

Eight-Year Weight Losses with an Intensive Lifestyle Intervention: The Look AHEAD Study

The Look AHEAD Research Group

Objective: To evaluate 8-year weight losses achieved with intensive lifestyle intervention (ILI) in the Look AHEAD (Action for Health in Diabetes) study.

Design and Methods: Look AHEAD assessed the effects of intentional weight loss on cardiovascular morbidity and mortality in 5,145 overweight/obese adults with type 2 diabetes, randomly assigned to ILI or usual care (i.e., diabetes support and education [DSE]). The ILI provided comprehensive behavioral weight loss counseling over 8 years; DSE participants received periodic group education only.

Results: All participants had the opportunity to complete 8 years of intervention before Look AHEAD was halted in September 2012; $\geq 88\%$ of both groups completed the 8-year outcomes assessment. ILI and DSE participants lost (mean \pm SE) $4.7\% \pm 0.2\%$ and $2.1 \pm 0.2\%$ of initial weight, respectively ($P < 0.001$) at year 8; 50.3% and 35.7% , respectively, lost $\geq 5\%$ ($P < 0.001$), and 26.9% and 17.2% , respectively, lost $\geq 10\%$ ($P < 0.001$). Across the 8 years ILI participants, compared with DSE, reported greater practice of several key weight-control behaviors. These behaviors also distinguished ILI participants who lost $\geq 10\%$ and kept it off from those who lost but regained.

Conclusions: Look AHEAD's ILI produced clinically meaningful weight loss ($\geq 5\%$) at year 8 in 50% of patients with type 2 diabetes and can be used to manage other obesity-related co-morbid conditions.

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Introduction

The Look AHEAD (Action for Health in Diabetes) study was designed to assess the effects of an intensive lifestyle intervention (ILI) on clinically important health outcomes in overweight/obese individuals with type 2 diabetes (1). The trial's primary outcome was cardiovascular morbidity and mortality, on which no significant differences were observed between participants assigned to ILI or a

usual care group (i.e., diabetes support and education [DSE]) after a mean follow-up of 9.6 years (2). Investigators currently are examining changes in secondary outcomes in Look AHEAD including mood (3), quality of life (4), sleep apnea (5), and physical function (6), all of which were improved by the ILI during the trial's initial years.

Look AHEAD provides the largest and longest randomized evaluation to date of an ILI for weight reduction. The trial offers

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invaluable information about the feasibility of inducing and maintaining clinically significant weight loss, defined as a $\geq 5\%$ reduction in initial body weight (7-10). Weight loss of this size confers additional health benefits beyond those described above. These include prevention and resolution of type 2 diabetes (11,12), reduction in blood pressure and lipids (13,14), amelioration of non-alcoholic fatty liver disease (15), and improvements in urinary incontinence and sexual dysfunction (16,17).

The present report provides a detailed analysis of changes in body weight in ILI and DSE participants over the first 8 years of the intervention, which all participants had the opportunity to complete before the trial was halted. ILI participants were provided frequent treatment visits the first year to induce weight loss, followed by a comprehensive weight loss maintenance program in years 2-8 (18). Our primary hypotheses were that the ILI group, as compared with DSE, would achieve significantly greater mean weight losses at all years and be more successful in achieving reductions $\geq 5\%$ and $\geq 10\%$ of initial weight. Consistent with these hypotheses, we predicted that ILI participants, compared with DSE, would report greater practice of numerous weight control behaviors (e.g., reducing energy intake, increasing physical activity) recommended by the intervention. The study's large sample size ($N = 5,145$) allowed us to examine the effect on 8-year weight loss of age, gender, and race/ethnicity, as evaluated previously for years 1 and 4 (19). The large sample also allowed us to examine, within the ILI group, the percentage of participants that lost $\geq 10\%$ of initial weight the first year and sustained the loss at year 8. Behavioral characteristics of these weight-loss maintainers were compared with those of participants who initially lost $\geq 10\%$ but regained it.

Methods

Participants

A total of 5,145 men and women were enrolled in Look AHEAD at 16 centers throughout the United States (1,2). Eligible individuals had type 2 diabetes, were 45-76 years of age, and had a body mass index (BMI) $\geq 25 \text{ kg/m}^2$ (or $\geq 27 \text{ kg/m}^2$ if taking insulin). Additional eligibility criteria have been reported and included applicants' completing a graded exercise test and a test of behavioral adherence (1,2). Those who remained eligible were randomly assigned, with equal probability, to ILI or DSE. All participants signed a consent form approved by their center's institutional review board.

Interventions

The ILI and DSE interventions have been described previously and are only briefly summarized here (18,20). Participants in both groups received all usual medical care from their own primary care providers.

ILI. In year 1, ILI participants received a comprehensive lifestyle intervention designed to induce an average, study-wide loss $\geq 7\%$ of initial weight (with an individual goal of losing $\geq 10\%$) (1,19). The intervention was adapted from the Diabetes Prevention Program (DPP) (11,21) and delivered to groups of approximately 10-20 persons by experienced interventionists. In months 1-6, participants attended group sessions (of 60-75 minutes) for the first 3 weeks of each month; the fourth week, they met individually with their interventionist (for 20-30 minutes), and group sessions were not held. In months 7-12, they continued to have a monthly individual meeting, but group sessions were reduced to two per month. Participants

were prescribed 1,200-1,800 kcal/day (depending on initial body weight) with $\leq 30\%$ of calories from fat ($< 10\%$ from saturated fat) and $\geq 15\%$ of calories from protein. Structured meal plans (22) and meal replacements (18) were provided (free of charge) for the first 4 months, with patients encouraged to replace two meals and one snack daily with liquid shakes and meal bars. From months 5-12, they were instructed to replace one meal and one snack daily. Participants were prescribed ≥ 175 minutes/week of moderate intensity physical activity, to be achieved by month 6, with a further increase to ≥ 200 minutes/week for those who met this goal. The activity program relied on unsupervised exercise that, for most, consisted of brisk walking (1,18). Participants were instructed to keep daily records of their food intake, physical activity, and other targeted behaviors.

In years 2-8, the intervention focused principally on maintaining the weight losses and duration of physical activity achieved during year 1, as well as helping unsuccessful individuals achieve the study goals (18,19). Lifestyle counseling was provided primarily in individual sessions to allow tailoring to participants' specific treatment needs. Each month, participants had an individual, on-site meeting (20-30 minutes), with a second individual contact by telephone or e-mail, approximately 2 weeks later. (This second contact was discontinued beginning in year 5.) Participants had individualized calorie goals, based on their desire to maintain their weight loss, lose more (if their BMI was $> 23 \text{ kg/m}^2$), or reverse weight gain. All were encouraged to continue to use meal replacements (at no charge) to replace one meal or snack per day, to exercise ≥ 200 minutes/week, and to monitor weight weekly or more often.

During years 2-8, all sites offered a monthly group meeting at which members weighed-in, reviewed diet and activity records, and participated in a lifestyle modification session. Each year sites also offered at least one Refresher Group and one National Campaign, as used in the DPP (21). Refresher Groups typically lasted 6-8 weeks and were organized around a weight loss and/or physical activity theme (19). National Campaigns were similar in providing a group experience for 8-10 weeks but challenged participants to meet a specific goal (e.g., losing 5 lb), for which they received a small prize. Participants were strongly encouraged but not required to attend the various group offerings.

Interventionists included registered dietitians, psychologists, and exercise specialists, all of whom were certified annually. In addition to cognitive behavioral therapy, they incorporated elements of problem solving, motivational interviewing, and cultural tailoring in their counseling (23-25). They also could select more intensive interventions from a toolbox, described previously (18,19).

DSE. For the first 4 years, DSE participants were provided three 1-hour group meetings per year that discussed diet, physical activity, and social support, respectively (20). These sessions offered information but not specific behavioral strategies for adhering to the diet and physical activity recommendations. Years 5 to 8 provided one such session per year. Persons who desired more help with weight loss were referred to their PCPs, who were free to recommend whatever interventions they considered appropriate.

Assessments

Weight was measured at baseline and annually thereafter with a digital scale (model BWB-800; Tanita, Willobrook, IL), by certified

staff who were masked to intervention assignment. Physical activity was assessed at baseline and years 1, 4, and 8 by the Paffenbarger Activity Questionnaire (PAQ) (26), which provides an estimate of weekly energy expenditure from moderate intensity physical activity (e.g., climbing stairs, walking, and other fitness, sport, and recreational activities). At baseline and years 1 and 4, only participants at eight centers (i.e., the same each year) completed the questionnaire; in year 8, participants at all sites completed it. All participants also reported at baseline and years 1-4, as well as at year 8, the number of weeks in the prior year that they engaged in behaviors previously determined to be associated with long-term weight control: a) increasing physical activity (27-29); b) monitoring body weight (30,31); c) reducing calorie and fat intake (32,33); and d) using meal replacements (33). These items were included in a questionnaire developed by study investigators (available on request).

Statistical analyses

The present analyses focused on the first 8 years of intervention, which all participants had the opportunity to complete before the trial was halted in September 2012. (Weight data reported in the primary endpoint paper included participants at different stages of intervention, ranging from 8.2 to 11 years.) Differences between the DSE and ILI groups in changes in weight over the 8 years were analyzed using a mixed effects analysis of covariance, which included baseline weight, clinical center, and treatment arm. The analyses followed the intention-to-treat principle in which participants were grouped according to intervention assignment, regardless of adherence, and all follow-up data were included. The percentage of participants in each group who met different categorical weight losses (e.g., $\geq 5\%$ or $\geq 10\%$ loss) at years 1 and 8 were compared using generalized estimating equations (GEE). For behavioral outcomes (e.g., physical activity), differences between groups on continuous measures were analyzed using analysis of covariance (adjusting for clinical center and baseline value of the outcome) and using GEE for categorical measures. Within the two intervention groups, a mixed effects analysis of covariance was used to examine the relationship between weight loss (at years 1, 4, and 8) and gender, age, and race/ethnicity (controlling for baseline weight, clinical center, and interactions of each of the subgroup variables with year and intervention group). All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

Body weight data for participants who died during the 8-year trial were included in the analyses until censored at the time of death. In addition, all analyses were conducted with and without censoring weights of participants (in both groups) who underwent bariatric surgery. In year 1, 5 ILI and 10 DSE participants had surgery, which increased by year 8 to a total of 76 and 84, respectively (the latter values representing 3.0% and 3.3% of participants randomized to ILI and DSE, respectively). The two sets of analyses yielded the same statistical conclusions concerning differences between groups. Mean weight losses for both sets of analyses are reported; however, we focus primarily on weight changes in which bariatric surgery patients were censored (at the time of surgery) to provide the most accurate estimate of the efficacy of the lifestyle intervention.

For the ILI participants only, weight loss trajectories over the 8 years were determined for participants who at year 1 had lost $\geq 10\%$ of initial weight, 5% to $<10\%$, or $<5\%$. Logistic regression was used to determine the odds of achieving a loss $\geq 10\%$ or $\geq 5\%$ at

year 8, based on having achieved these categorical losses at year 1. Data for the 8-year trajectories comprised a completers' sample as a result of not including participants who had been censored or had failed to provide a measured body weight at both years 1 and 8.

Results

Participants' baseline characteristics

ILI and DSE participants did not differ significantly on baseline characteristics, as reported previously (see Table 1) (2,33). Overall, average (\pm SD) age was 58.7 ± 6.8 years, BMI was 36.0 ± 5.9 kg/m², and duration of type 2 diabetes was 6.8 ± 6.5 years. Figure 1 shows that 89.9% and 88.3% of ILI and DSE participants, respectively, completed the 8-year outcomes assessment ($P = 0.077$). Year-8 retention was 94.0% (across the two groups) when deceased participants were removed from the denominator.

Weight loss

At year 1, ILI participants lost a mean (\pm SE) of $8.5\% \pm 0.2\%$ of initial weight, compared with $0.6\% \pm 0.2\%$ for DSE ($P < 0.001$; see Figure 2). (Mean losses, not censored for bariatric surgery, were $8.6\% \pm 0.2\%$ and $0.6\% \pm 0.2\%$, respectively.) As reported previously (33), more ILI than DSE participants lost $\geq 5\%$ of initial weight (68.0% vs. 13.3%; $P < 0.001$), as well as $\geq 10\%$ (37.7% vs.

TABLE 1 Baseline characteristics of participants in the ILI and DSE groups

Characteristic	ILI N = 2,570	DSE N = 2,575	P Value
Sex (no. of subjects)			
Female	1,526 (59.3)	1,537 (59.6)	0.85
Male	1,044 (40.7)	1,038 (40.4)	
Ethnicity			
African American	399 (15.5)	404 (15.7)	0.28
American Indian/Alaskan Native	130 (5.1)	128 (5.0)	
Asian/Pacific Islander	29 (1.1)	21 (0.8)	
Hispanic/Latino	339 (13.2)	338 (13.2)	
Non-Hispanic White	1,618 (63.1)	1,628 (63.3)	
Other/multiple	48 (1.9)	50 (1.9)	
Use of insulin	381 (14.8)	408 (15.8)	0.31
Age (yr)	58.6 ± 6.8	58.9 ± 6.9	0.12
Weight (kg)			
Females	94.8 ± 17.9	95.4 ± 17.3	0.34
Males	108.9 ± 19.0	109.0 ± 18.0	0.94
Body mass index (kg/m ²)			
Females	36.3 ± 6.2	36.6 ± 6.0	0.15
Males	35.3 ± 5.7	35.1 ± 5.2	0.41
Body mass index (kg/m ²)			
<30	403 (15.7)	362 (14.1)	0.13
30 to <35	918 (35.7)	899 (34.9)	
35 to <40	672 (26.1)	740 (28.7)	
≥ 40	577 (22.5)	574 (22.3)	

Values shown are means \pm SDs or frequency counts (with percentages).

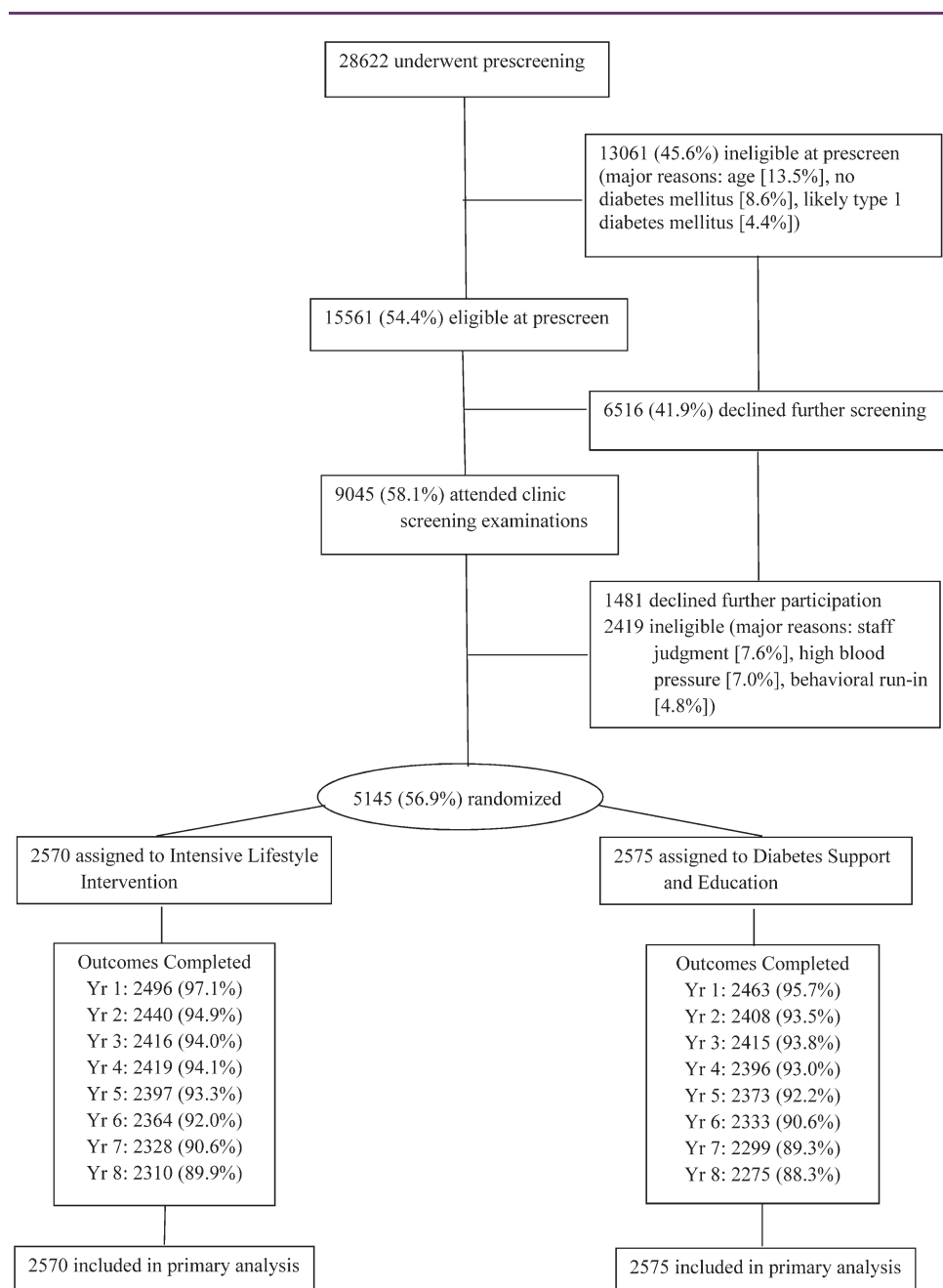


Figure 1 Flowchart for screening, randomization, and follow-up of participants. Participants who did not complete outcome assessments in years 1 through 8 had either died, withdrawn from the study, or missed the assessment.

2.9%; $P < 0.001$). (The percentage of participants who lost $\geq 5\%$ includes those who lost $\geq 10\%$.) Figure 3a shows that ILI was superior to DSE on other measures of categorical weight loss.

At year 8, ILI participants lost $4.7\% \pm 0.2\%$ of initial weight, compared with $2.1\% \pm 0.2\%$ for DSE ($P < 0.001$). (Mean losses, including participants who had bariatric surgery, were $5.3\% \pm 0.2\%$ and $2.7\% \pm 0.2\%$, respectively.) More ILI than DSE participants met the $\geq 5\%$ (50.3% vs. 35.7%; $P < 0.001$) and $\geq 10\%$ (26.9% vs. 17.2%; $P < 0.001$) categorical losses. Fewer participants in ILI than DSE (26.4% vs. 39.2%; $P < 0.001$) exceeded their baseline weight

at year 8 (see Figure 3b). Figure 2 shows that ILI produced greater mean weight loss than DSE at all years and that weight regain in ILI, following maximum weight loss at year 1, plateaued between years 4 and 6.

Weight loss according to demographic characteristics

Table 2 presents weight loss according to gender, age, and race/ethnicity at years 1, 4, and 8. (Data not censored for bariatric surgery are presented in Table 1, Supporting Information.) At all

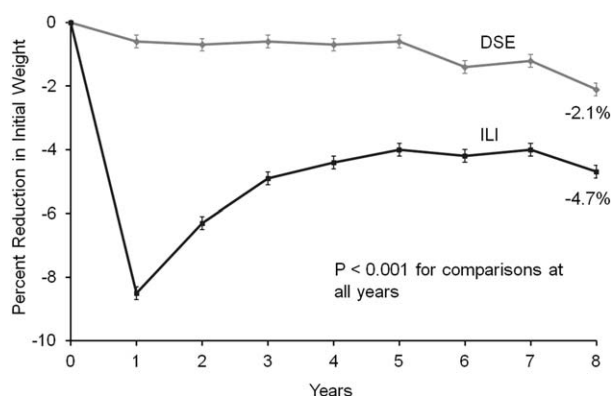


Figure 2 Figure shows mean (±SE) weight losses over 8 years for participants randomly assigned to an intensive lifestyle intervention (ILI) or diabetes support and education (DSE; usual care group). Differences between groups were significant ($P < 0.001$) at all years.

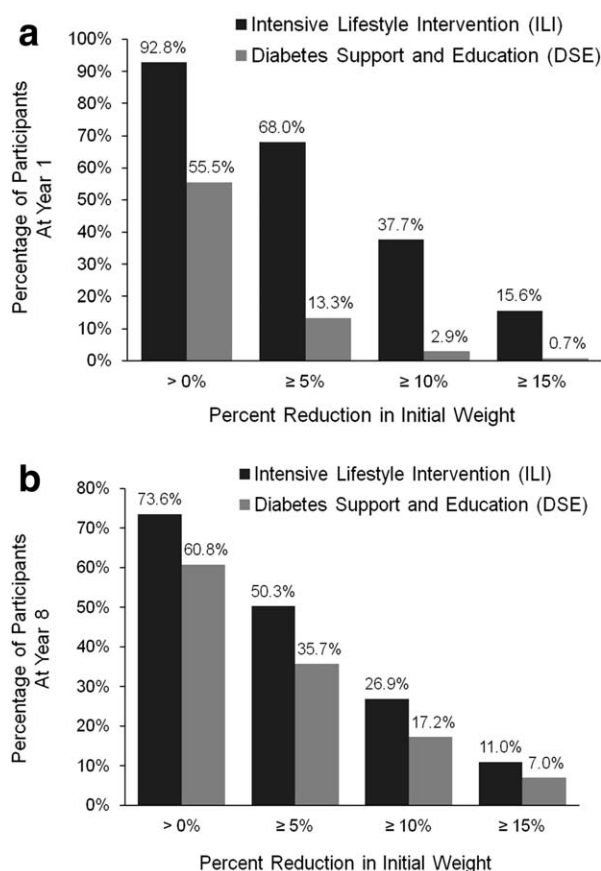


Figure 3 (a) Percentage of participants in the ILI and DSE groups who achieved different categorical weight losses at year 1. The percentages are cumulative such that the 68% of ILI participants who lost 5% or more of initial weight includes those who also lost ≥10% and ≥15%. $P < 0.001$ for all comparisons between treatment groups. (b) Percentage of participants in the ILI and DSE groups who achieved different categorical weight losses at year 8. The percentages are cumulative as described for Figure 1(A). $P < 0.001$ for all comparisons between treatment groups.

years, participants in ILI lost significantly more weight than their corresponding peers in DSE (see Table 2 for means and P values). Within the ILI group, men and women achieved comparable weight losses over the 8 years, with mean differences between them ranging from 0.3% (year 1) to 0.9% (year 8) (Table 2). By contrast, the oldest ILI individuals (65-76 years at baseline) consistently lost more weight than the youngest participants (45-54 years), with differences ranging from 0.9% (year 1) to 3.0% (year 8). Non-Hispanic white participants in ILI lost significantly more weight at year 1 than participants who self-identified as African American, Hispanic, and American Indian/Other. However, at years 4 and 8, mean weight losses were comparable among the four racial/ethnic groups, as they were among DSE participants at all years. Older DSE participants lost more weight than their younger counterparts, with the greatest difference (1.9%) between age groups occurring at year 8.

Physical activity and weight control behaviors

At baseline, participants in both groups reported expending approximately 860 kcal/week in moderate intensity physical activity, as determined by the PAQ. ILI participants, compared with DSE, achieved significantly greater increases on this measure at all subsequent assessments (see Table 3). Reported energy expenditure more than doubled in ILI participants the first year (1737.8 ± 47.6 kcal/week) but declined in subsequent years. Table 3 also presents the number of weeks in the past year that participants reported engaging in selected weight control behaviors. Groups did not differ at baseline on any measures; however, at all subsequent assessments, ILI participants, compared with DSE, significantly increased the number of weeks in which they reported exercising, reducing their calorie and fat intake, and using meal replacements (see Table 3). Practice of all behaviors increased the most during the first year. At years 1, 4, and 8, significantly more ILI than DSE participants also reported measuring their body weight weekly or more often, as well as daily or more often.

Achievement of categorical weight losses in ILI over 8 years

Figure 4a presents the weight loss trajectories of 825 ILI participants who lost ≥10% of weight at year 1 and qualified for data analysis at year 8 (as described in the Methods section). Of these 825 participants, 324 (39.3%) achieved a ≥10% loss at year 8, 213 (25.8%) a loss of 5% to <10%, 171 (20.7%) a loss of 0% to <5%, and 117 (14.2%) gained above their baseline weight. A comparison of participants who at year 8 maintained the ≥10% loss versus gained above baseline weight revealed that maintainers reported (at year 8) a higher activity-related energy expenditure (1471.9 ± 121.1 vs. 799.9 ± 100.9 kcal/week, $P < 0.001$) and a greater number of weeks (in the prior year) reducing their calorie and fat intake (both P values <0.001; see Table 4). Weight maintainers also were more likely than full regainers to weigh themselves daily or more often (47.8% vs. 28.4%), as well as weekly or more (82.4% vs. 69.8%) (both $P < 0.001$).

Figure 4b presents weight loss trajectories of the 633 participants who at year 1 lost 5% to <10% of initial weight and shows that 303 (47.9%) had a loss of ≥5% at year 8. Figure 4c presents similar results for the 656 participants who lost <5% at year 1, of whom 226 (34.5%) achieved a ≥5% loss at year 8. The odds of achieving

TABLE 2 Percent reduction in initial weight in the ILI and DSE groups at years 1, 4, and 8 according to gender, age and race/ethnicity

Characteristic	Year 1			Year 4			Year 8		
	ILI	DSE	P value	ILI	DSE	P value	ILI	DSE	P value
Total sample	8.5 ± 0.2	0.6 ± 0.2	<0.001	4.4 ± 0.2	0.7 ± 0.2	<0.001	4.7 ± 0.2	2.1 ± 0.2	<0.001
Gender									
Female	8.4 ± 0.2 ^a	0.8 ± 0.2 ^a	<0.001	4.3 ± 0.2 ^a	1.1 ± 0.2 ^a	<0.001	5.1 ± 0.2 ^a	2.6 ± 0.2 ^a	<0.001
Male	8.7 ± 0.3 ^a	0.3 ± 0.3 ^a	<0.001	4.6 ± 0.3 ^a	0.1 ± 0.3 ^b	<0.001	4.2 ± 0.3 ^b	1.3 ± 0.3 ^b	<0.001
Age									
45-55 yr	8.2 ± 0.3 ^a	0.3 ± 0.3 ^a	<0.001	3.6 ± 0.3 ^a	0.1 ± 0.3 ^a	<0.001	3.8 ± 0.3 ^a	1.2 ± 0.3 ^a	<0.001
56-65 yr	8.6 ± 0.2 ^{ab}	0.6 ± 0.2 ^a	<0.001	4.4 ± 0.2 ^b	0.7 ± 0.2 ^b	<0.001	4.7 ± 0.2 ^b	2.2 ± 0.2 ^b	<0.001
66-76 yr	9.1 ± 0.4 ^b	0.9 ± 0.4 ^a	<0.001	6.0 ± 0.4 ^c	1.8 ± 0.4 ^c	<0.001	6.8 ± 0.4 ^c	3.1 ± 0.4 ^c	<0.001
Race/ethnicity									
Non-Hispanic White	9.4 ± 0.2 ^a	0.8 ± 0.2 ^a	<0.001	4.6 ± 0.2 ^a	0.8 ± 0.2 ^a	<0.001	4.7 ± 0.2 ^a	2.1 ± 0.2 ^a	<0.001
Hispanic	7.2 ± 0.5 ^b	−0.0 ± 0.5 ^a	<0.001	4.6 ± 0.5 ^a	0.4 ± 0.5 ^a	<0.001	4.8 ± 0.5 ^a	2.1 ± 0.5 ^a	<0.001
African American	6.4 ± 0.4 ^{bc}	−0.0 ± 0.4 ^a	<0.001	3.8 ± 0.4 ^a	0.7 ± 0.4 ^a	<0.001	5.0 ± 0.4 ^a	1.8 ± 0.4 ^a	<0.001
American Indian/Other	5.3 ± 0.6 ^c	0.2 ± 0.6 ^a	<0.001	3.9 ± 0.6 ^a	0.2 ± 0.6 ^a	<0.001	5.0 ± 0.6 ^a	1.9 ± 0.6 ^a	<0.001

Note: Values shown are means ± SEs for the intention-to-treat population (ILI = 2,570; DSE = 2,575). Weights of participants who died were censored at the time of death. Data for participants who underwent bariatric surgery also were censored (at the time of surgery). In ILI, the cumulative numbers of participants who had surgery in years 1, 4, and 8 were 5, 30, and 76, respectively. Corresponding values in DSE were 10, 45, and 84, respectively.

Within columns and demographic groupings, values with different superscripts (i.e., a, b, c, etc.) differ significantly from each other. For example, at year 1, ILI participants 45–55 years of age lost significantly less weight than those 66–76 years (“a” vs. “b”), whereas weight loss of those 56–65 year did not differ significantly from either group (as shown by sharing a superscript “ab” with each group). At year 1, there were no significant differences between men and women in ILI, as shown by the shared superscript “a.” All analyses were adjusted for clinical site and baseline weight. Each family of comparisons, at each assessment time, was conducted using the Bonferroni correction. This yielded $P < 0.05$ for comparison of gender, $P \leq 0.017$ for comparison of different age groups, and $P < 0.008$ for comparison of racial/ethnic groups.

a $\geq 10\%$ weight loss at year 8 were 2.3 (95% CI: 1.83, 2.97) times greater for participants who at year 1 lost $\geq 10\%$, compared with those who lost 5% to $<10\%$, and 3.9 (95% CI: 2.99, 5.15) times greater compared with those who lost $<5\%$ at year 1. The odds of achieving $\geq 5\%$ loss at year 8 were 2.1 (95% CI: 1.70, 2.64) times greater for participants who at 1 year lost $\geq 10\%$, compared with those who lost 5% to $<10\%$, and 3.9 (95% CI: 3.10, 4.92) times greater compared with participants who lost $<5\%$ at year 1.

Discussion

Look AHEAD is the longest randomized controlled evaluation to date of an ILI for weight management. Overweight/obese individuals with type 2 diabetes lost 4.7% of initial body weight at year 8, compared with 2.1% for participants assigned to DSE (i.e., usual care). Fifty percent of ILI participants lost $\geq 5\%$ of initial weight, a common criterion of clinically meaningful weight loss (7-9), and 26.9% lost $\geq 10\%$. The same statistical differences were observed between the ILI and DSE groups when including or censoring weight losses of participants who had bariatric surgery. The Diabetes Prevention Program Outcomes Study (34) reported 10 years of follow-up of a lifestyle weight-loss intervention, but both the lifestyle group and the comparison groups received weight loss counseling after a mean of 3.2 years since randomization.

Look AHEAD's lifestyle intervention was effective over 8 years in both men and women and across an ethnically and racially diverse population. Weight losses of African Americans were among the largest reported in the literature. Older participants also lost more weight than their younger counterparts (as also observed in the DPP

(35)). Some of their weight loss, however, probably was attributable to the combined effects of diabetes (36) and aging, since it also occurred in older participants in Look AHEAD's DSE group and in the original placebo-treated group of the Diabetes Prevention Program Outcomes Study (34).

Look AHEAD's long-term weight loss maintenance intervention, which included monthly or twice monthly individual contacts combined with periodic group meetings (i.e., refresher groups and national campaigns), was modeled on the DPP (11,21) and similar protocols (30,37). Look AHEAD, however, has demonstrated that the extended provision of a weight loss maintenance intervention can facilitate clinically meaningful weight loss for up to 8 years—two to three times the duration examined in previous randomized trials (30,37,38). Sustaining weight loss for longer periods may further improve the prevention of type 2 diabetes in at-risk individuals (34), as well as maintain improvements in sleep apnea (5), physical mobility (6), and other health conditions ameliorated by weight loss (7-9).

ILI participants achieved their maximum weight loss (of 8.5%) in the first year, when they received the most intensive intervention and reported their highest adherence to the prescribed weight control behaviors, compared with DSE. The ILI group, on average, regained weight from years 1 to 5, at which time body weight stabilized at approximately a 4.0%–4.7% loss for the remainder of the trial (compared with 0.7%–2.1% for DSE at this time). Look AHEAD's large sample size permitted examination of patterns of long-term weight change among subgroups of participants, rather than simply the mean change. This analysis revealed that of 825 individuals who

TABLE 3 ILI and DSE participants' reports of their physical activity, calorie restriction, and other weight control behaviors

Variable	Baseline				Year 1				Year 4				Year 8			
	ILI	DSE	P value	ILI	DSE	P value	ILI	DSE	ILI	DSE	P value	ILI	DSE	P value	ILI	P value
Physical activity (kcal/wk)	859.5 ± 31.9	862.4 ± 34.3	0.376	1737.8 ± 47.6	968.9 ± 40.9	<0.001	1245.4 ± 43.2	974.7 ± 36.0	1040.2 ± 35.3	853.2 ± 27.3	<0.001	1040.2 ± 35.3	853.2 ± 27.3	<0.001	1040.2 ± 35.3	853.2 ± 27.3
Increased exercise (no. wk/yr)	10.3 ± 0.3	10.1 ± 0.3	0.696	35.6 ± 0.4	12.2 ± 0.4	<0.001	13.8 ± 0.4	10.2 ± 0.4	10.9 ± 0.4	8.7 ± 0.4	<0.001	10.9 ± 0.4	8.7 ± 0.4	<0.001	10.9 ± 0.4	8.7 ± 0.4
Reduced kcal (no. wk/yr)	8.8 ± 0.3	9.3 ± 0.3	0.222	40.1 ± 0.4	12.6 ± 0.4	<0.001	21.0 ± 0.4	12.1 ± 0.4	17.9 ± 0.4	11.0 ± 0.4	<0.001	17.9 ± 0.4	11.0 ± 0.4	<0.001	17.9 ± 0.4	11.0 ± 0.4
Reduced fat (no. wk/yr)	12.6 ± 0.4	12.8 ± 0.4	0.627	41.2 ± 0.4	16.4 ± 0.4	<0.001	24.4 ± 0.5	16.2 ± 0.5	20.8 ± 0.5	14.1 ± 0.5	<0.001	20.8 ± 0.5	14.1 ± 0.5	<0.001	20.8 ± 0.5	14.1 ± 0.5
Meal replacements (no. wk/yr)	1.6 ± 0.1	1.6 ± 0.1	0.720	39.0 ± 0.3	3.5 ± 0.3	<0.001	24.3 ± 0.4	2.0 ± 0.4	17.2 ± 0.4	1.8 ± 0.4	<0.001	17.2 ± 0.4	1.8 ± 0.4	<0.001	17.2 ± 0.4	1.8 ± 0.4
Monitored weight																
≥ Weekly, N (%)	1,041 (40.5)	1,052 (40.9)	0.798	2,290 (91.1)	1,085 (43.7)	<0.001	1,769 (73.1)	1,045 (43.5)	1,555 (67.2)	1,027 (45.1)	<0.001	1,555 (67.2)	1,027 (45.1)	<0.001	1,555 (67.2)	1,027 (45.1)
≥ Daily, N (%)	301 (11.7)	318 (12.3)	0.479	1,162 (46.2)	318 (12.8)	<0.001	822 (34.0)	315 (13.1)	754 (32.6)	319 (14.0)	<0.001	754 (32.6)	319 (14.0)	<0.001	754 (32.6)	319 (14.0)

Values shown for physical activity are raw means ± SE; the p value is from a model that uses the log-transformed value of the measure. P values are adjusted for clinical site and the log of the baseline value (for years 1, 4, and 8). All other values are LS means ± SE or frequency count (percentage). P values are adjusted for clinical site and baseline value (for years 1, 4, and 8). (As noted in the Methods section, at baseline and years 1 and 4, only participants at eight centers [i.e., the same each year] completed the Paffenbarger Activity Questionnaire (27); in year 8, participants at all sites completed it.)

TABLE 4 Weight control behaviors at Year 8 for ILI participants who maintained (N = 324) versus regained (N = 117) their ≥10% weight loss, achieved at Year 1

Year 8 behaviors	Year 8 weight change		
	Maintained ≥10% Loss	Gained above baseline weight	P value
Physical activity (kcal/wk)	1471.9 ± 121.2	799.9 ± 100.9	0.001
Reduced Kcal (no. wk/yr)	20.4 ± 1.4	11.9 ± 2.1	<0.001
Reduced fat (no. wk/yr)	24.2 ± 1.5	15.6 ± 2.2	<0.001
Increased exercise (no. wk/yr)	12.9 ± 1.3	8.2 ± 1.8	0.013
Meal replacements (no. wk/yr)	22.8 ± 2.0	17.3 ± 2.9	0.072
Monitored weight			
≥ Weekly, N (%)	262 (82.4)	81 (69.8)	0.001
≥ Daily, N (%)	152 (47.8)	33 (28.4)	<0.001

Values shown are LS means (raw means for Paffenbarger) ± standard error or frequency count (percentage).
P values are adjusted for clinical site and baseline value.

lost ≥10% of initial weight at year 1, 39% maintained this degree of weight loss at year 8, and another 26% maintained a loss of 5% to <10%. Those who maintained the full ≥10% loss at year 8, compared with those who regained above baseline, reported greater practice of several weight-maintenance behaviors, including high levels of physical activity, reduced calorie intake, and frequent monitoring of body weight. These behaviors have been identified in prior studies of successful weight loss maintainers (28-32).

The lifestyle intervention's strengths are offset by findings that 32% of ILI participants did not lose at least 5% of initial weight in the first year, and only 34.5% of these individuals achieved this goal at year 8. Logistic regression analyses clearly revealed the importance of successful first-year weight loss for achieving a clinically meaningful loss at year 8. This finding highlights the need for research on methods of inducing weight loss in persons who do not have an early, favorable response to lifestyle modification.

Nearly 36% of DSE participants achieved a ≥5% weight loss at year 8, compared with 13.3% at year 1. Several factors may have contributed to more of these participants reaching this criterion over time. DSE participants were permitted, in consultation with their PCPs, to pursue whatever weight loss options they wished. Their weight loss also could have been unintentional (39) and reflect the effects of aging (40) or illness (39) (including diabetes (36)), as discussed with weight loss in older ILI participants.

In summary, Look AHEAD advances the management of obesity by showing that a comprehensive, long-term lifestyle intervention produced ≥5% weight loss at 8 years in 50% of participants. While efforts clearly are needed to translate the current treatment approach into clinical practice, Look AHEAD provides new optimism for the long-term management of obesity and its many co-morbid conditions that are ameliorated by weight loss. **O**

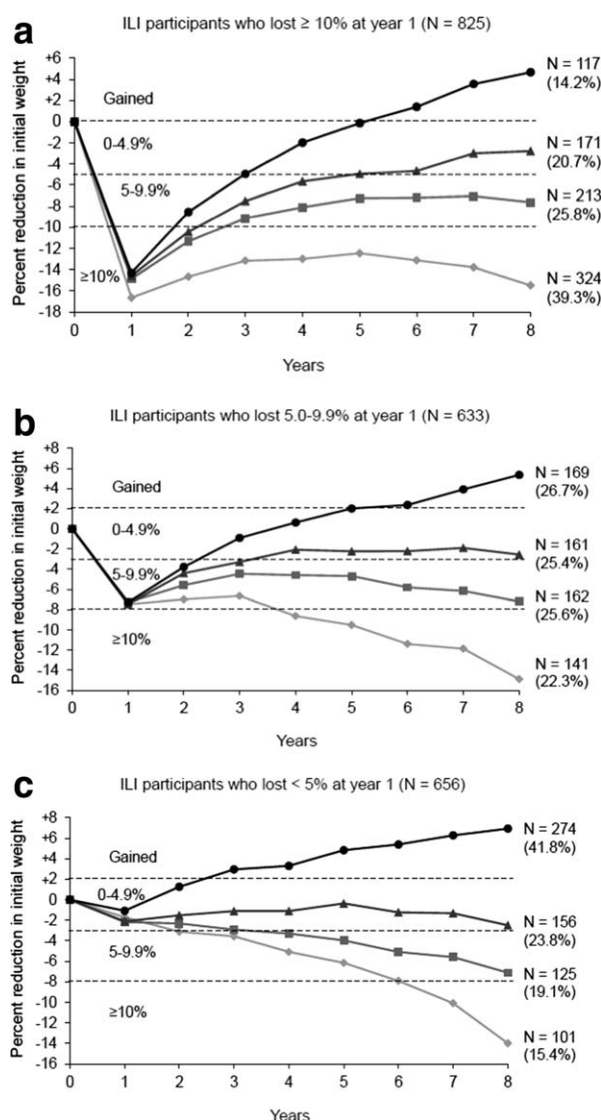


Figure 4 (a) Weight loss trajectories over 8 years in 825 participants in the intensive lifestyle intervention (ILI) who, at year 1, lost $\geq 10\%$ of initial weight and, at year 8, provided a measured body weight. The figure shows the number of participants who, at year 8, maintained a loss of 10% or more of initial weight (N = 324), of 5%-9.9% (N = 213), of 0%-4.9% (N = 171), or who gained above their baseline weight (N = 117). The percentages shown in parentheses are based on the sample size for the subgroup. Thus, the 324 of 825 participants who maintained a $\geq 10\%$ loss at year 8 comprised 39.3% of this subgroup of participants. (b) Weight loss trajectories over 8 years in 633 ILI participants who, at year 1, lost 5%-9.9% of initial weight and, at year 8, provided a measured body weight. The four categories of weight change that these participants achieved at year 8 are presented in the same manner as in Figure 4(a). (c) Weight loss trajectories over 8 years in 656 ILI participants who, at year 1, lost $< 5\%$ of initial weight and, at year 8, provided a measured body weight. The four categories of weight change that these participants achieved at year 8 are presented in the same manner as in Figure 4(a).

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REFERENCES

- Look AHEAD Research Group, Ryan DA. Look AHEAD (Action for Health in Diabetes): design and methods for a clinical trial of weight loss for the prevention of cardiovascular disease in type 2 diabetes. *Control Clin Trials* 2003;24:610-628.
- Look AHEAD Research Group, Wing RR. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;369:145-154.
- Faulconbridge LF, Wadden TA, Rubin RR, et al. One-year changes in symptoms of depression and weight in overweight/obese individuals with type 2 diabetes in the Look AHEAD study. *Obesity* 2012;20:783-793.
- Williamson DA, Rejeski J, Lang W, et al. Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. *Arch Intern Med* 2009;169:163-171.
- Kuna ST, Reboussin DM, Borradaile KE, et al. Long-term effect of weight loss on obstructive sleep apnea severity in obese patients with type 2 diabetes. *Sleep* 2013;36:641-649.
- Rejeski WJ, Ip EH, Bertoni AG, et al; Look AHEAD Research Group. Lifestyle change and mobility in obese adults with type 2 diabetes. *N Engl J Med* 2012;366:1209-17.
- National Institutes of Health/National Heart, Lung, and Blood Institute. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. *Obes Res* 1998;6:51S-210S.
- Institute of Medicine. *Weighing the Options: Criteria for Evaluating Weight Management Programs*. Washington, DC: National Academy Press; 1995.
- World Health Organization. *Obesity: Preventing and Managing the Global Epidemic*. Geneva, Switzerland: Author; 1998.
- Wing RR, Lang W, Wadden TA, et al; Look AHEAD Research Group. 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.
- Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393-403.
- Gregg EW, Chen H, Wagenknecht LE, et al. Association of an intensive lifestyle intervention with remission of type 2 diabetes. *JAMA* 2012;308:2489-2896.
- Stevens VJ, Obarzanek E, Cook NR, et al. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Ann Intern Med* 2001;134:1-11.

14. Poobalan A, Aucott L, Smith WC, et al. Effects of weight loss in overweight/obese individuals and long-term lipid outcomes—a systematic review. *Obes Rev* 2004;5: 43-50.
15. Shah K, Stufflebam A, Hilton TN, et al. Diet and exercise interventions reduce intrahepatic fat content and improve insulin sensitivity in obese older adults. *Obesity* 2009;17:2162-2168.
16. Subak LL, Wing R, West DS, et al. Weight loss to treat urinary incontinence in overweight and obese women. *N Engl J Med* 2009;360:481-490.
17. Wing RR, Bond DS, Gendrano IN 3rd, et al. Effect of intensive lifestyle intervention on sexual dysfunction in women with type 2 diabetes: results from an ancillary Look AHEAD study. *Diabetes Care* 2013;36:2937-2944.
18. Look AHEAD Research Group, Wadden TA. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity* 2006;14:737-752.
19. Wadden TA, Neiberg RH, Wing RR, et al. Four-year weight losses in the Look AHEAD study: factors associated with long-term success. *Obesity* 2011;19:1987-1998.
20. Look AHEAD Research Group, Wescbe-Thobaben JA. The development and description of the comparison group in the Look AHEAD trial. *Clin Trials* 2011;8: 320-329.
21. The Diabetes Prevention Program Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care* 2002;25:2165-2171.
22. Wing RR, Jeffrey RW, Burton LR, Thorson C, Nissinoff KS, Baxter JE. Food provision vs structured meal plans in the behavioral treatment of obesity. *Int J Obes Relat Metab Disord* 1996;20:56-62.
23. Perri MG, Nezu AM, McKelvey WF, et al. Relapse prevention training and problem-solving therapy in the long-term management of obesity. *J Consult Clin Psychol* 2001;69:722-726.
24. West DS, DiLillo V, Bursac Z, Gore SA, Greene PG. Motivational interviewing improves weight loss in women with type 2 diabetes. *Diabetes Care* 2007;30:1081-1087.
25. Kumanyika SK. Obesity treatment in minorities. In: Wadden TA, Stunkard AJ (eds). *Handbook of Obesity Treatment*. New York, Guilford Press; 2002, pp 416-446.
26. 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.
27. 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.
28. Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr* 2003;78:684-689.
29. 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.
30. Wing RR, Tate DF, Gorin AA, Raynor HA, Fava JL. A self-regulation program for maintenance of weight loss. *N Engl J Med* 2006;355:1563-1571.
31. Butryn ML, Phelan S, Hill JO, Wing RR. Consistent self-monitoring of weight: a key component of successful weight loss maintenance. *Obesity* 2007;15:3091-3096.
32. Wing RR, Hill JO. Successful weight loss maintenance. *Annu Rev Nutr* 2001;21: 323-341.
33. Look AHEAD Research Group, Wadden TA, West DS, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity* 2009;17: 713-722.
34. Knowler WC, Fowler SE, Hamman RF, et al; Diabetes Prevention Program Research Group. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet* 2009;374:1677-1686.
35. Wing RR, Hamman RF, Bray GA, et al; Diabetes Prevention Program Research Group. Achieving weight and activity goals among diabetes prevention program lifestyle participants. *Obes Res* 2004;12:1426-1434.
36. Looker HC, Knowler WC, Hanson RL. Changes in body mass index and weight before and after the development of type 2 diabetes. *Diabetes Care* 2001;24:1917-1922.
37. Svetkey LP, Stevens VJ, Brantley PJ, et al; Weight Loss Maintenance Collaborative Research Group. Comparison of strategies for sustaining weight loss: the weight loss maintenance randomized controlled trial. *JAMA* 2008;299:1139-1148.
38. Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155-161.
39. French SA, Folsom AR, Jeffery RW, Williamson DF. Prospective study of intentionality of weight loss and mortality in older women: the Iowa Women's Health Study. *Am J Epidemiol* 1999;149:504-514.
40. Villareal DT, Apovian CM, Kushner RF, Klein S; American Society for Nutrition; NAASO, The Obesity Society. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Obes Res* 2005;13:1849-1863.