

## Effectiveness of Lifestyle Interventions for Individuals With Severe Obesity and Type 2 Diabetes

Results from the Look AHEAD trial

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**OBJECTIVE**—Rates of severe obesity (BMI  $\geq 40$  kg/m<sup>2</sup>) are on the rise, and effective treatment options are needed. We examined the effect of an intensive lifestyle intervention (ILI) on weight loss, cardiovascular disease (CVD) risk, and program adherence in participants with type 2 diabetes who were severely obese compared with overweight (BMI 25 to  $<30$  kg/m<sup>2</sup>), class I (BMI 30 to  $<35$  kg/m<sup>2</sup>), and class II (BMI 35 to  $<40$  kg/m<sup>2</sup>) obese participants.

**RESEARCH DESIGN AND METHODS**—Participants in the Action for Health in Diabetes (Look AHEAD) trial were randomly assigned to ILI or diabetes support and education (DSE). DSE participants received a less intense educational intervention, whereas ILI participants received an intensive behavioral treatment to increase physical activity (PA) and reduce caloric intake. This article focuses on the 2,503 ILI participants (age  $58.6 \pm 6.8$  years).

**RESULTS**—At 1 year, severely obese participants in the ILI group lost  $-9.04 \pm 7.6\%$  of initial body weight, which was significantly greater ( $P < 0.05$ ) than ILI participants who were overweight ( $-7.43 \pm 5.6\%$ ) and comparable to class I ( $-8.72 \pm 6.4\%$ ) and class II obese ( $-8.64 \pm 7.4\%$ ) participants. All BMI groups had comparable improvements in fitness, PA, LDL cholesterol, triglycerides, blood pressure, fasting glucose, and HbA<sub>1c</sub> at 1 year. ILI treatment session attendance was excellent and did not differ among weight categories (severe obese 80% vs. others 83%;  $P = 0.43$ ).

**CONCLUSIONS**—Severely obese participants in the ILI group had similar adherence, percentage of weight loss, and improvement in CVD risk compared with less obese participants. Behavioral weight loss programs should be considered an effective option for this population.

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Although the prevalence of overweight and mild obesity has begun to stabilize in recent years (1), rates of severe obesity (BMI  $\geq 40$  kg/m<sup>2</sup>) continue to rise (1,2). Recent estimates suggest that the prevalence of severe obesity

rose by 52% in 5 years (2). The extreme categories of obesity represent the fastest growing segment of the overweight population, posing a significant public health concern (2). Severe obesity is associated with a significantly higher prevalence of

comorbid conditions, including diabetes, and also results in higher mortality rates compared with overweight or moderate obesity (i.e., BMI  $<40$  kg/m<sup>2</sup>) (3). For these reasons, it is critical that effective treatment options for this population be identified and implemented.

In the past, severely obese individuals have been excluded from the majority of clinical weight loss trials because of upper BMI exclusionary criteria and/or other comorbid conditions (4). Moreover, despite a lack of empirical evidence, it was suggested that this population cannot be effectively treated with lifestyle interventions (5). Currently, bariatric surgery is the recommended treatment approach for individuals with severe obesity “when less invasive methods of weight loss have failed” (5). Although surgical procedures are an effective strategy for reducing body weight and improving cardiovascular disease (CVD) risk factors, particularly diabetes (6), they may not be an ideal treatment approach for a large percentage of severely obese individuals (7,8). In addition, surgery is limited in reach, with only  $\sim 1\%$  of the severely obese population undergoing surgical procedures each year (1,9). Thus, investigators have recently called for a reexamination of the effectiveness of lifestyle interventions for treating severe obesity (10).

A recent study by Goodpaster et al. (11) was the first to examine the effectiveness of an intensive lifestyle intervention on weight loss, abdominal fat, hepatic steatosis, and other CVD risk factors in a severely obese population. Study participants with a BMI  $>40$  kg/m<sup>2</sup> lost  $\sim 10\%$  of their initial body weight at 1 year and experienced favorable changes in CVD risk factors. In addition, severely obese participants lost significantly more weight than class II obese participants (BMI 35 to  $<40$  kg/m<sup>2</sup>); however, the sample size was small (class II:  $n = 17$ ; severely obese:  $n = 50$ ) and individuals with diabetes were excluded. Given that diabetes may make it more difficult for individuals to lose weight compared with individuals without diabetes (12), it is important to assess the

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effects of intensive lifestyle interventions in individuals with diabetes.

The current study used the 1-year results from the Action for Health in Diabetes (Look AHEAD) trial to compare initial weight losses, changes in CVD risk factors, and compliance to dietary and exercise recommendations between the severely obese (BMI  $\geq 40$  kg/m<sup>2</sup>) and overweight (25 to  $< 30$  kg/m<sup>2</sup>), class I obese (30 to  $< 35$  kg/m<sup>2</sup>), and class II obese (35 to  $< 40$  kg/m<sup>2</sup>) participants.

## RESEARCH DESIGN AND METHODS

**—**The Look AHEAD trial enrolled 5,145 participants from 16 centers across the U.S. Subject characteristics and inclusion/exclusion criteria were previously described (13). In short, participants had type 2 diabetes, were aged 45–76 years, had a BMI  $\geq 25$  kg/m<sup>2</sup> (or  $\geq 27$  kg/m<sup>2</sup> if taking insulin) and body weight  $\leq 400$  lb, HbA<sub>1c</sub>  $\leq 11\%$ , triglycerides  $< 600$  mg/dL, and systolic and diastolic blood pressure  $\leq 160$  and  $\leq 100$  mmHg, respectively. Participants completed a maximal graded exercise test, as previously described (13), to ensure that exercise could be tolerated. A 2-week behavioral run-in period was used to determine participants' adherence to recording their physical activity (PA) and food intake. All participants provided written informed consent, and study procedures were approved by each center's institutional review board.

## Treatment conditions

Participants were randomized to either an intensive lifestyle intervention (ILI) or a diabetes support and education (DSE) intervention. Participants randomized to the DSE group attended four meetings during year 1 and received general recommendations related to healthy eating and PA (13). Initial analyses revealed that the difference in weight loss between the ILI group and DSE group at 1 year, as previously reported (13), was similar across BMI categories; thus, all subsequent analyses focus solely on ILI participants and the comparison across BMI groups.

Details regarding the ILI used in the Look AHEAD trial have been published elsewhere (13,14). Briefly, this intervention was designed to induce an average 1-year weight loss of at least 7% across the 16 centers, whereas individual participants were given a goal of losing  $\geq 10\%$  of initial weight. Modeled after the Diabetes Prevention Program (15), participants were taught various behavioral strategies to modify their eating and exercise behaviors

to assist with weight loss. During the first 6 months, participants attended three weekly group sessions per month and one individual counseling session with a registered dietitian, behavioral psychologist, or exercise physiologist. During months 7–12, participants attended two group meetings and one individual session per month.

Participants in the ILI group were prescribed a calorie goal of 1,200–1,800 kcal/day, depending on initial body weight, and were instructed to consume  $< 30\%$  of calories as fat. To assist individuals in their weight loss efforts, meal replacements were provided free of charge and participants were instructed to replace two meals and one snack per day with a meal replacement product for the first 4 months and then one meal and one snack per day for months 5–12.

Participants were given a home-based exercise plan to gradually increase their PA to  $\geq 175$  min/week in the first 6 months. The goal of 175 min/week was chosen based on recent evidence that higher levels of exercise are related to better weight loss and maintenance (16). Any activity that was at least of a moderate intensity (e.g., brisk walking) and  $\geq 10$  min in duration could be counted toward the exercise goal. Participants were also given a pedometer to assist in motivating them to reach these goals.

The treatment program incorporated behavioral techniques to help participants achieve their diet and exercise goals, stressing daily self-monitoring of diet and PA. Goal-setting, stimulus control, and problem-solving were also important aspects of the ILI program. For participants struggling to meet their dietary, exercise, and weight loss goals, a "toolbox" strategy, consistent with that used in the Diabetes Prevention Program (15), was used. This "toolbox" consisted of advanced behavioral strategies such as motivational interviewing and problem-solving techniques, but also included the use of pharmacotherapy (orlistat) for participants who failed to meet their 6-month weight loss goal. Specific protocols outlining when to initiate and discontinue medication usage have been described elsewhere (14). Overall, 519 participants used orlistat before the end of the first year.

## Assessments

All assessments were conducted at baseline and 1 year. Weight, height, BMI, waist circumference, and blood pressure were assessed using standard procedures

previously described (13). Serum measures were analyzed by the Central Biochemistry Laboratory (Northwest Lipid Research Laboratories, University of Washington, Seattle, WA). Frozen specimens were shipped for the analysis of HbA<sub>1c</sub>, fasting serum glucose, total triglycerides, HDL, and LDL using methods described elsewhere (13). Use of insulin, lipid-lowering medications, and blood pressure medications was determined via standardized interviewer-administered questionnaires.

PA (expressed in kcal/week) was only assessed on a subsample of subjects (approximately half) using the Paffenbarger Physical Activity Questionnaire (17). Participants reported the number of city blocks walked, stair flights climbed, and the duration and frequency of sports and recreational activities performed during the past week, which was used to quantify activity-related energy expenditure.

Cardiorespiratory fitness was assessed using a maximal graded exercise treadmill test at baseline and a submaximal test at 1 year. The maximal exercise test at baseline was terminated at the point of volitional fatigue or when the American College of Sports Medicine (18) test termination criteria were observed. At 1 year, the submaximal exercise test was terminated when 80% of maximal heart rate was achieved or, for patients taking  $\beta$ -blockers, when a 16 on the rating of perceived exertion scale was attained. Cardiorespiratory fitness was defined as the estimated metabolic equivalent (MET) level, determined by the speed and grade of the treadmill (18), when 80% of maximal heart rate or a rating of perceived exertion of 16 was attained. Thus, the change in fitness was calculated as the difference in MET levels between baseline and 1 year (13).

## Behavioral adherence

Using procedures similar to those of Wadden et al. (14), adherence to the prescribed treatment regimen was assessed by attendance at treatment sessions and self-reported use of meal replacements (shakes and bars) from weekly diaries. If participants failed to turn in their weekly diary, they were asked to do so at a subsequent visit. If a diary was never submitted, a 0 was assumed for each missing variable.

## Statistical analysis

All statistical analyses were performed using an assumed type I error rate of 0.05. Baseline measures are presented as relative frequencies for discrete responses and

means and SDs for continuous responses. Frequency comparisons for discrete responses were performed using the Cochran-Mantel-Haenszel test for general association. Pairwise comparisons were performed by creating simultaneous Wald CIs of odds ratios in a logistic regression framework to conserve family-wise error rates. Comparisons of group means were performed using one-way ANOVA. Bonferroni method for controlling family-wise error rate was used for post hoc comparisons between BMI groups. If the initial ANOVA was not significant, no further pairwise comparisons were performed. Statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

**RESULTS**—The baseline characteristics of ILI study participants are presented in Table 1. Compared with participants with a BMI <40 kg/m<sup>2</sup>, the severely obese were younger and had lower PA and fitness, and a larger proportion were female.

Baseline values for CVD factors were similar between the severely obese and participants with a BMI <40 kg/m<sup>2</sup>, except for systolic blood pressure, which was significantly higher among individuals with severe obesity.

### Changes in body weight, fitness, PA, and CVD risk factors

Baseline to 1-year changes in body weight, fitness, PA, and CVD risk factors for ILI participants are displayed in Table 2. Presented below and in the tables are the unadjusted means and adjusted *P* values (controlling for age, sex, ethnicity, and baseline values and medication usage when appropriate). All analyses were repeated, excluding the very small number of individuals who underwent bariatric surgery during that year and also adjusting for and excluding orlistat users; the results were not altered.

**Body weight.** As shown in Table 2, the percentage of weight change achieved by ILI participants who were severely obese

was -9.04%, which was comparable to class I (-8.72%) and class II obese (-8.64%) and significantly greater than overweight participants (-7.43%; *P* < 0.05). The percentage of severely obese individuals achieving a ≥5% weight loss at 1 year was 67.0%, which was similar to overweight (66.3%), class I (70.2%), and class II (68%) obese participants (*P* = 0.45). However, the proportion of severely obese participants achieving a ≥10% weight loss at 1 year was 39.2%, which was similar to class I (41.4%) and class II (38.8%) participants but significantly greater than overweight (30.1%) participants (*P* < 0.05).

**Fitness and PA.** All BMI groups experienced similar improvements in absolute fitness and PA at year 1 (Table 2). However, since the severely obese had lower fitness and PA levels at baseline, their fitness (5.4 ± 1.6 METs) was significantly lower than that of overweight (6.6 ± 2.0 METs), class I (6.5 ± 2.1 METs), and class II (6.0 ± 1.8 METs) obese participants at

**Table 1—Baseline characteristics of ILI participants**

	Overall	Overweight	Class I	Class II	Severely obese	<i>P</i> value for mean/proportional equivalence across groups
<i>n</i>	2,503	395	892	654	562	
Age	58.6 (6.8)	60.0 (7.1) <sup>a</sup>	59.5 (6.7) <sup>a</sup>	58.4 (6.6) <sup>b</sup>	56.4 (6.4) <sup>c</sup>	<0.01
Sex (%)						<0.01
Male	40.6	41.2 <sup>a,b</sup>	46.6 <sup>a,b</sup>	37.9 <sup>a,c</sup>	33.8 <sup>c</sup>	
Female	59.4	58.7 <sup>a,b</sup>	53.4 <sup>a,b</sup>	62.1 <sup>a,c</sup>	66.2 <sup>c</sup>	
Ethnicity (%)						<0.01
African American	15.6	14.4	13.4	16.8	18.9	
American Indian/Alaskan Native	5.1	6.8	4.9	4.4	5.0	
Asian/Pacific Islander	1.2	4.1	1.0	0.3	0.36	
Hispanic/Latino	12.8	15.4	14.4	11.5	10.1	
Non-Hispanic white	63.3	57.0	64.9	64.4	64.1	
Other/multiple	1.9	2.3	1.5	2.6	1.60	
Obesity measures						
BMI	35.8 (6.0)	28.3 (1.3) <sup>a</sup>	32.6 (1.4) <sup>b</sup>	37.4 (1.5) <sup>c</sup>	44.8 (3.9) <sup>d</sup>	<0.01
Weight (kg)	100.6 (19.7)	79.7 (9.5) <sup>a</sup>	92.2 (11.7) <sup>b</sup>	105 (12.7) <sup>c</sup>	124 (16.6) <sup>d</sup>	<0.01
Waist circumference (cm)	113.8 (14.4)	98.4 (8.7) <sup>a</sup>	108 (9.1) <sup>b</sup>	118 (10.7) <sup>c</sup>	129 (11.8) <sup>d</sup>	<0.01
CVD risk factors						
HDL (mg/dL)	43.5 (11.8)	45.5 (13.8) <sup>a</sup>	42.5 (11.3) <sup>a,b</sup>	43.2 (11.6) <sup>b</sup>	43.8 (11.2) <sup>b</sup>	<0.01
LDL (mg/dL)	112 (32.2)	115 (33.3) <sup>a</sup>	110 (31.2) <sup>a</sup>	112 (33.3) <sup>a</sup>	114 (31.3) <sup>a</sup>	0.02
Triglycerides (mg/dL)	183 (116)	171 (109) <sup>a</sup>	185 (116) <sup>a</sup>	189 (126) <sup>a</sup>	180 (109) <sup>a</sup>	0.07
Systolic blood pressure (mmHg)	128 (17.3)	124 (16.5) <sup>a</sup>	127 (16.7) <sup>b</sup>	130 (17.3) <sup>c</sup>	132 (17.8) <sup>c</sup>	<0.01
Diastolic blood pressure (mmHg)	69.9 (9.55)	69.3 (8.9) <sup>a</sup>	70.3 (9.6) <sup>a</sup>	70.1 (9.5) <sup>a</sup>	69.6 (10) <sup>a</sup>	0.32
HbA <sub>1c</sub> (%)	7.25 (1.1)	7.18 (1.1) <sup>a</sup>	7.17 (1.1) <sup>a</sup>	7.31 (1.1) <sup>a</sup>	7.33 (1.2) <sup>a</sup>	0.02
Fasting glucose (mg/dL)	152 (44.5)	150 (44.5) <sup>a</sup>	150 (43.0) <sup>a</sup>	155 (46.1) <sup>a</sup>	153 (44.8) <sup>a</sup>	0.09
Exercise variables						
PA (kcal/week)	863.87 (1,107)	1,017 (1,257) <sup>a</sup>	962 (1,077) <sup>a</sup>	832 (1,077) <sup>a,b</sup>	684 (1,072) <sup>b</sup>	<0.01
Fitness (80% maximal METs)	5.18 (1.5)	5.73 (1.6) <sup>a</sup>	5.53 (1.6) <sup>a</sup>	5.02 (1.3) <sup>b</sup>	4.41 (1.2) <sup>c</sup>	<0.01

Data are means (SD) or percent, unless otherwise designated. Values with different superscript letters across columns are significantly different from one another (*P* < 0.05). These comparisons were only performed when the group comparison *P* value was <0.05.

**Table 2—Change in body weight, fitness, PA, and CVD risk factors from baseline to 1 year**

	n	BMI groups					P value for means across groups*
		Overall	Overweight	Class I	Class II	Severely obese	
<b>Obesity measures</b>							
Body weight (kg)	2,475	-8.71 (7.6)	-5.97 (4.7) <sup>a</sup>	-8.10 (6.2) <sup>b</sup>	-9.09 (8.0) <sup>b</sup>	-11.2 (9.7) <sup>c</sup>	<0.01
BMI (kg/m <sup>2</sup> )	2,475	-3.08 (2.6)	-2.10 (1.6) <sup>a</sup>	-2.84 (2.08) <sup>b</sup>	-3.23 (2.8) <sup>c</sup>	-4.01 (3.4) <sup>d</sup>	<0.01
Weight change (%)	2,475	-8.56 (6.9)	-7.43 (5.6) <sup>a</sup>	-8.72 (6.4) <sup>b</sup>	-8.64 (7.4) <sup>b</sup>	-9.04 (7.6) <sup>b</sup>	<0.01
Waist circumference (cm)	2,453	-7.61 (8.7)	-6.67 (7.4)	-7.72 (7.9)	-7.85 (10.1)	-7.84 (8.8)	0.06
<b>Exercise variables</b>							
Fitness (80% maximal METs)	2,256	0.957 (1.4)	0.881 (0.97)	0.974 (1.4)	0.961 (1.3)	0.979 (1.2)	0.92
% Change in fitness	2,256	20.9 (29.1)	18.3 (19.6) <sup>a</sup>	19.6 (28.1) <sup>a,b</sup>	21.3 (29.4) <sup>b</sup>	24.4 (30.1) <sup>b</sup>	0.03
PA (kcal/week)	1,120	881 (1,617)	825 (1,662)	878 (1,574)	1,027 (1,618)	761 (1,645)	0.25
<b>CVD risk factors†</b>							
HDL (mg/dL)	2,310	3.10 (7.2)	4.49 (8.2) <sup>a</sup>	3.99 (7.29) <sup>a,b</sup>	3.34 (7.16) <sup>b</sup>	1.83 (6.02) <sup>c</sup>	<0.01
LDL (mg/dL)	2,309	-5.21 (28.0)	-6.97 (28.4)	-3.93 (27.9)	-5.42 (29.3)	-5.68 (26.3)	0.52
Triglycerides (mg/dL)	2,379	-30.3 (102)	-25.4 (97.9)	-32.9 (107)	-32.4 (107)	-27.2 (88.9)	0.88
Systolic blood pressure (mmHg)	2,445	-6.77 (17.2)	-4.77 (15.4)	-6.39 (17.4)	-7.69 (16.8)	-7.74 (18.5)	0.49
Diastolic blood pressure (mmHg)	2,445	-3.00 (8.5)	-2.43 (7.9)	-3.12 (8.4)	-3.13 (8.4)	-3.08 (9.38)	0.19
HbA <sub>1c</sub> (%)	2,378	-0.643 (0.99)	-0.617 (1.0)	-0.589 (0.97)	-0.662 (0.95)	-0.723 (1.02)	0.20

Data are unadjusted means (SD). Values with different superscript letters across columns are significantly different from one another ( $P < 0.05$ ). \*All  $P$  values adjusted for age, sex, and ethnicity. † $P$  values for all CVD risk factors are also adjusted for baseline values and baseline medication usage (HDL, LDL, and triglyceride adjusted for lipid-lowering medication at baseline; systolic and diastolic blood pressure adjusted for hypertension medications; and HbA<sub>1c</sub> and fasting glucose adjusted for insulin usage at baseline).

1 year ( $P < 0.01$ ). Similarly, severely obese participants had significantly lower ( $P < 0.01$ ) absolute physical levels at 1 year ( $1,450 \pm 1,584$  kcal/week) compared with class I ( $1,857 \pm 617$  kcal/week) and class II ( $1,810 \pm 1,645$  kcal/week) obese and similar to overweight ( $1,841 \pm 1,479$  kcal/week) participants ( $P = 0.08$ ).

**CVD risk factors.** Favorable improvements in lipids, blood pressure, and glycemic control were seen across all BMI categories from baseline to 1 year (Table 2). Controlling for baseline values and medication usage, severely obese participants experienced similar improvements in LDL cholesterol, triglycerides, systolic and diastolic blood pressure, HbA<sub>1c</sub>, and fasting glucose compared with their less obese peers ( $P > 0.05$ ). However, the severely obese had smaller improvements in HDL cholesterol compared with individuals with a lesser degree of obesity ( $P < 0.01$ ). The percentage of participants using insulin, lipid-lowering, and hypertension medication at baseline and who discontinued usage at 1 year was similar across weight categories. Similarly, the percentage of participants not using these medications at baseline but who initiated usage at 1 year did not differ between BMI groups (Supplementary Table A1).

Participants in each of the BMI categories who met the American Diabetes

Association goals for LDL cholesterol ( $<100$  mg/dL), blood pressure ( $<130/80$  mmHg), and HbA<sub>1c</sub> ( $<7\%$ ) were compared at baseline and 1 year. The percentage of severely obese participants meeting the American Diabetes Association goal for LDL cholesterol (41.9%), HbA<sub>1c</sub> (71.3%), and blood pressure (65.7%) at 1 year was significantly greater than the percentage meeting these goals at baseline (34.1, 45.0, and 44.5%, respectively;  $P < 0.05$ ). In addition, the proportion of participants meeting each of these goals at 1 year was similar across BMI categories ( $P > 0.05$ ). For example, at 1 year, 71.3% of severely obese participants met the HbA<sub>1c</sub> goal, which was similar to the percentage of overweight (75.4%), class I (74.5%), and class II (70.1%) obese participants meeting this goal (Supplementary Table A2).

#### Program adherence

Severely obese individuals attended 80% of the treatment sessions over year 1, which was similar to all other BMI categories ( $P = 0.43$ ). Similarly, meal replacement usage did not differ by BMI categories ( $P = 0.58$ ).

**CONCLUSIONS**—The large number of participants with severe obesity ( $n = 562$ ; 22% of the participants) treated in the intensive lifestyle group in Look

AHEAD provides an unusual opportunity to consider whether severely obese individuals with type 2 diabetes can achieve significant initial weight losses and improvements in CVD risk factors when treated in a 1-year standard behavioral intervention. Nearly 40% of severely obese ILL participants lost  $\geq 10\%$  of initial body weight at 1 year. Additionally, 42% achieved the American Diabetes Association goal for LDL cholesterol, 66% for blood pressure, and 71% for HbA<sub>1c</sub>, all significantly greater than at baseline and comparable to individuals with a BMI  $<40$  kg/m<sup>2</sup>. These promising findings suggest that severely obese individuals with type 2 diabetes can be successfully treated through behavioral weight loss programs.

Previous studies have reported favorable weight loss outcomes among severely obese participants (11,19–22). For example, the Louisiana Obese Subjects Study examined nonsurgical weight loss for the severely obese within the primary care setting (21). Despite low retention rates (51%), completers' analyses revealed that the average weight loss at 2 years was 9.7%. Similar weight loss outcomes (10.9%) and significantly better retention rates (78%) were also reported by Goodpaster et al. (11) after a 1-year ILL for severely obese individuals. However, we are the first group to examine the effectiveness of a lifestyle intervention for

severely obese individuals with type 2 diabetes, and our results are equally impressive. After 1 year, the average retention rate was 98.4%, and the mean weight loss was 11.2 kg, or 9% of initial body weight. In addition, this magnitude of weight loss resulted in a 9 and 10% improvement in fasting glucose and HbA<sub>1c</sub>, respectively. Additionally, 17% of severely obese participants using insulin at baseline were no longer using insulin after 1 year of treatment.

Another novel finding from this study was that after a 1-year ILI, severely obese participants achieved weight losses and improvements in fitness, PA, blood pressure, LDL cholesterol, triglycerides, fasting glucose, and HbA<sub>1c</sub> that were comparable to individuals with lesser degrees of obesity. This was the first study to examine whether there were differences in these outcome variables across various BMI categories. In a previous Look AHEAD publication (23), it was determined that the relationship between weight loss and CVD risk did not depend on baseline weight for all risk factors except HDL. Thus, the current article expands on the previous finding by stratifying participants according to baseline BMI and comparing changes in weight and CVD risk factors across BMI categories. The finding that the severely obese achieve similar weight losses and improvements in CVD risk factors compared with those with lesser degrees of obesity counters the notion that "severely obese individuals often do not benefit from more conservative treatments for weight loss and weight maintenance," as stated in the current National Heart, Lung, and Blood Institute obesity guidelines (5).

We do not suggest that the weight losses achieved through lifestyle interventions are comparable or superior to bariatric surgery, or do we suggest that remission in diabetes that is often seen in the majority of bariatric surgery patients after surgery is similar when lifestyle interventions are used. Rather we propose that lifestyle interventions be considered as one possible strategy to treat individuals with severe obesity. Given that a large percentage of severely obese individuals report that they would not choose surgical procedures as a method of weight reduction (8) and that the number of bariatric surgery procedures capable of being performed yearly is small in comparison with the number of individuals with severe obesity (1), it is critical that nonsurgical treatment approaches be developed and used.

Although the majority of severely obese participants in this study did not reach an ideal body weight, and many remained severely obese, marked improvements in their CVD risk factors were observed. As previously reported by Wing et al. (23), modest weight losses (5–10%) result in clinically significant improvements in CVD risk factors at 1 year after a lifestyle intervention. Other studies in severely obese individuals have also reported significant reductions in CVD risk factors (19–21). For example, Anderson et al. (19) reported a 17% reduction in LDL cholesterol, 14% reduction in triglycerides, and an ~9% improvement in blood pressure after an average weight loss of 35.3 kg. Furthermore, in a study that compared bariatric surgery to commercial weight loss camps and intermittent residential treatment programs, the surgery group lost significantly more weight than the lifestyle intervention groups (31 vs. 13 and 15%, respectively), yet all groups experienced similar improvements in risk factors and resolution of weight-related comorbidities (20). Look AHEAD will continue to follow participants to assess the long-term impact of these CVD risk factor improvements and determine whether a lifestyle intervention can reduce morbidity and mortality and also lower the costs associated with obesity among severely obese individuals.

One risk factor in which severely obese participants did not experience the same magnitude of improvement as their less obese peers was in HDL cholesterol. Explanations for this attenuated response are unclear; however, it is possible that, overall, lower levels of PA and fitness among the severely obese at 1 year may have contributed to this response (24). Although severely obese participants had similar improvements in fitness and PA after the 1-year intervention, their lower PA and fitness at baseline resulted in PA and fitness levels that were lower than the majority of their less obese peers at 1 year. These results are not surprising given previous research, which has indicated that severely obese individuals perform little moderate-to-vigorous PA (25). Thus, strategies to enhance PA within the context of behavioral weight loss treatment programs should be developed, targeting the special needs of this population.

There are several limitations to this study. First, participants were older (45–76 years of age) individuals with type 2

diabetes, at the lower end of the severe obesity range (95% of participants had a BMI between 40 and <52.5 kg/m<sup>2</sup>). They also were highly motivated individuals who completed a behavioral run-in and passed an exercise test; thus, the generalizability of these findings to other populations is uncertain. In addition, the measurement of meal replacements, medication usage, and PA were self-reported. Finally, severely obese individuals participated in group sessions along with those with lesser degrees of obesity; thus, it is unclear how they would respond when treated solely in groups with individuals with a similar BMI.

To summarize, an intensive behavioral weight loss program for older individuals with type 2 diabetes resulted in significant initial weight losses and improvements in CVD risk factors among the severely obese, both of which were comparable to those changes seen in participants with a lesser degree of obesity. Based on the current findings, behavioral therapy should be considered a viable treatment option for this population. All patients should be provided with a strong behavioral weight loss program, as described here, before undergoing bariatric surgery. In the future, strategies to enhance weight loss outcomes and PA compliance for individuals with severe obesity should be explored. Additionally, future efforts should examine whether weight losses achieved through lifestyle approaches can be sustained long-term.

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## References

1. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. *JAMA* 2010;303:235–241
2. Sturm R. Increases in morbid obesity in the USA: 2000–2005. *Public Health* 2007; 121:492–496
3. McTigue K, Larson JC, Valoski A, et al. Mortality and cardiac and vascular outcomes in extremely obese women. *JAMA* 2006;296:79–86
4. Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. *Arch Intern Med* 2008;168:1550–1559; discussion 1559–1560
5. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. *Obes Res* 1998;6(Suppl. 2):51S–209S
6. Tice JA, Karliner L, Walsh J, Petersen AJ, Feldman MD. Gastric banding or bypass? A systematic review comparing the two most popular bariatric procedures. *Am J Med* 2008;121:885–893
7. Henkel DS, Remington PL, Athens JK, Gould JC. Trends in bariatric surgery for morbid obesity in Wisconsin: a 6-year follow-up. *WMJ* 2010;109:21–27
8. Strommen M, Kulseng B, Vedul-Kjelsås E, Johnsen H, Johnsen G, Mårvik R. Bariatric surgery or lifestyle intervention? An exploratory study of severely obese patients' motivation for two different treatments. *Obes Res Clin Pract* 2009;3:193–201
9. Buchwald H, Oien DM. Metabolic/bariatric surgery worldwide 2008. *Obes Surg* 2009; 19:1605–1611
10. Blackburn GL, Wollner S, Heymsfield SB. Lifestyle interventions for the treatment of class III obesity: a primary target for nutrition medicine in the obesity epidemic. *Am J Clin Nutr* 2010;91:289S–292S
11. Goodpaster BH, Delany JP, Otto AD, et al. Effects of diet and physical activity interventions on weight loss and cardio-metabolic risk factors in severely obese adults: a randomized trial. *JAMA* 2010; 304:1795–1802
12. Khan MA, St Peter JV, Breen GA, Hartley GG, Vessey JT. Diabetes disease stage predicts weight loss outcomes with long-term appetite suppressants. *Obes Res* 2000;8: 43–48
13. The Look AHEAD Research Group. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the Look AHEAD trial. *Diabetes Care* 2007;30:1374–1383
14. Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity (Silver Spring)* 2009;17:713–722
15. Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care* 2002;25:2165–2171
16. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK; American College of Sports Medicine. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc* 2009;41:459–471
17. Paffenbarger RS Jr, Wing AL, Hyde RT. Physical activity as an index of heart attack risk in college alumni. *Am J Epidemiol* 1978;108:161–175
18. American College of Sports Medicine. *ACSM's Guidelines for Exercise Testing and Prescription*. 7th ed. Whaley MH, Ed. New York, Lippincott, 2006
19. Anderson JW, Brinkman-Kaplan VL, Lee H, Wood CL. Relationship of weight loss to cardiovascular risk factors in morbidly obese individuals. *J Am Coll Nutr* 1994; 13:256–261
20. Martins C, Strommen M, Stavne OA, Nossur R, Mårvik R, Kulseng B. Bariatric surgery versus lifestyle interventions for morbid obesity—changes in body weight, risk factors and comorbidities at 1 year. *Obes Surg* 2010;21:841–849
21. Ryan DH, Johnson WD, Myers VH, et al. Nonsurgical weight loss for extreme obesity in primary care settings: results of the Louisiana Obese Subjects Study. *Arch Intern Med* 2010;170:146–154
22. Wadden TA, Faulconbridge LF, Jones-Cornelle LR, et al. Binge eating disorder and the outcome of bariatric surgery at one year: a prospective, observational study. *Obesity (Silver Spring)* 2011;19:1220–1228
23. Wing RR, Lang W, Wadden TA, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care* 2011;34:1481–1486
24. Leon AS, Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. *Med Sci Sports Exerc* 2001;33(Suppl. 6):S502–S515; discussion S528–S529
25. Bond DS, Jakicic JM, Vithianathan S, et al. Objective quantification of physical activity in bariatric surgery candidates and normal-weight controls. *Surg Obes Relat Dis* 2010;6:72–78