One-year Weight Losses in the Look AHEAD Study: Factors Associated With Success

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This report provides a further analysis of the first year weight losses in the Look AHEAD (Action for Health in Diabetes) study and identifies factors associated with success. Participants were a total of 5,145 men and women with type 2 diabetes who were recruited at 16 sites and randomly assigned to an intensive lifestyle intervention (ILI) or a control condition, Diabetes Support and Education (DSE). During year 1, participants in ILI received comprehensive diet and physical activity counseling in a total of 42 group and individual sessions, compared with three educational sessions for DSE participants. As reported previously, at the end of the year, ILI participants lost 8.6% of initial weight, compared to 0.7% for DSE ($P < 0.001$). Within the ILI group, all racial/ethnic groups achieved clinically significant weight losses (>5.5%), although there were significant differences among groups. For the year, ILI participants attended an average of 35.4 treatment sessions and reported exercising a mean of 136.6 min/week and consuming a total of 360.9 meal replacement products. Greater self-reported physical activity was the strongest correlate of weight loss, followed by treatment attendance and consumption of meal replacements. The use of orlistat, during the second half of the year, increased weight loss only marginally in those ILI participants who had lost <5% of initial weight during the first 6 months and chose to take the medication thereafter as a toolbox option. The lifestyle intervention was clinically effective in all subsets of an ethnically and demographically diverse population.

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INTRODUCTION

The Look AHEAD (Action for Health in Diabetes) study is designed to assess the long-term health consequences of intentional weight loss in overweight and obese individuals with type 2 diabetes (1). More than 5,100 participants have been randomly assigned to a usual care condition or to an intensive lifestyle intervention (ILI) with a goal of inducing a loss of ≥7% of initial weight and increasing physical activity to ≥175 min/week. The study has statistical power to detect an 18% difference between the two groups in time for occurrence of myocardial infarction or stroke, as well as other cardiovascular outcomes. When completed, results of the trial should resolve (in diabetic patients) the conflicting findings from observational studies concerning the cardiovascular consequences of weight loss (2,3). Look AHEAD is the first randomized controlled trial to address this issue.

Results of the first year of treatment for Look AHEAD were reported recently (4) and revealed a loss of 8.6% of initial weight in the ILI, compared to a significantly smaller 0.7% for the usual care group, referred to as Diabetes Support and Education (DSE). As expected, participants in ILI also had significantly greater reductions in systolic and diastolic blood pressure, triglyceride levels, hemoglobin A_{1C}, and other cardiovascular risk factors than did those in DSE (4).

More than 2,500 individuals received the lifestyle intervention during the first year, making this by far the largest sample of individuals to receive the same program of behavioral weight control in a randomized controlled trial. The present study capitalized on this large sample to provide a detailed analysis of the influence of gender, age, education, ethnicity, and other factors on weight loss at 1 year. Based on previous investigations (5–7), we predicted that male gender, older age, and non-Hispanic white ethnicity would be associated with a greater percentage reduction in initial weight. We also predicted that measures of participants' treatment adherence,

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including attendance at intervention sessions, consumption of prescribed meals, and high levels of physical activity, would be associated with greater weight loss (8,9). Finally, we examined whether insulin use would attenuate weight loss, as suggested by prior reports (10–12).

METHODS AND PROCEDURES

Participants

Participants were a total of 5,145 men and women who were recruited at 16 centers across the United States. As described previously (4,13), participation was open to persons with type 2 diabetes who were 45–74 years of age and had a BMI ≥25 kg/m^2 (or ≥27 kg/m^2 if taking insulin). (The lower age criterion was raised to 55 years in the second year of recruitment to increase the rate of anticipated cardiovascular events.) For safety, participants were required to have blood pressure <160/100 mm Hg, hemoglobin A_{1c} <11%, and triglyceride levels <600 mg/dl. These measures were obtained during a screening visit, after applicants gave their written informed consent to participate (following the guidelines of the Helsinki Declaration and each site's institutional review board). In addition, applicants completed a graded exercise test as described previously (1,4,14) to ensure that they could safely adhere to the physical activity program prescribed in the ILI (15). All applicants also were required to have a primary care provider who would be responsible for providing their medical care (including for cardiovascular risk factors) during the 11.5-year trial.

In addition to these safety criteria, applicants were required to pass a test of behavioral adherence which consisted of recording their food intake and physical activity for two consecutive weeks. Candidates who did not keep satisfactory records for at least 12 of 14 days were not eligible to participate. This adherence criterion was included to facilitate the selection of highly motivated individuals who could meet the study's weight and activity goals.

Participants reported their age, education, race/ethnicity, and other demographic characteristics. The study's recruitment goals were to enroll approximately equal numbers of men and women, with ≥33% of participants from racial and ethnic minority groups.

Procedure

Before randomization, eligible participants received an initial session of diabetes education that included general recommendations for adopting healthy eating and activity habits and addressed the management of hypoglycemia and foot care. Participants who remained interested in the study were then randomly assigned with equal probability to the ILI and DSE conditions. Randomization was stratified by clinical center. Table 1 presents selected baseline characteristics of participants in the two conditions; a full description is provided elsewhere (13).

Treatment conditions

Previous reports have described the interventions for the DSE and ILI groups for the full 11.5 years of the planned trial (1,15). The present description is limited to the first year.

DSE. During the first year, participants in DSE were invited to attend three 1-h group meetings that addressed diet, physical activity, and social support, respectively. These sessions provided information, but not specific behavioral strategies for adopting the diet and activity recommendations. Participants who wanted more help losing weight were told to speak with their own primary care providers (who were permitted to provide their usual recommendations).

ILI. These participants were provided a comprehensive intervention, expected to induce an average loss (across the 16 centers) ≥7% of initial weight. Individual participants were given a goal of losing ≥10% of initial weight to increase the likelihood of their meeting the 7% study-wide goal. The weight control intervention was adapted from the Diabetes Prevention Program (16,17) and was delivered to participants in groups of ~10–20 persons. (Group sessions were led by lifestyle counselors who included registered dietitians, behavioral psychologists, and exercise specialists.) During the first 6 months, participants attended group sessions (of 60–75 min) for the first 3 weeks of each month. The fourth week each month, they had an individual meeting (of 20–30 min) with their lifestyle counselors, and group sessions were not held this week. These monthly individual meetings were used to tailor the intervention to participants' individual needs, including those related to dietary preferences (18,19). During months 7–12, participants continued to have a monthly individual meeting with their lifestyle counselors, but the number of group sessions was reduced from three to two per month.

During weeks 1–2, participants were instructed to eat a self-selected diet of conventional foods and to record their daily food and calorie intake in diaries provided. The energy goal for participants <114 kg (250 lb) was 1,200–1,500 kcal/day and for individuals ≥114 kg was 1,500–1,800 kcal/day (15). Participants were told to consume <30% of calories from fat, with <10% from saturated fat. During weeks 3–19, participants were prescribed a liquid-meal replacement plan, given findings that this approach significantly increased weight loss compared to a self-selected diet of conventional foods with the same calorie goal (20,21). They were instructed to replace two meals (i.e., breakfast and lunch) with a liquid shake and one snack with a bar. They potentially could choose from four meal replacement products (including Slimfast (Unilever, London, UK and Rotterdam, Netherlands), Glucerna (Abbott Laboratories, Abbott Park, IL), Optifast (Nestle, Vervey, Switzerland), and HMR (Health Management Resources Corporation, Boston, MA)) which were provided free of charge by their manufacturers. For dinner, participants were instructed to consume a meal of conventional foods, which included the option of prepared food entrées (22). They added fruits and vegetables to their diet until they met their daily calorie goal. Persons who declined the use of meal replacements were provided

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

Characteristic	ILI (*N* = 2,570)	DSE (*N* = 2,575)	*P* value
Sex (number of participants)			
Female	1,526 (59.3)	1,537 (59.6)	0.85[a]
Male	1,044 (40.7)	1,038 (40.4)	
Ethnicity			
African American	399 (15.5)	404 (15.7)	0.28[a]
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[a]
Age (years)	58.6 ± 6.8	58.9 ± 6.9	0.12[b]
BMI (kg/m^2)			
Females	36.3 ± 6.2	36.6 ± 6.0	0.15[b]
Males	35.3 ± 5.7	35.1 ± 5.2	0.41[b]
Weight (kg)			
Females	94.8 ± 17.9	95.4 ± 17.3	0.34[b]
Males	108.9 ± 19.0	109.0 ± 18.0	0.94[b]

Values shown are means ± s.d. or frequency counts (with percentages).
DSE, Diabetes Support and Education; ILI, intensive lifestyle intervention.
[a]χ^2-test. [b]Analysis of covariance, adjusted for clinical center.

menu plans that specified conventional foods to be consumed (17,23). Meal plans were culturally tailored. During months 7–12, participants were instructed to replace one meal and one snack a day with shakes and bars to facilitate the maintenance of lost weight (24). The dietary intervention during this time also focused on eating more fruits and vegetables and other foods consistent with a low-energy-density diet (25). For the entire year, participants were instructed to record daily their food and calorie intake and to submit their records at each visit. Lifestyle counselors provided feedback on the records.

The ILI's physical activity goal was ≥175 min/week of moderately intense activity, to be achieved gradually by month 6. Persons who achieved this goal were encouraged to increase to ≥200 min/week from months 7 to 12. The activity program relied on unsupervised (at home) exercise which, for most participants, consisted of brisk walking. Participants recorded their weekly activity in their diaries; only bouts ≥10 min counted toward the weekly goal.

The ILI included a toolbox approach to help unsuccessful participants meet the study's diet and activity goals (17). In addition to problem solving (26) and motivational interviewing approaches (27,28), the toolbox included the weight loss medication, orlistat (29,30). The medication was used in three circumstances. First, participants who, after the first 6 months, had lost <5% of initial weight were encouraged by their lifestyle counselors to try orlistat and were shown a videotape that explained it. Second, participants who had lost ≥5% of initial weight but <10% were informed that they were eligible for the medication but were not expressly encouraged to take it. Third, participants who had lost ≥10% were not offered the medication because of its lack of efficacy in increasing weight loss beyond this amount (31). However, individuals in this category who, after month 6, regained ≥2% above their lowest weight (e.g., had lost 12.5% but regained to 10.5%) were allowed to take the medication to prevent further weight gain. Participants who took orlistat were monitored by a study physician (or nurse practitioner).

Dependent measures

Weight. Weight was measured on all participants at randomization and 1 year later using a digital scale (model BWB-800; Tanita, Willowbrook, IL). These weights were obtained by study staff (masked to participants' treatment status) and comprised the study's formal outcome weights. (Height was measured on the same schedule using a wall-mounted stadiometer.) Individuals in ILI also were weighed at each treatment visit by (unmasked) intervention staff who informed participants of their weight change. These weights were entered in a tracking system that provided staff monthly reports of their participants' weight losses. These data were used in the present report to provide information about weight loss during different phases of treatment.

Behavioral adherence. Three measures were used to estimate adherence to the prescribed treatment regimen. First, participants' attendance at all group and individual meetings was recorded by study staff. Second, we summed the weekly number of minutes of brisk physical activity that participants reported in their diaries. Third, weekly use of meal replacement products (shakes and bars), as recorded in food diaries, also was tracked. In cases in which participants failed to submit records of their physical activity or meal replacement use, they were asked to bring the data to their next visit. If they did not, they received a value of 0 for data missing for the week in question.

Statistical analyses

Differences between the DSE and the ILI groups in changes in weight were examined using ANOVA. The percentages of participants in the two groups who met different weight loss criteria (e.g., weight loss ≥7%) were compared using χ^2-tests. Randomization and 1-year weights, obtained by masked assessors, were used for all of these comparisons. Within the ILI condition, similar analyses were used to assess differences in weight loss among participants that were related to demographic factors. Data from the tracking system were used to compare differences between ILI participants that were related to session attendance, adherence to meal replacement and physical activity prescriptions, and the use of orlistat. For each family of comparisons, alpha was controlled using Bonferroni's method. As reported previously (4), the two groups did not differ significantly on any of the baseline characteristics shown in **Table 1**.

A total of 2,496 (97.1%) ILI and 2,463 (95.7%) DSE participants completed the 1-year assessment ($P = 0.004$). The 186 persons who did not complete the assessment were significantly ($P < 0.001$) more likely to be taking insulin than were completers (21.0 vs. 15.1%, respectively). The noncompleters included 101 individuals who missed the scheduled assessment and will be contacted for future follow-up visits. As described elsewhere (4), an additional 76 participants withdrew from the trial, and nine individuals died during the first year.

RESULTS

Weight loss in ILI and DSE groups

As reported previously (4), at the end of year 1, ILI participants lost 8.6 ± 6.9% of initial weight (8.6 ± 8.2 kg), compared to a significantly ($P < 0.001$) smaller 0.7 ± 4.8% (0.7 ± 5.0 kg) for individuals in DSE. As shown in **Figure 1**, 55.1% of ILI participants met the study-wide goal of losing ≥7% of initial weight, compared with only 7% of individuals in DSE ($P < 0.001$). As expected, significantly ($P < 0.001$) more ILI than DSE participants also lost ≥10% of initial weight (37.7 vs. 3.3%, respectively). Approximately 45% of DSE participants gained weight during the year, compared with only 7.3% of individuals in ILI ($P < 0.001$).

Use of insulin and other diabetes medications was associated with smaller weight losses. In the DSE group, weight losses for participants who took insulin, other diabetes medications, or no medications were 0.4 ± 5.1, 0.7 ± 4.7, and 1.0 ± 4.4%, respectively (with no significant differences among groups). Corresponding values in the ILI group were 7.4 ± 7.2, 8.7 ± 6.9, and 9.3 ± 6.8%, respectively. Participants on insulin lost significantly ($P < 0.002$) less weight than those in the two other groups (which did not differ significantly).

Weight loss within the ILI group

Participants in the ILI, taken together ($N = 2,570$), lost an average of 8.2 ± 5.7% at week 26, which increased to 8.7 ± 6.9% at 1 year. This 1-year value, which was calculated from data in the tracking system, differed by only 0.1% from that obtained when weights from the outcome ascertainment visits were analyzed (4).

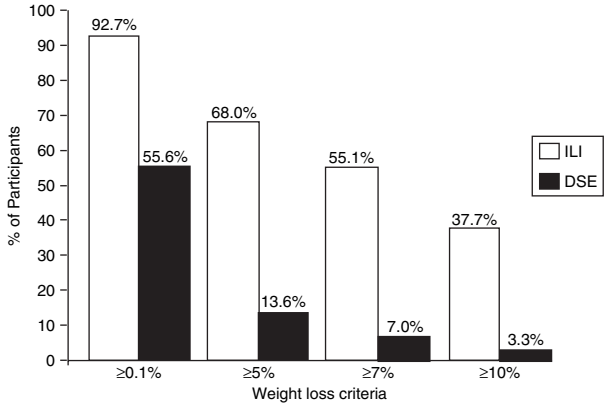

Figure 1 Percentage of participants in the intensive lifestyle intervention (ILI) and Diabetes Support and Education (DSE) groups that met different weight loss criteria.

Influence of demographic characteristics. Examining all participants in ILI, men lost significantly ($P < 0.001$) more weight than women at 1 year (9.2 ± 7.1 vs. 8.1 ± 6.8%). Among men, 58.5% met the study-wide criterion of a 7% weight loss, and 41.6% lost ≥10%. Comparable values for women were 52.9 and 35.2%, respectively. The study's oldest participants (65–74 years of age at baseline) lost a significantly ($P = 0.04$) greater percentage of initial weight than those in the middle group (55–64 years) or the youngest group (45–54 years), with 1-year losses of 9.4 ± 6.3, 8.5 ± 7.0, and 7.9 ± 7.2%, respectively. In each of these three age groups, 63.1, 54.6, and 50.0% met the 7% weight-loss criterion, respectively, and 44.7, 37.5, and 32.7% met the 10% criterion, respectively. No consistent effect of education on weight loss was observed. Participants with 13–16 years of education lost significantly ($P < 0.001$) less weight than those with >16 years, with participants with <13 years of education falling in between these two groups.

A significant relationship was observed between race/ethnicity and weight loss, as shown in **Figure 2**. At 1 year, non-Hispanic white participants lost 9.5 ± 7.3% of initial weight, compared to losses of 8.0 ± 6.2, 6.8 ± 5.4, and 5.5 ± 6.0% for Hispanic, African-American, and "other" participants, respectively (**Figure 3**). (Participants in the "other" category consisted principally of American Indians and are identified hereafter as American Indian/other.) ANOVA revealed that the four ethnic groups all differed significantly ($P < 0.001$) from each other, but there was not a statistically significant ethnicity-by-gender interaction. Additional analyses that controlled for age, education, income, and insulin use did not change the statistical differences among the four ethnic groups. Among the four groups, 60.5% of non-Hispanic whites, 53.3% of Hispanics, 45.5% of African Americans, and 35.8% of American Indians/others met the 7% weight-loss criterion. In addition, 43.5, 38.1, 24.7, and 18.8% of participants in the four groups, respectively, lost ≥10% of initial weight.

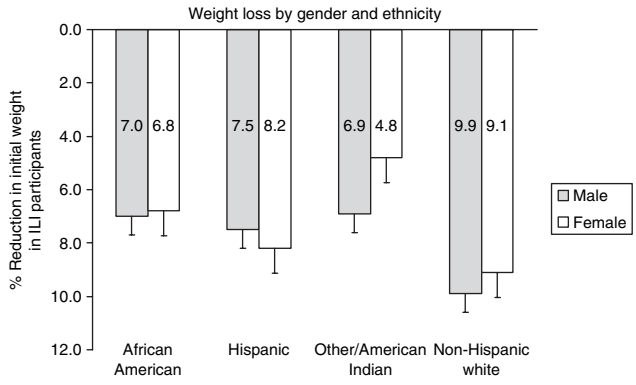

Figure 2 Percentage reduction in initial weight (in the ILI group) based on gender and ethnicity. ILI, intensive lifestyle intervention.

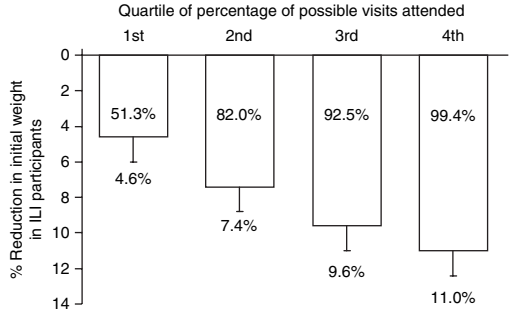

Figure 3 Percentage reduction in initial weight at 1 year based on quartile of percentage of possible visits attended. The number within each bar shows the mean percentage of visits attended for that quartile.

Treatment adherence and weight loss

During the first year, participants in ILI attended an average of 35.4 ± 7.3 of a possible 42 group and individual sessions. Correlation analysis revealed that the more sessions participants attended, the greater their weight loss at month 12 ($r = 0.31$, $P < 0.001$). Additional analyses, which divided participants into quartiles of attendance for year 1, showed that the odds (95% confidence interval) in favor of reaching the 7 and 10% weight loss goals for those in the highest quartile of attendance were 5.3 (4.0–7.0) and 8.1 (5.7–11.5) times the odds of the lowest quartile reaching the goals, respectively. **Figure 4** presents the weight losses for each of the four quartiles, based on percentage of possible treatment sessions attended during the first year.

Physical activity. Participants reported engaging in brisk physical activity an average of 136.7 ± 110.4 min/week during the

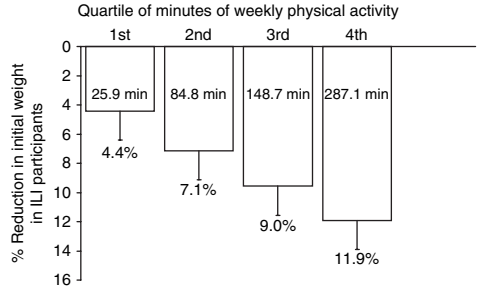

Figure 4 Percentage reduction in initial weight at 1 year based on quartile of average weekly minutes of self-reported physical activity. The number within each bar shows the mean number of weekly minutes of physical activity.

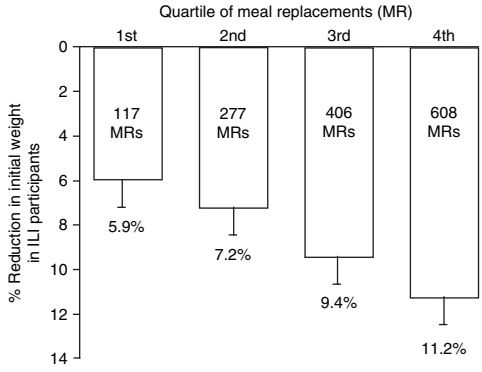

Figure 5 Percentage reduction in initial weight at 1 year based on quartile of meal replacement (MR) products used. The number within each bar shows the mean number of products used in that quartile.

first year. Correlation analysis revealed that the greater the minutes of weekly physical activity, the greater participants' weight loss at month 12 ($r = 0.41$, $P < 0.001$). The odds of reaching the 7 and 10% weight loss goals for participants in the highest quartile of physical activity were 7.5 (5.7–9.9) and 9.4 (6.8–13.0) times greater than the odds of participants in the lowest quartile, respectively. **Figure 5** presents weight loss based on quartiles of weekly minutes of physical activity.

Meal replacements. ILI participants reported consuming an average total of 233.3 ± 113.3 meal replacement products during the first 6 months, equal to 9.7 ± 5.1 per week during weeks 3–26 (when meal replacements were recommended). They consumed an average total of 127.6 ± 100.8 meal replacements from months 7 to 12, equal to 4.6 ± 4.1 per week during this time. The self-reported total consumption for the year averaged 360.9 ± 193.5. The number of meal replacements consumed in the first 6 months was significantly related to weight loss at week 26 ($r = 0.32$, $P < 0.001$), as was the total number consumed for the year to weight loss at week 52 ($r = 0.30$, $P < 0.001$). Participants in the highest quartile of meal replacement use had 4.0 (3.1–5.1) times greater odds of reaching the 7% weight loss goal and 4.1 (3.1–5.4) times greater odds of reaching the 10% goal than did participants in the lowest quartile. **Figure 6** presents the relation between quartile of meal replacement use and weight loss.

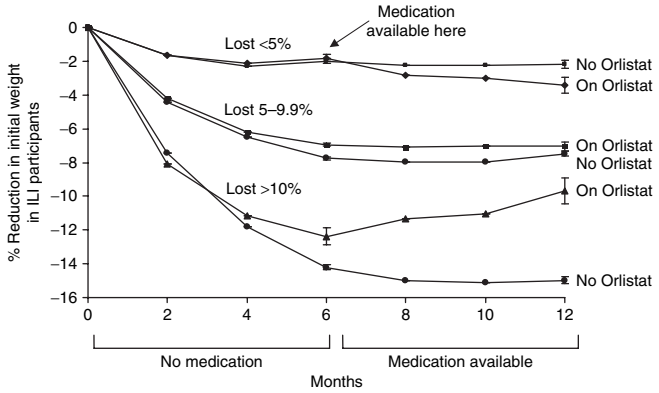

Figure 6 Percentage reduction in initial weight (in the ILI group) for individuals who did and did not receive orlistat after month 6. Individuals who had lost <5% of initial weight at month 6 were encouraged to use the medication. Those who had lost 5.0–9.9% were allowed to use orlistat upon request. For participants who had lost ≥10% at month 6, only those who had regained ≥2% points above their lowest weight were allowed to use medication. (Participants were not randomized to medication conditions.)

Intercorrelation of measures. Additional analyses showed that the three measures of adherence were highly correlated. Attendance correlated with physical activity ($r = 0.47$, $P < 0.001$) and meal replacement use ($r = 0.56$, $P < 0.001$), and the two latter variables also were positively related ($r = 0.51$, $P < 0.001$). Stepwise multiple regression, which allowed the model to enter the strongest variable first (i.e., Maximum R^2 procedure), revealed that minutes of physical activity accounted for 16.1% of the variance. This value increased to 19.0% with the addition of attendance and to 19.6% with the inclusion of meal replacements. All three variables contributed significantly ($P < 0.001$).

Adherence in relation to demographic characteristics

Table 2 presents findings for treatment adherence according to gender, age, and ethnicity. Over the year, men reported more weekly minutes of physical activity ($P < 0.05$) and greater total consumption of meal replacements ($P < 0.05$) than women. The study's oldest participants (65–74 years) had significantly ($P < 0.05$) better treatment attendance than did participants in the

Table 2 Participants' attendance at treatment sessions and self-reported physical activity and consumption of meal replacements

Characteristic	Number of treatment sessions attended during year 1	Average minutes of weekly physical activity during year 1	Total number of meal replacements used	
			6 Months	12 Months
Gender				
Male	35.8 ± 7.4[a]	173.7 ± 124.4[a]	239.4 ± 117.1[a]	374.2 ± 201.8[a]
Female	35.2 ± 7.2[a]	129.4 ± 96.2[b]	229.2 ± 110.5[b]	351.7 ± 187.0[b]
Age				
45–54 years	34.9 ± 7.3[a]	129.9 ± 97.5[a]	236.3 ± 113.0[a,b]	353.2 ± 197.3[a]
55–64 years	35.3 ± 7.5[a]	143.3 ± 109.7[a]	227.5 ± 111.8[a]	352.7 ± 189.3[a]
65–74 years	36.8 ± 6.4[b]	179.0 ± 121.5[b]	245.5 ± 116.8[b]	391.8 ± 197.4[b]
Ethnicity				
Non-Hispanic white	35.9 ± 6.9[a]	155.6 ± 115.5[a]	243.4 ± 115.8[a]	378.3 ± 199.8[a]
African American	35.6 ± 7.1[a,b]	125.8 ± 99.6[b]	228.2 ± 110.2[a,b]	343.1 ± 184.5[b]
Hispanic	34.5 ± 7.8[b]	151.2 ± 94.9[a]	215.2 ± 93.2[b,c]	340.0 ± 160.3[b]
American Indian/Other	32.2 ± 8.8[c]	113.8 ± 104.5[b]	186.4 ± 115.2[c]	280.5 ± 182.8[c]

Within columns and demographic groupings, values with different superscript letters (i.e., a, b, and c) differ significantly from each other ($P < 0.05$). Thus, for example, examining minutes of physical activity, men reported exercising significantly more minutes than women (a vs. b). By contrast, there was no significant difference between men and women in attendance, as shown by the shared superscript letter "a".

two younger age categories and reported significantly ($P < 0.05$) greater minutes of physical activity and total consumption of meal replacements. Examining race/ethnicity, non-Hispanic white, and African-American participants both attended ~36 treatment sessions during the year, which was significantly ($P < 0.001$) greater than the attendance observed in the American Indian/other group, with Hispanic participants falling in between these two groups. Self-reported physical activity was significantly ($P < 0.05$) greater in non-Hispanic white and Hispanic participants than in the African-American and American Indian/other groups. Non-Hispanic white participants reported significantly ($P < 0.05$) greater consumption of meal replacements over the year than all other groups, with Hispanic and African-American participants reporting significantly ($P < 0.05$) greater use than the American Indian/other group.

Weight loss controlling for treatment adherence. Differences in weight losses related to comparisons of gender, age, and race/ethnicity groups were reanalyzed (using analysis of covariance) to control for differences among these groups on the three measures of treatment adherence—attendance, physical activity, and meal replacements. Differences in weight loss, neither between men and women nor those among age groups, remained statistically significant after controlling for differences in treatment adherence. By contrast, weight losses of both non-Hispanic white and Hispanic participants remained significantly greater than those of African-American participants, as did differences among non-Hispanic whites and participants in the American Indian/other group. None of the remaining comparisons among the race/ethnicity groups remained statistically significant after controlling for the three measures of treatment adherence.

Use of orlistat

Of the 722 participants who lost <5% of initial weight in the first 6 months and were encouraged to take orlistat, 291 did so. **Figure 6** shows that those who took the medication had lost 1.8 ± 3.0% at month 6, compared with 2.0 ± 2.7% for those who did not. One-year weight losses of these two groups were 3.4 ± 7.3 and 2.2 ± 4.0%, respectively ($P < 0.02$). Of the 780 participants who had lost 5.0–9.9% at month 6 and were eligible (but not encouraged) to take medication, only 201 chose to. Six-month weight losses of those who elected to use the medication were significantly ($P < 0.001$) smaller than those of participants who declined it (6.9 ± 1.2 vs. 7.7 ± 1.5%). One-year weight losses were 6.9 ± 3.3 vs. 7.5 ± 3.4%, respectively ($P < 0.04$). Of the 838 participants who had lost ≥10% in the first 6 months, 412 were eligible to take the medication from months 7 to 12 by virtue of regaining ≥2% of their lost weight. The 31 individuals who chose to use orlistat had a mean loss of 12.6 ± 2.3% at month 6, compared to 14.1 ± 3.5% for those who did not use it ($P < 0.03$). One-year weight losses for the two groups were 9.8 ± 4.1 and 14.8 ± 6.0%, respectively ($P < 0.001$). The 523 total participants who took orlistat reported doing so for an average of 16.7 ± 8.8 weeks from months 7 to 12.

Further analyses showed that participants who were encouraged to take orlistat (i.e., <5% loss) attended significantly ($P < 0.001$) fewer treatment sessions during the first 6 months than those who were eligible (but not expressly encouraged) to take the medication (i.e., <10% loss) who, in turn, attended significantly ($P < 0.001$) fewer sessions than individuals who were ineligible to take the drug (i.e., >10% loss) (attendance of 21.4 ± 4.5, 23.3 ± 3.3, and 24.3 ± 2.7 sessions, respectively). A similar set of significant ($P < 0.001$) differences was observed between these three groups in their average minutes of physical activity per week during the first 6 months (i.e., 101.5 ± 82.9, 147.1 ± 98.6, and 196.1 ± 116.9 min/week, respectively) and in their total consumption of meal replacements during this time (i.e., 195.1 ± 112.3, 237.9 ± 105.8, and 270.7 ± 102.4 meals, respectively).

DISCUSSION

This study's principal finding was that an ILI induced a clinically significant weight loss in all subsets of a demographically and ethnically diverse population. Although a statistically significant difference in weight loss was observed between men and women (as expected), the absolute difference was small, and both genders achieved clinically significant reductions. The study's oldest participants (65–74 years) achieved significantly greater weight losses than the two younger age groups, but all three groups were within 1.5% of each other (with mean losses ranging from 7.9 to 9.4%). Similarly, African-American and Hispanic participants lost significantly less weight than non-Hispanic whites, consistent with findings from other multisite trials (5–7). However, weight losses achieved in this study are among the largest reported for either African-American or Hispanic participants, demonstrating the wide-scale acceptability of Look AHEAD's lifestyle intervention. American Indian/other participants achieved a mean loss of 5.5% which, while smaller than that of other ethnicities, is still sufficiently large to engender improvements in cardiovascular risk factors (2,16).

Participants' weight losses were related to their adherence to the study's treatment recommendations. Of the three measures of adherence, physical activity correlated most strongly with weight loss, accounting for 16.1% of the variance, as determined by multiple regression analysis. Participants in the highest quartile of self-reported physical activity lost 11.9% of initial weight, compared with only 4.4% for those in the lowest quartile. More frequent attendance at treatment sessions and greater consumption of meal replacements also were associated with greater weight loss, although to a lesser degree than physical activity (as determined by the regression analysis).

The design of this study prevents us from concluding that adherence to any of the three treatment factors caused greater weight loss. For example, participants who achieved high levels of physical activity may have done so because they had lost more weight (and felt more comfortable exercising), rather than activity causing their weight loss. However, randomized trials (32,33), as well as observational studies (34), have reported a positive relationship between weight loss and high levels of physical activity. In addition to burning calories, increased physical activity may contribute to weight management by sparing the loss of fat-free mass or by facilitating dietary adherence by controlling appetite and improving mood (35).

Randomized trials similarly have shown that meal replacements increase weight loss, compared with the consumption of a self-selected diet of conventional foods with the same calorie goal (20–22). Liquid meal replacements and other portion-controlled approaches appear to facilitate patients' adherence to their prescribed calorie targets (20–24). Controlled trials also have shown that the more treatment sessions participants are provided, the more weight they lose (35). Greater weight loss probably results from strengthening adherence to diet and activity recommendations, as suggested by the robust intercorrelations among the three measures in this study.

Differences in weight loss among some of the study's demographic groups appeared to be explained by differences in treatment adherence. Thus, the significantly greater weight losses observed in men than women and in the study's oldest participants (65 to 74 years) appeared to result from their greater treatment attendance, minutes of physical activity, and consumption of meal replacements. The analyses suggest that women would have lost as much weight as men, and younger participants as much as older ones, if they had adhered as closely to the study's treatment recommendations. By contrast, the significantly greater weight loss observed in non-Hispanic white participants, as compared with African Americans and Native Americans, was not eliminated by controlling for differences in physical activity, treatment attendance, and consumption of meal replacements. Smaller weight losses in these latter two groups could have been attributable to a variety of nontreatment-related factors. African-American women, for example, were found in previous studies to have a lower resting energy expenditure than age- and weight-matched non-Hispanic white women (36,37) and to have greater reductions in resting energy expenditure in response to weight loss (38,39), each of which could limit weight loss.

We note that the significantly lower treatment attendance of America Indian/other participants may have reflected significant economic barriers (e.g., lack of transportation) known at the study's outset. In addition, their lower reported minutes of physical activity and consumption of meal replacements are also likely a consequence of their attending fewer treatment sessions and, thus, having fewer opportunities to report their activity and food intake. Moreover, we believe that the data reported here underestimate physical activity and meal replacement use for all participants. If participants forgot to record these events in their diaries, or failed to submit a diary for a given week, they received a value of 0 for the number of minutes of physical activity for the week (as well as for the number of meal replacements consumed).

In addition to underscoring the importance of treatment adherence, the results of this study offer two other practical findings. The first is that insulin users can achieve clinically significant weight loss by participating in a comprehensive weight loss intervention (10–12). Although insulin users lost ~2% less weight than participants who took no diabetes medications, the more important finding was that patients on insulin still lost an impressive 7.4% of initial weight. The second finding is that persons 65–74 years of age appear to be acceptable candidates for weight loss trials, from which they now are frequently excluded. The oldest participants in this study were model citizens, in terms of their treatment adherence. Their achieving the largest weight losses of the three age groups confirms findings from the Diabetes Prevention Program (5). Older individuals may have more time and fewer barriers to participating than their younger counterparts. Analysis of body composition, however, is needed to ensure that the greater weight loss in older individuals was not attributable to a greater loss of lean tissue or bone (40).

Despite the lifestyle intervention's clear strengths, we note three limitations, the first of which is that the ILI participants were highly motivated and were provided intensive treatment, free of charge. Thus, the generalizability of the present findings to primary care practice is not known. Second, participants in ILI were weighed at each treatment visit by unmasked intervention staff, and these data were included in this report. To fully understand the treatment effects, the reader should use these data in conjunction with weight data obtained by masked study staff (on all participants) at outcome visits. A third limitation is that nearly one-third of ILI participants did not achieve a 5% reduction initial weight, a benchmark of clinically significant weight loss (16). During the first 6 months, these participants had significantly poorer adherence to the study's treatment recommendations than did those who lost ≥5% of initial weight. The use of orlistat by 291 of the former participants, during the second 6 months of treatment, increased weight loss only marginally, in contrast to expected reductions (29). There has been little research in weight management on methods to assist suboptimal or nonresponders. Over time, Look AHEAD will provide a rich data set with which to examine the effects of different "rescue" interventions for the induction or maintenance of weight loss.

In summary, an intensive group lifestyle intervention induced a mean loss of 8.6% of initial weight in overweight and obese participants with type 2 diabetes. The intervention was clinically effective in all subsets of an ethnically and demographically diverse population. Greater self-reported physical activity and consumption of meal replacements, as well as more frequent treatment attendance, were associated with greater weight loss. Study efforts are currently devoted to helping participants maintain their lost weight to have the best opportunity to determine whether intentional weight loss reduces cardiovascular mortality and morbidity.

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