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Effect of Improved Fitness beyond Weight Loss on Cardiovascular Risk Factors in Individuals with Type 2 Diabetes in the Look AHEAD Study

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Abstract

Background—Because lifestyle-induced improvements in cardiovascular risk factors vary substantially across individuals with type 2 diabetes, we investigated the extent to which increases in fitness explain cardiovascular risk factor improvements independent of weight loss in a lifestyle intervention.

Methods—We studied 1-year changes in Look AHEAD, a randomized trial comparing an intensive lifestyle intervention (ILI) to a diabetes support and education control group (DSE) in adults with type 2 diabetes. Assessments included weight, fitness, blood pressure (BP), glucose, HbA1c, and lipids. We evaluated the effects of changes in weight and fitness on changes in cardiovascular risk factors by study arm, using R^2 from multiple linear regression.

Results—Analyses included participants with fitness data at baseline and 1-year ($n=4,408$; 41% male, 36% non-White, mean age 58.7 ± 6.8 years). Weight change alone improved R^2 for explaining changes in risk factors up to 8.2% in ILI and 1.7% in DSE. Fitness change alone improved R^2 up to 3.9% in ILI and 0.8% in DSE. After adjusting for weight change, fitness was

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DISCLOSURES

None

independently associated ($p < 0.05$) with improvements in R^2 for glucose (+0.7%), HbA1c (+1.1%), HDL cholesterol (+0.4%) and triglycerides (+0.2%) in ILI and DBP (+0.3%), glucose (+0.3%), HbA1c (+0.4%), and triglycerides (+0.1%) in DSE. Taken together, weight and fitness changes explained from 0.1–9.3% of the variability in cardiovascular risk factor changes.

Conclusion—Increased fitness explained statistically significant but small improvements in several cardiovascular risk factors beyond weight loss. Further research identifying other factors that explain cardiovascular risk factor change is needed.

Keywords

cardiovascular risk factor; lifestyle intervention; fitness; obesity

Individuals with type 2 diabetes (T2DM) are at increased risk for cardiovascular disease, and weight loss is known to improve cardiovascular risk factors including hypertension, glycemia, and hyperlipidemia. (1) Yet, risk factor improvement with weight loss varies considerably across individuals. For example, among participants with T2DM in the lifestyle intervention of the Look AHEAD trial with an average 1-year weight loss of 8.6%, HbA1c decreased by a mean of $-0.6\% \pm 1.5\%$ but ranged from -5.2% to $+5.6\%$. (2) Identifying determinants other than weight loss that could explain variability in individual response could be valuable for designing cost-effective lifestyle interventions that maximize cardiovascular risk reduction. Increasing fitness through an active lifestyle may contribute to changes in these risk factors independently of weight loss, (3, 4) and thus may help to explain differences in lifestyle-induced cardiovascular risk factor change across individuals with similar weight loss. However, it is unclear whether changes in fitness explain a large or small amount of variability in cardiovascular risk factor change after accounting for changes in weight.

We sought to determine if and how much of the variability in cardiovascular risk factor change, independent of weight change, could be explained by changes in cardiorespiratory fitness during the first year of the Look AHEAD, a randomized trial comparing an intensive lifestyle intervention (ILI) group to a diabetes support and education (DSE) control group. We investigated this aim separately in the ILI and the DSE control group to understand whether an independent effect of fitness change differed in the presence of greater (ILI) or lesser average (DSE) weight loss. A secondary objective was to ascertain the overall amount of variability in cardiovascular risk factor change that is explained by changes in weight and fitness, taken together.

RESEARCH DESIGN AND METHODS

Look AHEAD is a multi-center clinical trial investigating the long-term effects of an ILI on cardiovascular disease endpoints in overweight or obese adults with T2DM. Previously reported details of the study (5) are summarized below.

Participants

Look AHEAD recruited adults aged 45–76 years with BMI $\geq 25 \text{ kg/m}^2$ ($\geq 27 \text{ kg/m}^2$ if taking insulin), HbA1c $< 11\%$, systolic/diastolic BP (SBP/DBP) $< 160/100 \text{ mmHg}$, and triglycerides

<600 mg/dL. Participants also had to pass a maximal graded exercise test (GXT) by achieving 4 METS and reaching 85% of age-predicted maximal heart rate ($220 - \text{age}$) or an 18 on the Borg Rate of Perceived Exertion (RPE) scale for participants taking a β -blocker. (6) All participants gave informed written consent approved by a local Institutional Review Board before screening.

Interventions

The ILI's goal was to decrease weight by at least 7% at 6 months through diet, physical activity, and behavior modification. Participants had 3 group and 1 individual session during months 1–6, and 2 group and 1 individual session during months 7–12. Caloric intake reduction was encouraged through various methods, e.g. portion control and liquid meal replacements. The physical activity component of the ILI was progressive and home-based, and encouraged participants to build up to 175 minutes/week of moderate or vigorous physical activity. DSE participants were offered 3 group sessions, distinct from the ILI, which focused generally on diet, physical activity, and social support during the first year with no individual counseling. Further details of both programs are reported elsewhere. (7)

Assessments

Baseline and 1-year assessments were performed by blinded study staff. Weight (digital scale) and height (stadiometer) were measured in duplicate.

BP was measured in duplicate using an automated device after 5 minutes of quiet sitting. Participants were required to fast for 12 hours prior to the collection of blood specimen. Frozen serum was shipped to a Central Biochemistry Laboratory (Northwest Lipid Research Laboratories, University of Washington, Seattle, WA). Glucose was measured enzymatically on a Hitachi 917 autoanalyzer using hexokinase and glucose-6-phosphatase dehydrogenase. HbA1c was measured by a dedicated ion exchange high-performance liquid chromatography instrument (Biorad Variant 11). Total cholesterol and triglycerides were measured enzymatically by standard methods. HDL cholesterol was analyzed by treating whole plasma with dextran sulfate minus Mg^{2+} to precipitate all of the apolipoprotein B-containing lipoproteins. LDL cholesterol was estimated using the Friedewald equation. (8) Participants were asked to bring in all medications to assessment visits and these were recorded.

Baseline cardiorespiratory fitness was measured during screening by a maximal GXT. Participants chose a comfortable walking speed (2.4–6.4 mph) on a treadmill. The grade began at 0% and was increased by 1.0% each minute until volitional fatigue or achieving the American College of Sports Medicine criteria for test termination. (9) A test was considered valid if a participant reached 85% of his or her age-predicted maximum heart rate (if not taking a β -blocker) or a rate of perceived exertion (RPE) of at least 18 (if taking a β -blocker). At 1 year, participants performed a submaximal GXT using the walking speed from the baseline test. The 1-year test was terminated when the participant reached 80% of age-predicted maximal heart rate for participants not taking a β -blocker at either test or an RPE of 16. Change in fitness was computed as the difference in estimated metabolic equivalents (METS) calculated based on the specific workload (9) between points during the baseline test when >80% of maximal heart rate was attained and termination of the 1-year

test. For participants taking β -blockers at either time point, change in fitness was computed as the difference in METS at an RPE of 16.

Statistical Analysis

All analyses were conducted using SAS version 9.2 (Cary, North Carolina). Type 1 error level was set at 0.05 and all variables were checked for normality. Of 5,145 randomized participants, we included 4,408 (86%) participants with weight and fitness assessments at baseline and 1-year. We conducted analyses separately by study arm to examine relationships in an intervention and control setting. We also repeated analyses stratified by gender to examine the possibility of effect modification.

Multiple linear regression models were used to investigate associations and improvements in model fit for changes in weight and fitness with changes in cardiovascular risk factors. To do this, we report R^2 from a baseline model with change in cardiovascular risk factor as the outcome and covariates including demographics (age, race/ethnicity, gender), change in the number of outcome-related medications, and baseline value of the cardiovascular risk factor. Next, changes in weight and fitness (METS) were added to the model one at a time to understand how changes in each of these factors explained the remaining variability. Finally, a model with all covariates evaluated independent contributions of changes in weight and fitness.

Our primary objective evaluated whether and to what extent increasing fitness could explain changes in cardiovascular risk factors independently of weight loss. To evaluate our secondary objective, we calculated the change in R^2 when change in weight and fitness were added together.

RESULTS

The study population included 1803 (41%) men, 1578 (36%) non-Whites, and had an average age of 58.7 years (SD=6.8). Almost a fourth of participants (n=1027, 23.3%) were taking beta-blockers at either or both baseline and 1 year. Changes in weight, fitness, and cardiovascular risk factors (Table 1) were similar to those previously reported in the full study population. (2, 10) The primary reason for exclusion from the current analysis was missing (n=393) or invalid (n=217) fitness data at 1 year. At baseline, participants excluded vs. included in the current analysis had slightly though significantly higher weight (102.6 kg vs. 100.4 kg, $p=0.003$), resting SBP (130 mmHg vs. 129 mmHg, $p=0.01$), glucose (157 mg/dL vs. 152 mg/dL, $p=0.007$), HbA1c (7.4 vs. 7.3, $p=0.02$), and number of diabetes (1.64 vs. 1.56, $p=0.05$) and hypertension (1.55 vs. 1.35, $p<0.001$) medications.

Individual and Independent Effects of Changes in Weight and Fitness on Cardiovascular Risk Factors

Weight change taken alone (Tables 2 and 3) was significantly associated with changes in each cardiovascular risk factor except for LDL cholesterol in both the ILI and DSE groups. Weight change explained a median of 3.5% and a maximum of 8.2% (HbA1c) of variability in the ILI group, while weight change explained a median of 1.0% and a maximum of 1.7% (HbA1c) in the DSE group.

Fitness change taken individually (Tables 2 and 3) was also significantly associated with changes in each cardiovascular risk factor except for LDL cholesterol in both groups. In the ILI group, change in fitness explained less variability than weight change (median of 1.3%, maximum of 3.9% for HbA1c). Similarly in the DSE group, change in fitness explained less variability than weight change and the effect was smaller than observed in the ILI, with a median of 0.4% and up to 0.8% (HbA1c).

Including all variables, weight change continued to be associated with changes in SBP, DBP, fasting glucose, HbA1c, HDL cholesterol and triglycerides, though the associations were no longer significant ($p=0.07$) for changes in DBP in the DSE group.

With respect to our primary objective, fitness remained an independent predictor of changes in fasting glucose, HbA1c, HDL cholesterol (ILI only) and triglycerides. Fitness was not independently associated with changes in SBP in either group, though it remained a significant predictor of DBP changes in the DSE group. The amount of variability (change in R^2) explained by changes in fitness after adjustment for change in weight was generally small (range 0–1.1%), but was greatest for 1-year changes in HbA1c and fasting glucose and was higher in ILI compared to DSE (Table 4).

When we repeated these analyses stratifying by gender, results were similar (Appendix Table).

Overall Variability Explained by Changes in Weight and Fitness

The Figure displays the increase in R^2 from the basic model beside each bar, depicting the individual and overall explanatory power of weight and fitness changes beyond the basic model. Generally, weight change explains more variability than fitness change and associations were stronger in the ILI compared to the DSE group. Additionally, fully adjusted models are only able to account for 7.1% to 50.5% of the total variability in cardiovascular risk factor change.

DISCUSSION

We found that, though weight loss was the stronger predictor of cardiovascular risk factor improvement in the ILI and DSE groups, improvements in fitness explained additional variability in cardiovascular risk factor change. Increasing fitness had a small but statistically significant beneficial effect beyond weight change on fasting glucose, HbA1c, HDL cholesterol (ILI group only), triglycerides, and DBP (DSE group only). Perhaps our most interesting finding is that changes in weight and fitness taken together only explained from 0.1% to 9.3% of the total variability in 1-year cardiovascular risk factor change. Our findings support current recommendations for individuals with T2DM to increase physical activity in addition to decreasing body weight for the greatest reduction in cardiovascular risk factors, though the independent effect may be small.

We emphasize that our primary analysis evaluates the impact of increased fitness independent of weight loss. Exercise training modestly reduces weight, though not consistently in people with T2DM, (11) and improves weight loss outcomes when a

component of a weight loss intervention. (12) Thus, the effect of increased fitness on cardiovascular risk factors is likely greater than we have presented herein since the effect may be partially mediated by weight loss. Spearman rank correlations between change in weight and fitness (ILI $\rho = -0.39$; control $\rho = -0.21$) have been previously reported in this cohort (10) and are not nominal. This correlation does not necessarily imply cause and effect, but is likely due, at least in part, to the clustering of behaviors in participants who are successful in a lifestyle intervention. Thus, an independent association between changes in fitness and cardiovascular risk factors should be interpreted as an effect through pathways other than weight loss.

Increased fitness had an independent effect on improvements in glycemia, HDL cholesterol (ILI only), and triglycerides independent of weight change. Our results agree with several meta-analyses (11, 13, 14) showing that exercise or increased fitness improve HbA1c in adults with T2DM, even after adjustment for BMI changes. (13) Our findings are consistent with a mechanism where increased physical activity improves insulin action and glucose control through improved muscular insulin sensitivity and glucose uptake, (15) which can occur independently of weight loss. Though two meta-analyses differed with respect to an effect of exercise in triglycerides in T2DM populations and neither found an effect on HDL cholesterol, (11, 16) our findings agree with the established benefit of exercise training on lipid profile in normoglycemic individuals. (17) Exercise training has been shown to improve the lipid profile in the absence of weight loss (17) and an independent effect is further evidenced by favorable changes in triglycerides following a single bout of exercise. (18)

The DSE group did not participate in an intensive weight loss intervention and had less weight and fitness change on average in the first year, which may explain why changes in weight and fitness explained less variability in cardiovascular risk factor change in this group. A notable contrast between results in the ILI and DSE groups was that fitness change was a better predictor of change in DBP than weight loss and was nearly independently associated with change in SBP. This finding might indicate that in a usual care setting with little weight loss, increased fitness might be important for improving BP. Exercise training is known to decrease both SBP and DBP in hypertensive and normotensive adults, (19) though sparse and inconsistent data are available in populations with T2DM. (11, 20, 21) Fitness and physical activity are thought to improve BP through decreased total peripheral resistance from vascular adaptations, neural changes, and possibly gene-environment interactions, (19) which could occur independently of weight loss.

Concerning our secondary objective, we found that increased fitness and weight loss together explained a small portion of individual differences in cardiovascular risk factor change. Further, in our full models, 49%–93% of variability in risk factor change remained unexplained. Aside from a proportion attributable to measurement error, other factors that may be important for explaining cardiovascular risk factor change beyond weight loss might include changes in diet composition, (22, 23) psychosocial factors, (24, 25) or underlying genetic factors. (26) Interestingly, changes in waist circumference did not predict changes in cardiovascular risk factors independently from changes in fitness and weight, and so we did not include it in our analyses (data not shown). More proximal weight changes – for

example whether participants who lost weight were regaining, stable, or continuing to lose weight at the 1-year assessment – may also explain remaining variability. These deserve evaluation in future investigations.

Our results are strengthened by the large sample size, excellent retention of the Look AHEAD Study, and the comprehensive assessment of cardiovascular risk factors and fitness from a GXT. However, measurement error or the small changes observed in the DSE group, on average, could have limited our ability to explain variability and observe significant associations. Also, compared to participants excluded from the analysis, included participants were slightly but statistically significantly healthier with respect to several cardiovascular risk factors and this could have attenuated the strength of relationships we observed. We only had information on the number of medications and not changes in dosage, which may have explained additional variability. We only considered traditional cardiovascular risk factors as outcomes and it is possible that changes in fitness could have had a greater independent effect on other measures of cardiovascular risk (e.g. endothelial function (27)). Lastly, our study population consisted of participants with T2DM meeting eligibility criteria for Look AHEAD, which could limit generalizability to a broader population of adults with cardiovascular risk factors.

Conclusion

Our findings identify a small, independent contribution of increasing fitness beyond losing weight for cardiovascular risk reduction in adults with T2DM enrolled in a lifestyle intervention, but moreover highlight the need for further investigation of additional factors that influence cardiovascular risk reduction to improve the effectiveness of clinical interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure.

Variability (R^2) in 1-year Change in Cardiovascular Risk Factors in the Intensive Lifestyle Intervention Group (A) and the Diabetes Support and Education Group (B) Explained by Basic Model (age, race, gender, medication, and baseline value) + Weight Change (Wt), Basic Model + Submaximal Fitness Change (Fit), and Basic Model + Weight Change + Fitness Change (Basic + WC + Fit). Displayed % change is the amount of variability explained by (dark gray) and beyond (light gray and %) the basic model.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein; TG, triglycerides.

Table 1

Baseline, 1-year, and changes in weight, fitness, and cardiovascular risk factors among intensive lifestyle intervention (ILI) and diabetes support and education (DSE) participants in the Look AHEAD Study

		ILI (n=2,256)	DSE (n=2,152)	<i>p</i> -value comparing change
Weight (kg)	Baseline	100.3 (19.5)	100.5 (18.5)	
	1-year	91.4 (18.6)	99.7 (18.8)	
	Change	-8.9 (7.5)	-0.8 (4.9)	<0.001
Submaximal fitness (METS) *	Baseline	5.2 (1.5)	5.1 (1.6)	
	1-year	6.1 (2.0)	5.3 (1.6)	
	Change	1.1 (1.4)	0.2 (1.1)	<0.001
Systolic blood pressure (mmHg)	Baseline	128 (17)	129 (17)	
	1-year	121 (17)	126 (17)	
	Change	-7 (17)	-3 (16)	<0.001
Diastolic blood pressure (mmHg)	Baseline	70 (10)	70 (10)	
	1-year	67 (9)	69 (10)	
	Change	-3 (8)	-1 (9)	<0.001
Fasting glucose (mg/dL)	Baseline	152 (44)	153 (46)	
	1-year	130 (40)	147 (44)	
	Change	-22 (45)	-6 (46)	<0.001
HbA1c (%)	Baseline	7.2 (1.2)	7.3 (1.2)	
	1-year	6.6 (1.1)	7.2 (1.1)	
	Change	-0.7 (1.0)	-0.1 (1.0)	<0.001
LDL cholesterol (mg/dL)	Baseline	112 (32)	112 (32)	
	1-year	107 (32)	106 (32)	
	Change	-5 (28)	-6 (29)	0.444
HDL cholesterol (mg/dL)	Baseline	44 (12)	43 (12)	
	1-year	47 (13)	45 (12)	
	Change	3 (7)	2 (7)	<0.001
Triglycerides (mg/dL)	Baseline	182 (116)	180 (118)	
	1-year	151 (91)	165 (94)	
	Change	-31 (100)	-15 (89)	<0.001
Blood pressure medications (number)	Baseline	1.4 (1.2)	1.3 (1.2)	
	1-year	1.4 (1.1)	1.4 (1.2)	
	Change	0.0 (0.6)	0.1 (0.7)	<0.001
Diabetes Medications (number)	Baseline	1.6 (1.0)	1.6 (1.0)	
	1-year	1.3 (1.0)	1.7 (1.0)	

		ILI (n=2,256)	DSE (n=2,152)	<i>p-value</i> comparing change
	Change	−0.3 (0.7)	0.1 (0.7)	<0.001
Lipid Medications (number)	Baseline	0.5 (0.6)	0.5 (0.6)	
	1-year	0.6 (0.6)	0.6 (0.6)	
	Change	0.04 (0.40)	0.11 (0.46)	<0.001

Data presented as mean (SD)

* Submaximal metabolic equivalents (METs) from a graded exercise test at 80% of predicted maximal heart rate or RPE of 16 for participants on β -blockers

Table 2

Association of 1-year changes in weight and submaximal fitness (fit) with 1-year changes in cardiovascular risk factors in Intensive Lifestyle Intervention participants (n=2,256) of the Look AHEAD Study

		Basic model*	Basic model + weight change	Basic model + fit change	Basic model + weight & fit change
Systolic Blood Pressure (mmHg)	β weight change (kg)	-	0.37 (p<0.001)	-	0.36 (p<0.001)
	β fitness change (METs)	-	-	-0.95 (p<0.001)	-0.20 (p=0.43)
	R ²	26.6%	29.1%	27.1%	29.1%
Diastolic Blood Pressure (mmHg)	β weight change (kg)	-	0.17 (p<0.001)	-	0.16 (p<0.001)
	β fitness change (METs)	-	-	-0.46 (p<0.001)	-0.12 (p=0.37)
	R ²	24.2%	26.4%	24.7%	26.4%
Fasting Glucose (mg/dL)	β weight change (kg)	-	1.39 (p<0.001)	-	1.19 (p<0.001)
	β fitness change (METs)	-	-	-5.27 (p<0.001)	-3.02 (p<0.001)
	R ²	36.5%	41.2%	38.9%	41.9%
HbA1c (%)	β weight change (kg)	-	0.04 (p<0.001)	-	0.04 (p<0.001)
	β fitness change (METs)	-	-	-0.15 (p<0.001)	-0.08 (p<0.001)
	R ²	28.7%	36.9%	32.6%	38.0%
LDL cholesterol (mg/dL)	β weight change (kg)	-	0.10 (p=0.18)	-	0.06 (p=0.46)
	β fitness change (METs)	-	-	-0.67 (p=0.09)	-0.55 (p=0.22)
	R ²	28.8%	28.8%	28.9%	28.9%
HDL cholesterol (mg/dL)	β weight change (kg)	-	-0.19 (p<0.001)	-	-0.16 (p<0.001)
	β fitness change (METs)	-	-	0.70 (p<0.001)	0.36 (p=0.005)
	R ²	3.2%	6.7%	4.8%	7.1%
Triglycerides (mg/dL)	β weight change (kg)	-	3.00 (p<0.001)	-	2.77 (p<0.001)
	β fitness change (METs)	-	-	-9.02 (p<0.001)	-3.25 (p=0.01)
	R ²	45.8%	50.3%	47.1%	50.5%

Data are presented as β coefficients (p-value).

* Basic model includes adjustment for age, race, gender, change in medication, and baseline outcome value

Table 3

Association of 1-year changes in weight and submaximal fitness (fit) with 1-year changes in cardiovascular risk factors in Diabetes Support and Education participants (n=2,152) of the Look AHEAD Study

		Basic model*	Basic model + weight change	Basic model + fit change	Basic model + weight & fit change
Systolic Blood Pressure (mmHg)	β weight change (kg)	-	0.39 (p<0.001)	-	0.36 (p<0.001)
	β fitness change (METs)	-	-	-0.99 (p=0.001)	-0.60 (p=0.05)
	R ²	25.3%	26.6%	25.7%	26.7%
Diastolic Blood Pressure (mmHg)	β weight change (kg)	-	0.08 (p=0.01)	-	0.06 (p=0.07)
	β fitness change (METs)	-	-	-0.51 (p=0.001)	-0.44 (p=0.007)
	R ²	24.4%	24.6%	24.8%	24.9%
Fasting Glucose (mg/dL)	β weight change (kg)	-	0.94 (p<0.001)	-	0.83 (p<0.001)
	β fitness change (METs)	-	-	3.21 (p<0.001)	-2.39 (p=0.005)
	R ²	29.6%	30.6%	30.1%	30.9%
HbA1c (%)	β weight change (kg)	-	0.03 (p<0.001)	-	0.02 (p<0.001)
	β fitness change (METs)	-	-	-0.09 (p<0.001)	-0.06 (p=0.001)
	R ²	19.5%	21.2%	20.3%	21.6%
LDL cholesterol (mg/dL)	β weight change (kg)	-	0.08 (p=0.46)	-	0.12 (p=0.32)
	β fitness change (METs)	-	-	0.55 (p=0.29)	0.68 (p=0.21)
	R ²	31.0%	31.0%	31.0%	31.1%
HDL cholesterol (mg/dL)	β weight change (kg)	-	-0.11 (p<0.001)	-	-0.10 (p<0.001)
	β fitness change (METs)	-	-	0.32 (p=0.02)	0.21 (p=0.13)
	R ²	6.3%	7.0%	6.6%	7.1%
Triglycerides (mg/dL)	β weight change (kg)	-	1.90 (p<0.001)	-	1.73 (p<0.001)
	β fitness change (METs)	-	-	-5.24 (p<0.001)	-3.40 (p=0.02)
	R ²	39.5%	40.6%	39.9%	40.7%

Data are presented as β coefficients (p-value).

* Basic model includes adjustment for age, race, gender, change in medication, and baseline outcome value

Table 4

Amount of remaining variability (R^2) in 1-year cardiovascular risk factor changes explained by changes in fitness in Intensive Lifestyle Intervention (ILI) and Diabetes Support and Education (DSE) participants of the Look AHEAD Study

	ILI (n=2,256)		DSE (n=2,152)	
	in R^2 *	p-value	in R^2 *	p-value
Systolic blood pressure	0%	0.43	0.1%	0.05
Diastolic blood pressure	0%	0.37	0.3%	0.007
Fasting glucose	0.7%	<0.001	0.3%	0.005
HbA1c	1.1%	<0.001	0.4%	0.001
LDL cholesterol	0%	0.22	0.1%	0.21
HDL cholesterol	0.4%	0.005	0.1%	0.13
Triglycerides	0.2%	0.01	0.1%	0.02

* The change in R^2 when adding fitness to a model already adjusting for age, race, gender, change in medication, baseline outcome value, and change in weight

Independent associations of 1-year changes in weight and submaximal fitness (fit) with 1-year changes in cardiovascular risk factors by gender and group in the Look AHEAD Study

Appendix Table

	ILI Men (n=922)	ILI Women (n=1,334)	DSE Men (n=881)	DSE Women (n=1,271)
Systolic Blood Pressure (mmHg)				
β weight change (kg)	0.37 (p<0.001)	0.36 (p<0.001)	0.29 (p=0.003)	0.41 (p<0.001)
β fitness change (METs)	-0.56 (p=0.11)	0.12 (p=0.73)	-0.52 (p=0.21)	-0.65 (p=0.14)
R ²	31.4%	27.9%	26.3%	28.4%
Diastolic Blood Pressure (mmHg)				
β weight change (kg)	0.19 (p<0.001)	0.14 (p<0.001)	0.06 (p=0.26)	0.07 (p=0.14)
β fitness change (METs)	-0.11 (p=0.57)	-0.12 (p=0.50)	-0.46 (p=0.05)	-0.45 (p=0.05)
R ²	25.7%	26.4%	24.8%	26.2%
Fasting Glucose (mg/dL)				
β weight change (kg)	1.08 (p<0.001)	1.30 (p<0.001)	1.07 (p<0.001)	0.72 (p=0.003)
β fitness change (METs)	-2.42 (p=0.008)	-3.60 (p<0.001)	-2.98 (p=0.01)	-2.08 (p=0.09)
R ²	43.9%	40.8%	36.7%	26.9%
HbA1c (%)				
β weight change (kg)	0.04 (p<0.001)	0.04 (p<0.001)	0.04 (p<0.001)	0.02 (p=0.006)
β fitness change (METs)	-0.09 (p<0.001)	-0.08 (p<0.001)	-0.04 (p=0.09)	-0.09 (p=0.002)
R ²	42.9%	34.7%	28.7%	18.0%
LDL cholesterol (mg/dL)				
β weight change (kg)	0.20 (p=0.05)	-0.07 (p=0.58)	0.19 (p=0.28)	0.03 (p=0.86)
β fitness change (METs)	-0.66 (p=0.24)	-0.44 (p=0.49)	1.14 (p=0.12)	0.12 (p=0.88)
R ²	30.6%	28.8%	28.3%	34.0%
HDL cholesterol (mg/dL)				
β weight change (kg)	-0.19 (p<0.001)	-0.13 (p<0.001)	-0.13 (p<0.001)	-0.06 (p=0.12)
β fitness change (METs)	0.22 (p=0.18)	0.50 (p=0.009)	0.29 (p=0.11)	0.10 (p=0.63)
R ²	10.2%	5.5%	9.5%	6.9%
Triglycerides (mg/dL)				
β weight change (kg)	3.04 (p<0.001)	2.54 (p<0.001)	2.33 (p<0.001)	1.37 (p<0.001)
β fitness change (METs)	-2.90 (p=0.14)	-3.61 (p=0.04)	-4.15 (p=0.09)	-2.37 (p=0.20)
R ²	50.7%	50.2%	40.5%	42.4%

Data are presented as β coefficients (p-value). Coefficients are adjusted for age, race, gender, change in medication, baseline outcome value, change in weight, and change in fitness.