 (14.4)	0.2 (15.3)	<0.001	<0.001
Change in HbA1c, %	-4.6 (19.0)	0.6 (16.0)	0.8 (17.5)	-4.0 (19.3)	0.1 (15.8)	0.8 (17.4)	<0.001	<0.001

Categorical data presented as n (percentage) and continuous data presented as mean (standard deviation). Comparison across groups performed using generalized linear models. Follow-up variables were assessed post-baseline visit.

BMI = body mass index; BP = blood pressure; CRF = cardiorespiratory fitness; CVD = cardiovascular disease; FM = fat mass; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; ILI = intensive lifestyle intervention; LDL = low-density lipoprotein; LM = lean mass; METs = metabolic equivalents; MI = myocardial infarction; WC = waist circumference

Supplemental Table IV. Multivariable adjusted associations of changes in body composition measures from baseline to 4-year follow-up with risk of HF events

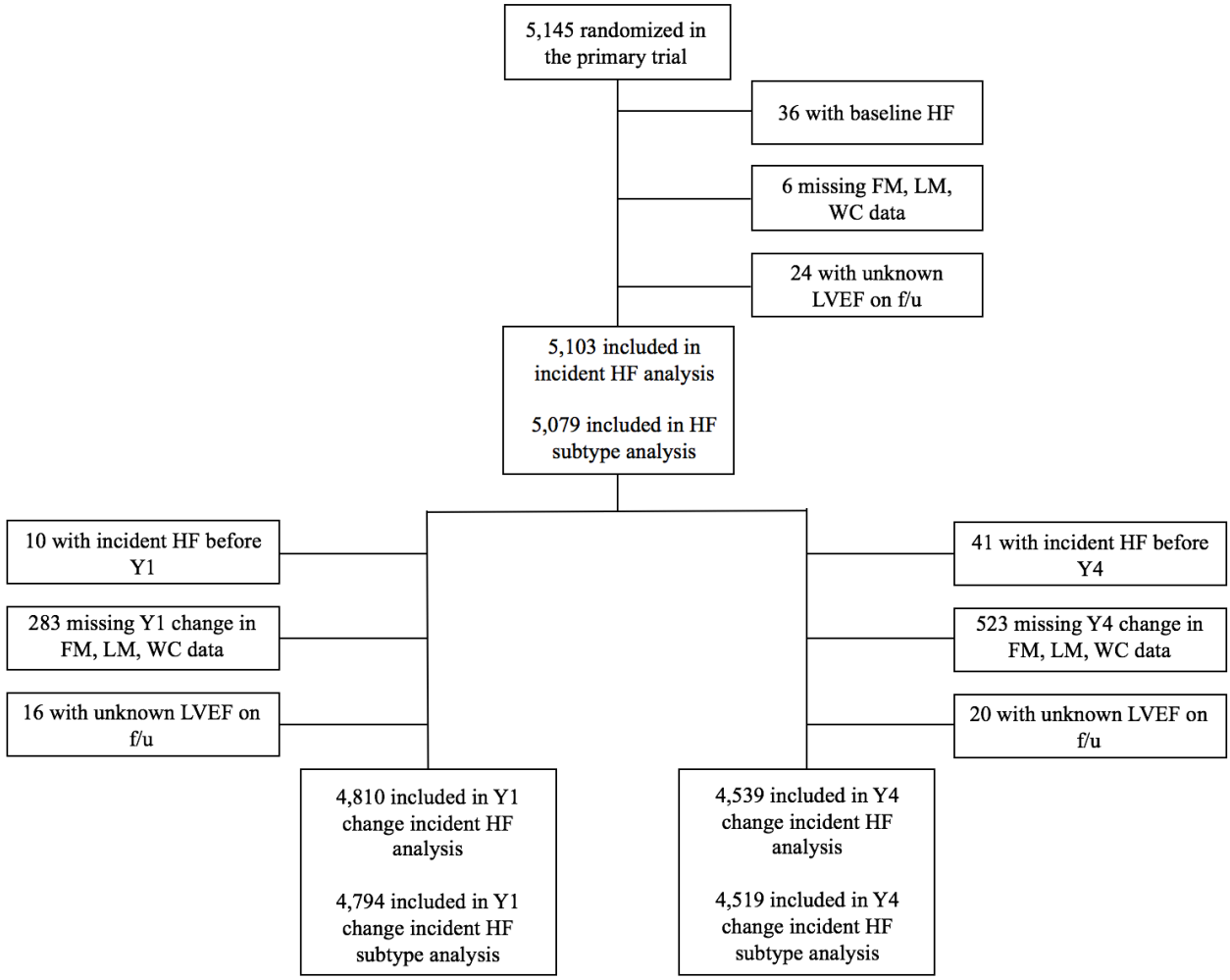
			Model 1		Model 2	
	Person-years	**Event rate per 1,000 person years**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Per 10% decrease in predicted fat mass from baseline to 4-year follow-up						
Overall HF	54,590	3.28	0.73 (0.64, 0.84)	<0.001	0.77 (0.65, 0.91)	0.002
HFpEF	54,478	1.63	0.68 (0.56, 0.81)	<0.001	0.78 (0.60, 0.998)	0.048
HFrEF	54,478	1.40	0.81 (0.66, 0.99)	0.04	0.77 (0.61, 0.97)	0.03
Per 10% decrease in predicted lean mass from baseline to 4-year follow-up						
Overall HF	54,590	3.28	0.65 (0.50, 0.83)	<0.001	0.93 (0.66, 1.31)	0.67
HFpEF	54,478	1.63	0.49 (0.35, 0.69)	<0.001	0.69 (0.42, 1.12)	0.14
HFrEF	54,478	1.40	0.93 (0.62, 1.39)	0.72	1.32 (0.81, 2.14)	0.26
Per 10% decrease in waist circumference from baseline to 4-year follow-up						
Overall HF	54,710	3.31	0.67 (0.56, 0.81)	<0.001	0.68 (0.56, 0.83)	<0.001
HFpEF	54,598	1.67	0.61 (0.46, 0.80)	<0.001	0.61 (0.46, 0.82)	<0.001
HFrEF	54,598	1.39	0.75 (0.56, 1.02)	0.07	0.77 (0.56, 1.06)	0.11

Multivariable adjusted Cox proportional hazard models were constructed for each HF outcome and body composition exposure variable with sequential adjustment for potential confounders

Model 1 included age, sex, race/ethnicity, education, income, treatment group, baseline CRF, history of hypertension, systolic BP, smoking status, alcohol use status, estimated GFR, diabetes duration, insulin use, HbA1c, history of CVD
Model 2 included Model 1 covariates plus year 4 percent change in predicted fat mass (except for WC model), year 4 percent change in predicted lean mass (except for WC model), year 4 percent change in HbA1c, year 4 percent change in systolic BP

Abbreviations: BP = blood pressure; CI = confidence interval; CRF = cardiorespiratory fitness; CVD = cardiovascular disease; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; HR = hazard ratio; WC = waist circumference

Supplemental Figure I. CONSORT flow diagram of study participants



Abbreviations: f/u = follow-up; FM = fat mass; HF = heart failure; LM = lean mass; LVEF = left ventricular ejection fraction; WC = waist circumference; Y = year

Supplemental Figure II. Bland-Altman plots of predicted versus measured fat mass (A, C) and lean mass (B, D) at years 1 (n=1,279) and 4 (n=1,166)

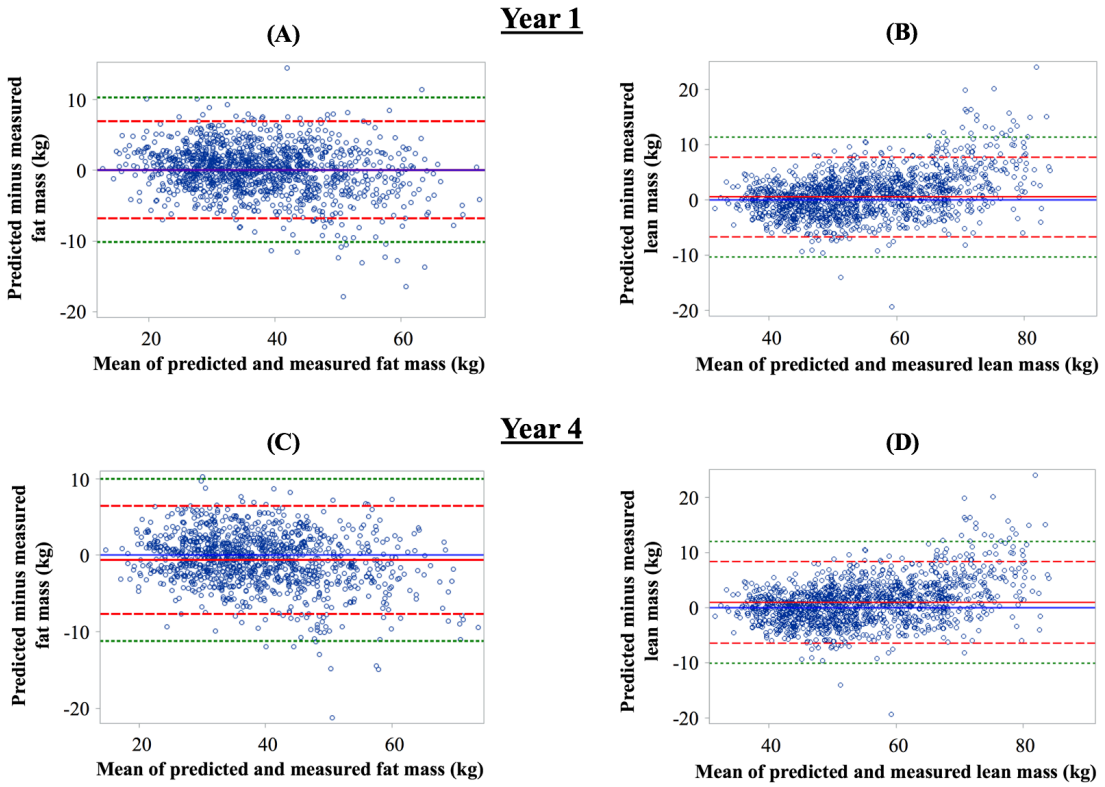
Solid red line is the mean of difference (dashed red line is +/- 2 standard deviations and dashed green line is +/- 3 standard deviations).

For year 1 predicted and measured fat mass, the bias (95% limits of agreement) was 0.06 (-0.13 to 0.24) kg and R^2 = 0.91.

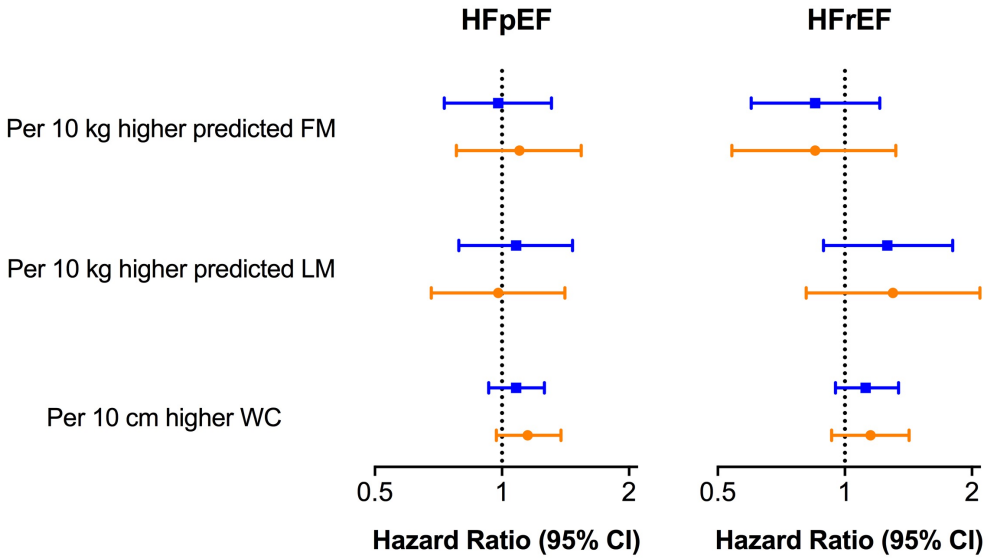
For year 1 predicted and measured lean mass, the bias (95% limits of agreement) was 0.53 (0.33 to 0.73) kg and R^2 = 0.92.

For year 4 predicted and measured fat mass, the bias (95% limits of agreement) was -0.60 (-0.80 to -0.39) kg and R^2 = 0.89.

For year 4 predicted and measured lean mass, the bias (95% limits of agreement) was 0.94 (0.73 to 1.15) kg and R^2 = 0.91.



Supplemental Figure III. Multivariable adjusted associations of baseline body composition measures with risk of HFpEF and HFrEF among all study participants (blue/squares) and those with no prior history of cardiovascular disease (orange/circles)

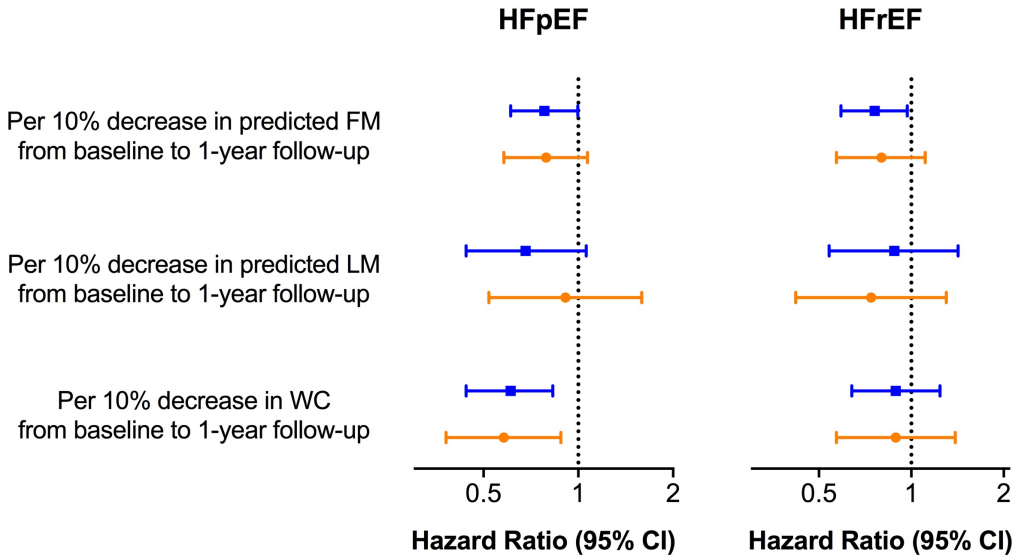


Hazard ratio (95% CI) for all study participants are shown in blue/squares. Hazard ratio (95% CI) for study participants with no prior history of cardiovascular disease are shown in orange/circles.

Multivariable adjusted Cox proportional hazard models were constructed for each HF outcome and body composition exposure variable with adjustment for the following potential confounders: Age, sex, race/ethnicity, education, income, treatment group, baseline CRF, history of hypertension, systolic BP, smoking status, alcohol use status, estimated GFR, diabetes duration, insulin use, HbA1c, history of CVD (only in the analysis including all study participants), predicted fat mass (except for WC model), predicted lean mass (except for WC model)

Abbreviations: BP = blood pressure; CI = confidence interval; CRF = cardiorespiratory fitness; CVD = cardiovascular disease; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; HR = hazard ratio; WC = waist circumference

Supplemental Figure IV. Multivariable adjusted associations of changes in body composition measures from baseline to 1-year follow-up with risk of HFpEF and HFrEF among all study participants (blue/squares) and those with no prior history of cardiovascular disease (orange/circles)



Hazard ratio (95% CI) for all study participants are shown in blue/squares. Hazard ratio (95% CI) for study participants with no prior history of cardiovascular disease are shown in orange/circles.

Multivariable adjusted Cox proportional hazard models were constructed for each HF outcome and body composition exposure variable with adjustment for the following potential confounders: Age, sex, race/ethnicity, education, income, treatment group, baseline CRF, history of hypertension, systolic BP, smoking status, alcohol use status, estimated GFR, diabetes duration, insulin use, HbA1c, history of CVD (only in the analysis including all study participants), year 1 percent change in predicted fat mass (except for WC model), year 1 percent change in predicted lean mass (except for WC model), year 1 percent change in HbA1c, year 1 percent change in systolic BP

Abbreviations: BP = blood pressure; CI = confidence interval; CRF = cardiorespiratory fitness; CVD = cardiovascular disease; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; HR = hazard ratio; WC = waist circumference

Online Appendix: Look AHEAD Research Group at End of Continuation

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