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Weight Change Two Years after the Termination of the Intensive Lifestyle Intervention in the Look AHEAD Study

Ariana M Chao^{1,2}, Thomas A Wadden², Robert I Berkowitz², George Blackburn³, Paula Bolin⁴, Jeanne M Clark⁵, Mace Coday⁶, Jeffrey M Curtis⁴, Linda M Delahanty⁷, Gareth R Dutton⁸, Mary Evans⁹, Linda J Ewing¹⁰, John P Foreyt¹¹, Linda J Gay¹², Edward W Gregg¹³, Helen P Hazuda¹⁴, James O Hill¹⁵, Edward S Horton¹⁶, Denise K Houston¹⁷, John M Jakicic¹⁰, Robert W Jeffery¹⁸, Karen C Johnson⁶, Steven E Kahn¹⁹, William C Knowler⁴, Anne Kure¹⁹, Katherine L Michalski⁵, Maria G Montez¹⁴, Rebecca H Neiberg¹⁷, Jennifer Patricio²⁰, Anne Peters²¹, Xavier Pi-Sunyer²⁰, Henry Pownall¹¹, David Reboussin¹⁷, Bruce Redmon¹⁸, W Jack Rejeski¹⁷, Helmut Steinburg⁶, Martha Walker²¹, Donald A Williamson²², Rena R Wing¹², Holly Wyatt¹⁵, Susan Z Yanovski⁹, Ping Zhang¹³

¹Department of Biobehavioral Health Sciences, School of Nursing, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

²Department of Psychiatry, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

³Division of Nutrition, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.

⁴Southwestern American Indian Center, National Institute of Diabetes and Digestive and Kidney Diseases and St. Joseph's Hospital and Medical Center, Phoenix, Arizona, USA.

⁵Division of General Internal Medicine, Johns Hopkins University, Baltimore, Maryland, USA.

⁶Departments of Preventive Medicine and Psychiatry, The University of Tennessee Health Science Center, Memphis, Tennessee, USA.

⁷Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA.

⁸Division of Preventive Medicine, Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA.

⁹Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland, USA.

Correspondence: Ariana M. Chao, Ph.D., CRNP, University of Pennsylvania School of Nursing, 418 Curie Blvd, Philadelphia, PA 19104; Tel.: 215-746-7183; Fax: 215-615-1285; arichao@upenn.edu.

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All other Look AHEAD staffs are listed alphabetically by site.

¹⁰Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

¹¹Department of Medicine, Baylor College of Medicine, Houston, Texas, USA.

¹²Department of Psychiatry, The Miriam Hospital, Brown Medical School, Providence, Rhode Island, USA.

¹³Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

¹⁴Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA.

¹⁵Anschutz Health and Wellness Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA.

¹⁶Department of Integrative Physiology and Metabolism, Joslin Diabetes Center, Boston, Massachusetts, USA.

¹⁷Department of Internal Medicine - Geriatrics, Wake Forest University, Winston-Salem, North Carolina, USA.

¹⁸Divisions of Epidemiology and Community Health, University of Minnesota, Minneapolis, Minnesota, USA.

¹⁹Division of Metabolism, Endocrinology and Nutrition, US Department of Veterans Affairs Puget Sound Health Care System, University of Washington, Seattle, Washington, USA.

²⁰Department of Medicine, St. Luke's Roosevelt Hospital Center, Columbia University, New York, New York, USA.

²¹Division of Endocrinology, University of Southern California, Los Angeles, California, USA.

²²Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA.

Abstract

Objective: To evaluate weight changes after cessation of the 10-year intensive lifestyle intervention (ILI) in the Look AHEAD (Action for Health in Diabetes) study. We hypothesized that ILI participants would be more likely to gain weight during the 2-year observational period following termination of weight-loss-maintenance counseling than would participants in the Diabetes Support and Education (DSE) control group.

Methods: Look AHEAD was an RCT that compared the effects of ILI and DSE on cardiovascular morbidity and mortality in participants with overweight/obesity and type 2 diabetes. Look AHEAD was converted to an observational study in September 2012.

Results: Two years after the EOI, ILI and DSE participants lost a mean±SE of 1.2±0.2 kg and 1.8±0.2 kg, respectively (p=0.003). Thirty-one percent of ILI and 23.9% of DSE participants gained 2% (p<0.001) of EOI weight, while 36.3% and 45.9% of the two groups, respectively, lost 2% of EOI weight (p=0.001). Two years after the EOI, ILI participants reported greater use of weight-control behaviors than DSE participants.

Conclusions: Both groups lost weight during the 2-year follow-up period, but more ILI than DSE participants gained 2% of EOI weight. Further understanding is needed of factors that affected long-term weight change in both groups.

Clinical trials registration: [NCT00017953](#)

Keywords

overweight; obesity; obesity treatment; type 2 diabetes; weight loss

INTRODUCTION

Keeping off lost weight remains a key challenge in the behavioral treatment of obesity. Perri and colleagues demonstrated in a seminal series of studies that participants who lost approximately 8–10 kg with short-term behavioral interventions regained 40% or more of their lost weight in the year following treatment.^{1–3} These investigators further showed that providing participants every-other-week weight-loss-maintenance counseling, following initial weight loss, substantially reduced or eliminated this weight regain in maintenance programs that lasted up to 1 year. This was true of counseling provided in person or by phone.⁴ The investigators, however, found that once maintenance sessions ended, participants began to gain weight, suggesting that this counseling only delayed, rather than prevented, weight regain.^{1–3} Other researchers have demonstrated the benefits of every-other-week, as well as monthly weight-loss-maintenance sessions, in addition to the problem of weight regain following the termination of such interventions.^{5–7}

Look AHEAD (Action for Health in Diabetes) was a multi-center, randomized controlled trial that assessed whether intentional weight loss, achieved with an intensive lifestyle intervention (ILI), would reduce cardiovascular morbidity and mortality in participants with type 2 diabetes and overweight or obesity.^{8,9} The ILI was designed to induce a mean loss of 7% or more of initial weight the first year and to sustain this loss, with the provision of every-other-week and later monthly weight-loss-maintenance counseling, during an expected follow-up period of 8 to 11.5 years. After the first year of the intervention, ILI participants lost a mean of 8.6% of initial weight, compared with 0.7% for participants randomly assigned to a usual care group ($p < .001$), referred to as Diabetes Support and Education (DSE).¹⁰

Look AHEAD was stopped on September 14, 2012, based on a futility analysis that found no significant differences between the ILI and the DSE groups on the study's primary outcome, a composite of death from cardiovascular causes, nonfatal myocardial infarction or stroke, or hospitalization for angina.⁹ At study termination, participants had completed a median of 9.6 years of intervention, with a range of 8.4 years (for the trial's last enrollees in April 2004) to 11.0 years for the first enrollees (in September 2001). When the intervention ended, ILI participants had a mean loss of 6.0%, as measured from randomization, compared to 3.5% for DSE.⁹

With the termination of the randomized trial, Look AHEAD was converted to an observational cohort study to assess the effects of the ILI, compared to DSE, on a variety of

subsequent outcomes. The present report describes changes in body weight in ILI and DSE participants a mean±SD of 2.0±1.1 years (median of 1.6 years) after the end of the intervention. It compares mean differences in weight change (in kg) between groups, as well as the percentages of participants who gained weight (i.e., any amount and 2, 5, or 10% of end-of-intervention weight), and the percentages who lost weight (using similar criteria). Based on Perri's findings, we hypothesized that ILI participants would be more likely than their DSE counterparts to gain weight following termination of weight-loss-maintenance counseling.^{3,7,11} The study also examined differences between groups in their self-reported practice of diet and physical activity behaviors, previously shown to be associated with long-term weight loss.^{12,13}

METHODS

Participants and Procedures

Recruitment and random assignment of Look AHEAD participants have been described previously.^{8,14} The study enrolled 5,145 men and women from 2001–2004 at 16 centers across the U.S. Participants were ages 45–76 years and were required to have type 2 diabetes and a body mass index (BMI) ≥ 25 kg/m² (or ≥ 27 kg/m² if taking insulin). Participants were randomly assigned in equal numbers to ILI or DSE.

ILI participants received a comprehensive lifestyle intervention that provided one individual and three group (in-person) visits per month for 6 months, followed by one individual and two group visits per month in months 7–12.¹⁵ Participants were prescribed a diet of 1200–1800 kcal/d, based upon body weight, which included the use of meal replacements (e.g., shakes and bars) to help participants achieve their calorie targets.^{15–17} In years 2–4, they were provided one individual, in-person visit per month, with an additional monthly contact by telephone, e-mail, or mail. They also were offered optional monthly group meetings, as well as two to three annual refresher groups and national campaigns that focused principally on maintaining the weight losses and high levels of physical activity achieved in year 1.¹⁵ After year 4, participants were provided at least one individual in-person visit per month until the ILI was terminated. They also were encouraged to participate in the optional group meetings described previously.^{9,15} Participants in the DSE were invited to three group sessions per year for the first four years, with one annual meeting thereafter.¹⁶

Upon termination of the randomized trial, all participants were informed of the study's outcome and of the transition to an observational study. All were invited to continue in the Look AHEAD observational follow-up and provided informed consent.

For the present analyses of changes in body weight, participants were included if they completed an annual study assessment 1 year before the end of the intervention (between September 14, 2011 and September 14, 2012) and at least one of two planned assessment visits following the termination of the trial. Participants who had undergone bariatric surgery were excluded.

Study Assessments

Weight and height were assessed, using methods described previously, at approximately annual visits during the first 2 years of the observational study.^{8,9} Participants completed questionnaires on physical activity as assessed by the Paffenbarger Activity Questionnaire (PAQ), and self-reported the number of weeks in the prior year in which they engaged in behaviors previously determined to be associated with long-term weight control: 1) increasing physical activity; 2) monitoring body weight; 3) reducing calorie and fat intake; and 4) using meal replacements.^{13,18} All participants completed these questionnaires at their 8-year post-randomization assessment and then again at an average of 2.0 years following the end of the intervention (average of 11.7 years post-randomization).

Statistical Analyses

The present analyses focused on the first two visits after the end of intervention (EOI). The baseline visit for this analysis was considered the last visit that occurred in the year prior to the EOI. Models of weight change (in kg) from the baseline EOI visit to visits 1 and 2 years after EOI (during the observational study) were adjusted for race, gender, current age, weight at EOI baseline, and repeated measures. Analyses were also repeated including, as a covariate, the amount of weight lost during the original randomized intervention. Differences between the original ILI and DSE groups in categorical weight changes from the EOI visit to a mean follow-up of 2.0 years were compared using a Chi-squared test. Categories of weight change included any weight gain (0%) and gains 2%, 5%, and 10% of EOI weight. Comparable weight loss categories were used (i.e., any loss and 2%, 5%, and 10% of EOI weight). A second analysis further categorized participants as: 1) having remained essentially weight stable during the 2-year period, as indicated by a gain or loss <2% of EOI; 2) having gained weight (i.e., 2% gain of EOI weight); or 3) having lost weight (2% loss of EOI weight). Similar criteria for weight stability have been used previously.¹⁹

Differences between the ILI and DSE groups in the practice of weight-control behaviors, after the EOI were analyzed using linear regression for continuous variables and logistic regression for categorical variables. Analyses were adjusted for weight change from randomization to EOI and weight change strategy use measured closest to the end of intervention (i.e., year 8). Within each randomization group, similar analyses were also conducted to examine differences in the practice of weight-control behaviors, based on weight stability during the 2-year period (gain or loss <2% of EOI weight), weight gain 2% of EOI weight, and weight loss 2% of EOI weight. In the linear regression analyses, pairwise tests used the Bonferroni adjustment for multiple comparisons. Correlations between weight change in ILI and DSE in the first 2 years after the EOI and each of the weight-control behaviors were investigated using partial correlation tests, adjusting for weight loss from randomization to the EOI and year 8 behavioral strategy use.

Additional analyses compared mean weight change in the two groups from the study's original randomization over a mean follow-up of 11.7 years (including a mean of 2 years of follow-up after the EOI). Analyses were adjusted for race, gender, baseline age, and baseline

weight in addition to repeated measures. Similar analyses were conducted examining categorical weight changes.

RESULTS

Participant Characteristics

Figure 1 shows the study's recruitment, randomization, enrollment, and follow-up. Of the 3965 surviving members of the original Look AHEAD study, 3739 participants continued to participate during the observational period and are included in the present analyses. Visits 1 and 2 after the EOI were completed by a similar proportion of participants in ILI (94.9% and 94.4%, respectively) and DSE (93.8% and 93.2%, respectively) (between-group difference after 1 year, $p=0.15$, after 2 years, $p=0.12$).

The characteristics of these 3739 participants are summarized in Table 1. The table shows their characteristics at the time of randomization to ILI and DSE and again at the EOI. ILI and DSE participants did not differ significantly on characteristics at randomization. At this time, the mean \pm SD weight for the ILI group was 99.6 \pm 19.3 kg, compared with 100.0 \pm 18.4 kg for DSE participants. At the EOI, ILI participants weighed 94.1 \pm 19.6 kg, which was significantly less than the 97.2 \pm 19.8 kg for DSE group ($p<0.001$).

Weight Change After EOI

On average, both the ILI and DSE participants lost weight 2 years after the EOI (Figure 2). ILI participants lost a mean \pm SE of 1.2 \pm 0.2 kg (1.1 \pm 0.2%) from EOI to 2 years post-EOI, compared to a significantly greater 1.8 \pm 0.2 kg (1.7 \pm 0.2%) for the DSE group ($p=0.003$ for kg and $p<0.001$ for percent weight loss between ILI and DSE). Similar results and statistical conclusions were obtained after adjusting for weight change from randomization to the EOI.

Figure 3 shows that over the mean 2 years of follow-up after the EOI, 48.9% and 38.9% of the original ILI and DSE participants, respectively, gained weight (i.e., any amount) ($p<0.001$). Approximately 31.0% and 23.9% of ILI and DSE participants, respectively, gained 2% of EOI weight ($p<0.001$), 13.9% and 11.6%, respectively, gained 5% ($p=0.05$), and 3.2% and 2.8%, respectively, gained 10% ($p=0.53$). (These values are cumulative. For example, the 31.0% of ILI participants who gained 2% of EOI weight includes the 13.9% who gained 5%.) By contrast, 51.1% of the ILI participants lost weight (i.e., any amount) after the EOI, compared with 61.2% of the DSE group ($p<0.001$); 36.3% and 45.9% of ILI and DSE participants, respectively, lost 2% of EOI weight ($p<0.001$), 20.1% and 24.4%, respectively, lost 5% ($p=0.003$), and 6.9% and 8.1%, respectively, lost 10% of EOI weight ($p=0.17$). Defining weight stability during the 2-year period as a gain or loss $<2\%$ of EOI weight revealed that 32.8% of ILI and 30.2% of DSE participants were weight stable ($p<0.001$).

Correlates of Weight Change After EOI

Weight change after the EOI was significantly associated with weight change during the intervention phase of Look AHEAD (as measured from randomization to the EOI; $\text{Rho}=-0.19$, $p<0.001$). The correlation between weight change (in kg) from Look AHEAD

randomization to the EOI and weight change (in kg) from EOI through the mean 2 years of follow-up after EOI was $r=-0.17$ ($p<0.001$) in ILI and $r=-0.19$ ($p<0.001$) in DSE. After adjusting for randomization weight (in kg), the correlation between weight change from Look AHEAD randomization to the EOI and the weight change from EOI through 2 years of follow-up after EOI was $r=-0.20$ ($p<0.001$) in ILI and $r=-0.20$ ($p<0.001$) in DSE. Thus, in both ILI and DSE participants, those who lost more weight during the randomized trial tended to have less weight loss in the 2 years of follow-up after EOI, although these effects were small. In a general linear model, weight change in kg from the EOI through 2 years of follow-up was associated with weight change from randomization to the EOI ($\beta = -0.15$, $SE=0.01$, $p<0.001$), age ($\beta = -0.06$, $SE=0.02$, $p=0.001$), female sex (vs male, $\beta = -0.72$, $SE=0.26$, $p=0.005$), and randomization weight in kg ($\beta = -0.05$, $SE=0.01$, $p<0.001$). Randomization arm ($p=0.12$), race ($p=0.35$), and duration of participation in the Look AHEAD trial (ranging from 8.2 to 11.0 years; $p=0.79$), were not significantly associated with weight change from EOI through 2 years of follow-up after EOI in these adjusted models.

Practice of Weight Control Behaviors After EOI

Table 2 presents participants' reports of their physical activity and practice of weight-control behaviors, as assessed 8 years following randomization and a mean of 2 years after the EOI, as well as the change in behaviors over this time. ILI participants, as compared with DSE, reported significantly more physical activity and weight-control behaviors 8 years following randomization. After the EOI, ILI participants continued to report significantly greater weekly energy expenditure (from leisure time physical activity) than DSE participants. However, they did not report trying to increase their physical activity in more weeks of the past year than did DSE participants. ILI participants, compared with DSE, reported using all other weight-control behaviors for a significantly greater number of weeks after the EOI (including reducing calorie and fat intake, using meal replacements, and weighing themselves on a regular basis). However, the frequency with which ILI participants reported practicing these behaviors was significantly less than reported at the 8-year assessment (Table 2). ILI participants, compared with DSE, reported a significantly greater reduction in the practice of all behaviors, except leisure time physical activity, during the EOI follow-up period (all $ps<0.001$; Table 2). ILI participants were less likely to weigh daily or weekly 2 years after the EOI compared to year 8, while the DSE group showed no difference in odds of daily or weekly self-weighing during the same time period (both $ps<0.01$).

Additional analyses within the ILI group revealed that greater practice of self-weighing, as well as reducing calorie and fat intake, reported 2 years following EOI, were associated with losing 2% from the EOI to 2 years of follow-up. (Table 3). No other behaviors were related to weight loss during this time. Within DSE, participants who gained 2% of EOI weight reported significantly fewer weeks of increased exercise compared to participants who lost 2% (Table 3). Partial correlations, shown in Table 4, also demonstrated that greater improvements in self-weighing, as well as in the number of reported weeks of reducing calorie and fat intake, were associated with greater weight loss from the EOI to 2 years afterwards. In the DSE group, greater increases in physical activity also were associated with greater weight loss. Correlations were very small ($r= -0.05$ to -0.13) in all cases.

Weight Loss from Randomization

Figure 4 presents percentage reduction in baseline weight for the original ILI and DSE participants as measured from randomization to 2 years after the EOI. When the intervention was terminated in September 2012, the 3739 ILI and DSE participants who provided an EOI weight had lost a mean of 5.3 and 2.6% of randomization weight, respectively ($p < 0.001$). Two years after EOI, these two groups achieved mean losses of -6.1% and -4.1% of randomization weight, respectively ($p < 0.001$; see Figure 4). From randomization to 2 years after EOI, a greater percentage of ILI than DSE participants lost 5% of body weight (57.2% vs 47.0% ; $p < 0.001$; see Figure S1), as well as 10% (34.8% vs 27.4% ; $p < 0.001$). The ILI group had a significantly smaller percentage of participants who exceeded their randomization weight at 2 years after EOI than did the DSE (23.7% vs 31.0% ; $p < 0.001$).

DISCUSSION

ILI participants, on average, lost 1.2 kg during the 2-year observational period following termination of the lifestyle intervention, compared with a mean loss of 1.8 kg for DSE participants. As anticipated, more ILI than DSE participants gained weight during the follow-up period; 31.0% vs 23.9% of these participants, respectively, gained 2% or more of their EOI weight over the 2 years. However, members of Look AHEAD's lifestyle intervention subcommittee had been concerned that substantially more ILI participants would be vulnerable to weight gain. This concern was based on findings of mean weight regain of 1–2 kg in the first year following termination of approximately 12–15 month weight-loss-maintenance programs.¹⁻⁵

Post-EOI weight losses in the ILI group are difficult to interpret in the absence of results from similar long-term (5 years) randomized trials of participants with characteristics similar to those of our Look AHEAD sample.^{5,20-22} ILI participants, on average, had already regained about 4 percentage points of their first-year weight loss in years 2–5 of the intervention, after which (on average) they began to lose weight again, which continued during the 2-year EOI period (Figure 4). This resumed, late weight loss may have been attributable, in part, to our participants' relatively older age (i.e., 68 years at the start of the EOI), compared to that of individuals in most prior behavioral weight-loss-maintenance trials (i.e., typically 40–55 years).⁵ Body weight generally increases until about age 60 years, when it tends to plateau and then starts to decrease.²³ Resumed, late weight loss may also be explained by our selection of patients with type 2 diabetes, who typically have not been included in long-term (5 years) behavioral weight loss trials. In a prospective, observational study, Looker et al found that individuals gained weight prior to their diagnosis with type 2 diabetes but then, on average, lost weight steadily through up to 25 years of follow-up.²⁴ Similar results have been reported in other cohort studies of patients with type 2 diabetes.²⁵⁻²⁷

The mean post-EOI weight loss of 1.8 kg in our DSE participants also is unusual for a control group in a weight-loss maintenance study.⁵ However, the losses are consistent with the prior accelerated reductions in body weight observed in these participants beginning at year 5 of Look AHEAD, as well as with long-term weight losses that may be associated with

aging, type 2 diabetes (or other illness), medication use, or other factors, as noted with our ILI participants.^{13,23-27}

On average, ILI participants had greater declines in the self-reported use of weight-control behaviors 2 years after the EOI than did DSE participants. However, the overall practice of these behaviors was still greater in ILI than DSE participants 2 years after the EOI. Consistent with previous studies, participants in the ILI group who reported more frequent daily or weekly self-monitoring of their weight and more weeks of reducing their calorie and fat intake were more likely to lose weight during the 2-year EOI period.¹² However, associations between weight change and change in behaviors from post-randomization year 8 to 2 years after the EOI were very modest; each variable explained less than 1% of the variance in weight change. The same modest associations were observed in the DSE participants as in the ILI group.

As measured from randomization to 2 years after EOI, ILI participants achieved a mean percentage reduction in initial weight of 6.1%, compared with a significantly smaller 4.1% for DSE. The ILI group has consistently had larger weight losses than the DSE group throughout the randomized trial -- and now after the first 2 years of the observational study. The differences, however, in both mean and categorical weight losses between the two groups have declined steadily since the end of the first year of the intervention, when ILI and DSE had lost 8.6% and 0.7% of randomized weight, respectively.¹⁰ The narrowing of the difference was due in years 2–5 to the previously described mean weight regain in ILI participants (Figure 4).^{13,28} Since approximately year 6, the narrowing has been more attributable to accelerated weight loss in the DSE group, which continued to be observed during the 2 year EOI follow-up.¹³ We note that DSE participants were not provided behavioral weight loss counseling at anytime during the 10-year intervention or the present 2-year EOI period, in contrast to participants in the control (placebo) arm of the Diabetes Prevention Program (DPP), who received a group behavioral intervention when that trial was terminated early because of treatment benefit.²¹

Set point theory would suggest that the ILI and DSE weight loss curves will eventually meet, as has been occurring.^{29,30} This theory would conjecture that the fall in body weight in the DSE group is the likely consequence of aging, illness, and other factors mentioned previously.^{23–27} If the ILI participants had not received the lifestyle intervention, their body weight could have been expected to follow the same pattern of gradual decline observed in the DSE group.

According to set point theory, the lifestyle intervention can be viewed as having driven down participants' body weight, at the end of the first year of the intervention, below their pre-treatment set point, only to have weight rebound toward the control group's (DSE's) weight in years 2–4. This rebound occurred despite ILI participants continuing to be provided weight-loss maintenance counseling during this time. Numerous laboratory studies have demonstrated this weight rebound in food- and weight-restricted animals relative to controls.^{31,32}

From a long-term perspective, of 15 or more years, the ILI could be viewed as expediting the weight loss that could be expected in an older population of individuals with type 2 diabetes. Even though the ILI and DSE participants may eventually achieve the identical long-term weight losses, the paths by which they achieved weight reduction differed markedly, and weight loss at 1, 4, and 8 years in the ILI was associated with clinically meaningful improvements in sleep apnea, chronic kidney disease, physical mobility, and physical health-related quality of life, as compared to the DSE.^{33–36} A critical question that Look AHEAD will ultimately address is whether intentional, substantial weight loss, even if followed by partial weight regain, has a net benefit to overall morbidity and mortality, compared to the pattern of weight change observed in the DSE group.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

Data sharing statement: Look AHEAD data are available through the NIH/NIDDK Central Repository. <https://repository.niddk.nih.gov/home/> These data sets include de-identified participant level data. At this time data are available beginning with the recruitment and randomization of participants (2001) through the end of the Look AHEAD intervention (2012), or approximately 9 years of trial data on each participant. The study protocol, data collection forms, and data dictionaries are provided at this link. Requests for data are made through the NIDDK.

Appendix

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Look AHEAD Research Group; Ariana M. Chao, PhD, CRNP; Thomas A. Wadden, PhD; Robert I. Berkowitz, MD; George Blackburn, MD, PhD; Paula Bolin, RN, MC; Jeanne M. Clark, MD, MPH; Mace Coday, PhD; Jeffrey M. Curtis, MD, MPH; Linda M. Delahanty, MS, RDN; Gareth R. Dutton, PhD; Mary Evans, PhD; Linda J. Ewing, PhD; John P. Foreyt, PhD; Linda J. Gay; Edward W. Gregg, PhD; Helen P. Hazuda, PhD; James O. Hill, PhD; Edward S. Horton, MD; Denise K. Houston, PhD; John M. Jakicic, PhD; Robert W. Jeffery, PhD; Karen C. Johnson, MD, MPH; Steven E. Kahn, MB, ChB; William C. Knowler, MD; Anne Kure, BS; Katherine L. Michalski, RD; Maria G. Montez, RN, MSHP, CDE; Rebecca H. Neiberg, MS; Jennifer Patricio, MS; Anne Peters, MD; Xavier Pi-Sunyer, MD; Henry Pownall, PhD; David Reboussin, PhD; Bruce Redmon, MD; W. Jack Rejeski, PhD; Helmut Steinburg, MD; Martha Walker, RD; Donald A. Williamson, PhD, FTOS; Rena R. Wing, PhD; Holly Wyatt, MD; Susan Z. Yanovski, MD; Ping Zhang, PhD

Correspondence: Ariana M. Chao, Ph.D., CRNP, University of Pennsylvania School of Nursing, 418 Curie Blvd, Philadelphia, PA 19104; Tel.: 215–746-7183; Fax: 215–615-1285; Email: arichao@upenn.edu

Look AHEAD Research Group

Members of the writing group included:

Ariana M. Chao, PhD, CRNP; Thomas A. Wadden, PhD; Edward S. Horton, MD; Denise K. Houston, PhD; Steven E. Kahn, MB, ChB; Rebecca Neiberg, MS; Anne L. Peters, MD; F. Xavier Pi-Sunyer, MD; David M. Reboussin, PhD; Rena R. Wing, PhD; Susan Z. Yanovski, MD

Study authors included:

Ariana M. Chao, PhD, CRNP; Thomas A. Wadden, PhD; Robert I. Berkowitz, MD; George Blackburn, MD, PhD; Paula Bolin, RN, MC; Jeanne M. Clark, MD, MPH; Mace Coday, PhD; Jeffrey M. Curtis, MD, MPH; Linda M. Delahanty, MS, RDN; Gareth R. Dutton, PhD; Mary Evans, PhD; Linda J. Ewing, PhD; John P. Foreyt, PhD; Linda J. Gay; Edward W. Gregg, PhD; Helen P. Hazuda, PhD; James O. Hill, PhD; Edward S. Horton, MD; Denise K. Houston, PhD; John M. Jakicic, PhD; Robert W. Jeffery, PhD; Karen C. Johnson, MD, MPH; Steven E. Kahn, MB, ChB; William C. Knowler, MD; Anne Kure, BS; Katherine L. Michalski, RD; Maria G. Montez, RN, MSHP, CDE; Rebecca H. Neiberg, MS; Jennifer Patricio, MS; Anne Peters, MD; Xavier Pi-Sunyer, MD; Henry Pownall, PhD; David Reboussin, PhD; Bruce Redmon, MD; W. Jack Rejeski, PhD; Helmut Steinburg, MD; Martha Walker, RD; Donald A. Williamson, PhD, FTOS; Rena R. Wing, PhD; Holly Wyatt, MD; Susan Z. Yanovski, MD; Ping Zhang, PhD

Look AHEAD Research Group at End of Continuation

Clinical Sites

The Johns Hopkins University: Frederick L. Brancati, MD, MHS^{1*}; Jeanne M. Clark, MD, MPH¹ (Co-Principal Investigators); Lee Swartz²; Jeanne Charleston, RN³; Lawrence Cheskin, MD³; Richard Rubin, PhD^{3*}; Jean Arceci, RN; David Bolen; Danielle Diggins; Mia Johnson; Joyce Lambert; Sarah Longenecker; Kathy Michalski, RD; Dawn Jiggetts; Chanchai Sapun; Maria Sowers; Kathy Tyler

Pennington Biomedical Research Center: George A. Bray, MD¹; Allison Strate, RN²; Frank L. Greenway, MD³; Donna H. Ryan, MD³; Donald Williamson, PhD³; Timothy Church, MD³; Catherine Champagne, PhD, RD; Valerie Myers, PhD; Jennifer Arceneaux, RN; Kristi Rau; Michelle Begnaud, LDN, RD, CDE; Barbara Cerniauskas, LDN, RD, CDE; Crystal Duncan, LPN; Helen Guay, LDN, LPC, RD; Carolyn Johnson, LPN, Lisa Jones; Kim Landry; Missy Lingle; Jennifer Perault; Cindy Puckett; Marisa Smith; Lauren Cox; Monica Lockett, LPN

The University of Alabama at Birmingham: Cora E. Lewis, MD, MSPH¹; Sheikilya Thomas, PhD, MPH²; Monika Safford, MD³; Stephen Glasser, MD³; Vicki DiLillo, PhD³; Gareth Dutton, PhD, Charlotte Bragg, MS, RD, LD; Amy Dobelstein; Sara Hannum; Anne

¹Principal Investigator

*deceased

²Program Coordinator

³Co-Investigator

Hubbell, MS; Jane King, MLT; DeLavallade Lee; Andre Morgan; L. Christie Oden; Janet Wallace, MS; Cathy Roche, PhD, RN, BSN; Jackie Roche; Janet Turman

Harvard Center

Massachusetts General Hospital.: David M. Nathan, MD¹; Enrico Cagliero, MD³; Heather Turgeon, RN, BS, CDE²; Barbara Steiner, EdM; Valerie Goldman, MS, RDN²; Linda Delahanty, MS, RDN³; Ellen Anderson, MS, RDN³; Laurie Bissett, MS, RDN; Christine Stevens, RN; Mary Larkin, RN; Kristen Dalton, BS, Roshni Singh, BS

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The University of Tennessee Health Science Center

University of Tennessee East.: Karen C. Johnson, MD, MPH; Karen L. Wilson, BSN; Mace Coday, PhD³; Beate Griffin, RN, BS; Donna Valenski; Polly Edwards; Brenda Fonda; Kim Ward

University of Tennessee Downtown.: Helmut Steinburg, MD³; Carolyn Gresham, BSN; Moana Mosby, RN; Debra Clark, LPN; Donna Green RN; Abbas E. Kitabchi, PhD, MD (retired)

University of Minnesota: Robert W. Jeffery, PhD¹; Tricia Skarphol, MA²; John P. Bantle, MD³; J. Bruce Redmon, MD³; Richard S. Crow, MD³; Scott J. Crow, MD³; Manami Bhattacharya, BS; Cindy Bjerck, MS, RD; Kerrin Brelje, MPH, RD; Carolyne Campbell; Mary Ann Forseth, BA; Melanie Jaeb, MPH, RD; Philip Lacher, BBA; Patti Laqua, BS, RD; Birgitta I. Rice, MS, RPh, CHES; Ann D. Tucker, BA; Mary Susan Voeller, BA

St. Luke's Roosevelt Hospital Center: Xavier Pi-Sunyer, MD¹; Jennifer Patricio, MS²; Carmen Pal, MD³; Lynn Allen, MD; Janet Crane, MA, RD, CDN; Lolline Chong, BS, RD; Diane Hirsch, RNC, MS, CDE; Mary Anne Holowaty, MS, CN; Michelle Horowitz, MS, RD; Raashi Mamtani, MS

University of Pennsylvania: Thomas A. Wadden, PhD¹; Barbara J. Maschak-Carey, MSN, CDE²; Robert I. Berkowitz, MD³; Gary Foster, PhD³; Henry Glick, PhD³; Shiriki Kumanyika, PhD RD, MPH³; Yuliis Bell, BA; Raymond Carvajal, PsyD; Helen Chomentowski; Renee Davenport; Lucy Faulconbridge, PhD; Louise Hesson, MSN, CRNP; Sharon Leonard, RD; Monica Mullen, RD, MPH

University of Pittsburgh: John M. Jakicic, PhD¹; David E. Kelley, MD¹; Jacqueline Wesche-Thobaben, RN, BSN, CDE²; Daniel Edmundowicz, MD³; Lin Ewing, PhD, RN³; Andrea Hergenroeder, PhD, PT, CCS³; Mary L. Klem, PhD, MLIS³; Mary Korytkowski, MD³; Andrea Kriska, PhD³; Lewis H. Kuller, MD, DrPH³; Amy D. Rickman, PhD, RD, LDN³; Rose Salata, MD³; Monica E. Yamamoto, DrPH, RD, FADA³; Janet Bonk, RN, MPH; Susan Copelli, BS, CTR; Rebecca Danchenko, BS; Tammy DeBruce, BA; Barbara Elnyczky; David O. Garcia, PhD; George A. Grove, MS; Patricia H. Harper, MS, RD, LDN; Susan Harrier, BS; Diane Heidingsfelder, MS, RD, CDE, LDN; Nicole L. Helbling, MS, RN; Diane Ives, MPH; Janet Krulia, RN, BSN, CDE; Juliet Mancino, MS, RD, CDE, LDN; Anne Mathews, PhD, RD, LDN; Lisa Martich, BS, RD, LDN; Meghan McGuire, MS; Tracey Y. Murray, BS; Anna Peluso, MS; Karen Quirin; Jennifer Rush, MPH; Joan R. Ritchea; Linda Semler, MS, RD, LDN; Karen Vujevich, RN-BC, MSN, CRNP; Kathy Williams, RN, MHA; Donna L. Wolf, PhD

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The University of Texas Health Science Center at San Antonio: Helen p. Hazuda, PhD¹; Maria G. Montez, RN, MSHP, CDE²; Carlos Lorenzo, MD³; Charles F. Coleman, MS, RD; Domingo Granado, RN; Kathy Hathaway, MS, RD; Juan Carlos Isaac, RC, BSN; Nora Ramirez, RN, BSN

VA Puget Sound Health Care System / University of Washington: Steven E. Kahn, MB, ChB¹; Anne Kure, BS²; Edward J. Boyko, MD, MPH³; Edward Lipkin, MD, PhD³; Dace Trencze, MD³; Subbulaxmi Trikudanathan, MD, MRCP, MMSc³; Elaine Tsai, MD³; Brenda Montgomery, RN, MS, CDE; Ivy Morgan-Taggart; Jolanta Socha, BS; Lonnesse Taylor, RN, BS; Alan Wesley, BA

Southwestern American Indian Center, Phoenix, Arizona and Shiprock, New Mexico:

William C. Knowler, MD, DrPH¹; Paula Bolin, RN, MC²; Tina Killean, BS²; Maria Cassidy-Begay, BSND, RND²; Katie Toledo, MS, LPC²; Cathy Manus, LPN³; Jonathan Krakoff, MD³; Jeffrey M. Curtis, MD, MPH³; Sara Michaels, MD³; Paul Bloomquist, MD³; Peter H. Bennett, MB, FRCP³; Bernadita Fallis, RN, RHIT, CCS; Diane F. Hollowbreast; Ruby Johnson; Maria Meacham, BSN, RN, CDE; Christina Morris, BA; Julie Nelson, RD; Carol Percy, RN, MS; Patricia Poorthunder; Sandra Sangster; Leigh A. Shovestull, RD, CDE; Miranda Smart; Janelia Smiley; Teddy Thomas, BS

University of Southern California: Anne Peters, MD; Siran Ghazarian, MD; Elizabeth Beale, MD; Kati Konersman, RD, CDE; Brenda Quintero-Varela; Edgar Ramirez; Gabriela Rios, RD; Gabriela Rodriguez, MA; Valerie Ruelas MSW, LCSW; Sara Serafin-Dokhan; Martha Walker, RD

Coordinating Center

Wake Forest University: Mark A. Espeland, PhD¹; Judy L. Bahnson, BA, CCRP³; Lynne E. Wagenknecht, DrPH¹; David Reboussin, PhD³; W. Jack Rejeski, PhD³; Alain G. Bertoni, MD, MPH³; Wei Lang, PhD³; David Lefkowitz, MD³; Patrick S. Reynolds, MD³; Denise Houston, PhD³; Mike E. Miller, PhD³; Laura D. Baker, PhD³; Nicholas Pajewski, PhD³; Stephen R. Rapp, PhD³; Stephen Kritchevsky, PhD³; Haiying Chen, PhD, MM³; Valerie Wilson, MD³; Delia S. West, PhD³; Ron Prineas, MD³; Tandaw Samdarshi, MD³; Amelia Hodges, BS, CCRP²; Karen Wall²; Carrie C. Williams, MA, CCRP²; Andrea Anderson, MS; Jerry M. Barnes, MA; Tara D. Beckner; Delilah R. Cook; Valery S. Effoe, MD, MS; Melanie Franks, BBA; Katie Garcia, MS; Sarah A. Gaussoin, MS; Candace Goode; Michelle Gordon, MS; Lea Harvin, BS; Mary A. Hontz, BA; Don G. Hire, BS; Patricia Hogan, MS; Mark King, BS; Kathy Lane, BS; Rebecca H. Neiberg, MS; Julia T. Rushing, MS; Debbie Steinberg, BS; Jennifer Walker, MS; Michael P. Walkup, MS;

Central Resources Centers

Central Laboratory, Northwest Lipid Metabolism and Diabetes Research Laboratories: Santica M. Marcovina, PhD, ScD¹; Jessica Hurting²; John J. Albers, PhD³; Vinod Gaur, PhD⁴

ECG Reading Center, EPICARE, Wake Forest University School of Medicine: Elsayed Z. Soliman MD, MSc, MS¹; Charles Campbell²; Zhu-Ming Zhang, MD³; Mary Barr; Susan Hensley; Julie Hu; Lisa Keasler; Yabing Li, MD

Hall-Foushee Communications, Inc.: Richard Foushee, PhD; Nancy J. Hall, MA

Federal Sponsors

National Institute of Diabetes and Digestive and Kidney Diseases: Mary Evans, PhD; Van S. Hubbard, MD, PhD; Susan Z. Yanovski, MD

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Centers for Disease Control and Prevention: Edward W. Gregg, PhD; Ping Zhang, PhD

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References

1. Perri MG, McAdoo WG, Spevak PA, Newlin DB. Effect of a multicomponent maintenance program on long-term weight loss. *J Consult Clin Psychol* 1984;52:480–1. [PubMed: 6747068]
2. Perri MG, McAdoo WG, McAllister DA, Lauer JB, Yancey DZ. Enhancing the efficacy of behavior therapy for obesity: effects of aerobic exercise and a multicomponent maintenance program. *J Consult Clin Psychol* 1986;54:670–5. [PubMed: 3771884]
3. Perri MG, McAllister DA, Gange JJ, Jordan RC, McAdoo WG, Nezu AM. Effects of four maintenance programs on the long-term management of obesity. *J Consult Clin Psychol* 1988;56:529–34. [PubMed: 2848874]

4. Perri MG, Limacher MC, Durning PE, et al. Extended-care programs for weight management in rural communities: the treatment of obesity in underserved rural settings (TOURS) randomized trial. *Arch Intern Med* 2008;168:2347–54. [PubMed: 19029500]
5. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *J Am Coll Cardiol* 2014;63:2985–3023. [PubMed: 24239920]
6. Wing RR, Tate DF, Gorin AA, Raynor HA, Fava JL. A self-regulation program for maintenance of weight loss. *N Engl J Med* 2006;355:1563–71. [PubMed: 17035649]
7. Svetkey LP, Stevens VJ, Brantley PJ, et al. Comparison of strategies for sustaining weight loss: the weight loss maintenance randomized controlled trial. *JAMA* 2008;299:1139–48. [PubMed: 18334689]
8. Look AHEAD Research Group. 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. *Clin Trials* 2003;24:610–28.
9. Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;369:145–54. [PubMed: 23796131]
10. Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity* 2009;17:713–22. [PubMed: 19180071]
11. Lowe MR, Butryn ML, Zhang F. Evaluation of meal replacements and a home food environment intervention for long-term weight loss: A randomized controlled trial. *The Am J Clin Nutr* 2018;107:12–9. [PubMed: 29381791]
12. Thomas JG, Bond DS, Phelan S, Hill JO, Wing RR. Weight-loss maintenance for 10 years in the National Weight Control Registry. *Am J Prev Med* 2014;46:17–23. [PubMed: 24355667]
13. Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the Look AHEAD study. *Obesity* 2014;22:5–13. [PubMed: 24307184]
14. Look AHEAD Research Group. Baseline characteristics of the randomised cohort from the Look AHEAD (Action for Health in Diabetes) study. *Diab Vasc Dis Res* 2006;3:202–15. [PubMed: 17160917]
15. Look AHEAD Research Group. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity* 2006;14:737–52. [PubMed: 16855180]
16. Look AHEAD Research Group. The development and description of the comparison group in the Look AHEAD trial. *Clin Trials* 2011;8:320–9. [PubMed: 21730080]
17. Heymsfield S, Van Mierlo C, Van der Knaap H, Heo M, Frier H. Weight management using a meal replacement strategy: meta and pooling analysis from six studies. *Int J Obes* 2003;27:537–49.
18. Paffenbarger RS Jr, Wing AL, Hyde RT. Physical activity as an index of heart attack risk in college alumni. *Am J Epidemiol* 1978;108:161–75. [PubMed: 707484]
19. 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;34:1481–6. [PubMed: 21593294]
20. Coughlin JW, Brantley PJ, Champagne CM, et al. The impact of continued intervention on weight: Five-year results from the weight loss maintenance trial. *Obesity* 2016;24:1046–53. [PubMed: 26991814]
21. Diabetes Prevention Program Research Group. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *The Lancet* 2009;374:1677–86.
22. Apolzan JW, Venditti EM, Edelstein SL, et al. Long-Term Weight Loss With Metformin or Lifestyle Intervention in the Diabetes Prevention Program Outcomes Study. *Ann Intern Med* 2019;170:682–90. [PubMed: 31009939]
23. Sheehan T, DuBrava S, DeChello L, Fang Z. Rates of weight change for black and white Americans over a twenty year period. *Int J Obes* 2003;27:498–504.
24. Looker HC, Knowler WC, Hanson RL. Changes in BMI and weight before and after the development of type 2 diabetes. *Diabetes Care* 2001;24:1917–22. [PubMed: 11679457]

25. Gregg EW, Gerzoff RB, Thompson TJ, Williamson DF. Trying to lose weight, losing weight, and 9-year mortality in overweight US adults with diabetes. *Diabetes Care* 2004;27:657–62. [PubMed: 14988281]
26. Wedick NM, Barrett-Connor E, Knoke JD, Wingard DL. The relationship between weight loss and all-cause mortality in older men and women with and without diabetes mellitus: the Rancho Bernardo study. *J Am Geriatr Soc* 2002;50:1810–5. [PubMed: 12410899]
27. Williamson DF, Thompson TJ, Thun M, Flanders D, Pamuk E, Byers T. Intentional weight loss and mortality among overweight individuals with diabetes. *Diabetes Care* 2000;23:1499–504. [PubMed: 11023143]
28. 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;19:1987–98. [PubMed: 21779086]
29. Leibel R. Molecular physiology of weight regulation in mice and humans. *Int J Obes* 2009;32:S98–108.
30. Speakman JR, Levitsky DA, Allison DB, et al. Set points, settling points and some alternative models: theoretical options to understand how genes and environments combine to regulate body adiposity. *Dis Model Mech* 2011;4:733–45. [PubMed: 22065844]
31. Kirchner H, Hofmann SM, Fischer-Rosinsky A, et al. Caloric restriction chronically impairs metabolic programming in mice. *Diabetes* 2012;61:2734–42. [PubMed: 22787140]
32. Schroeder M, Gelber V, Moran TH, Weller A. Long-term obesity levels in female OLETF rats following time-specific post-weaning food restriction. *Horm Behav* 2010;58:844–53. [PubMed: 20736013]
33. 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;36:641–9. [PubMed: 23633746]
34. Look AHEAD Research Group. Effect of a long-term behavioural weight loss intervention on nephropathy in overweight or obese adults with type 2 diabetes: a secondary analysis of the Look AHEAD randomised clinical trial. *Lancet Diabetes Endocrinol* 2014;2:801–9. [PubMed: 25127483]
35. Rejeski WJ, Bray GA, Chen S-H, et al. Aging and physical function in type 2 diabetes: 8 years of an intensive lifestyle intervention. *J Gerontol A Biol Sci Med Sci* 2014;70:345–53. [PubMed: 24986062]
36. Look AHEAD Research Group. Impact of intensive lifestyle intervention on depression and health-related quality of life in type 2 diabetes: the Look AHEAD Trial. *Diabetes Care* 2014;37:1544–53. [PubMed: 24855155]

Study Importance

What is already known about this subject?

- Keeping off lost weight remains a key challenge in the behavioral treatment of obesity.
- Few studies have assessed changes in weight and weight-control behaviors after termination of long-term (5 years) intensive lifestyle interventions.

What are the new findings in your manuscript?

- This study evaluates changes in weight and weight-control behaviors 2 years after the cessation of the 10-year intensive lifestyle intervention (ILI) in the Look AHEAD (Action for Health in Diabetes) study.
- During the 2-year observational period following termination of weight-loss-maintenance counseling, ILI participants lost a mean \pm SE of 1.2 \pm 0.2 kg compared to a significantly greater loss of 1.8 \pm 0.2 kg in the Diabetes Support and Education (DSE) control participants.

How might your results change the direction of research or the focus of clinical practice?

- While both groups lost weight, potentially due to participants' advanced age (i.e., 68 years) and long-term diagnosis of type 2 diabetes, ILI participants reported greater use of weight control behaviors than DSE participants.

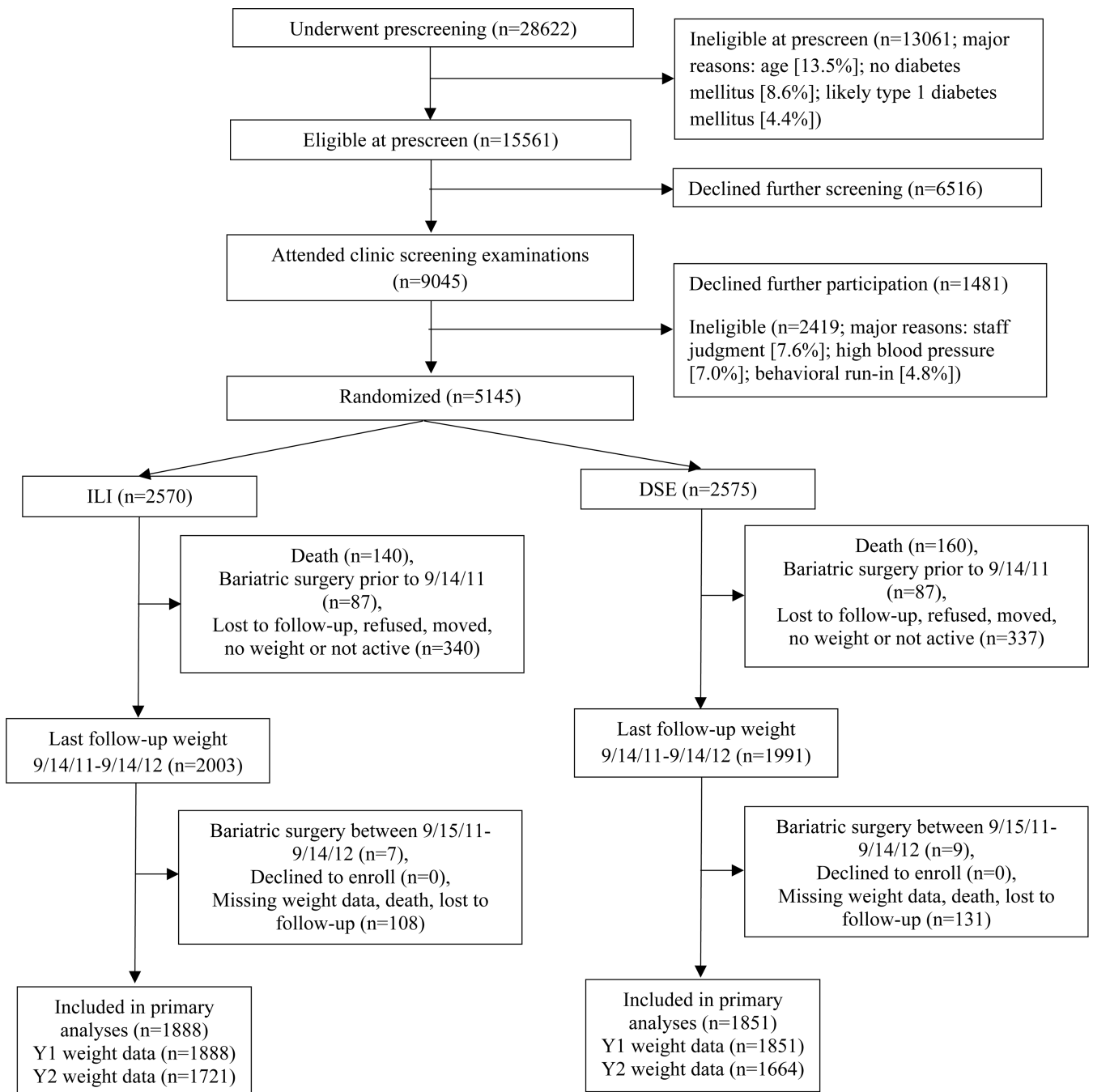


Figure 1:

The figure shows the CONSORT flow diagram of participants through the approximately 10-year Look AHEAD randomized trial and 2 years following the end of the intervention. ILI = intensive lifestyle intervention; DSE = diabetes support and education. Y1 = Year 1 visit after EOI; Y2 = Year 2 visit after EOI.

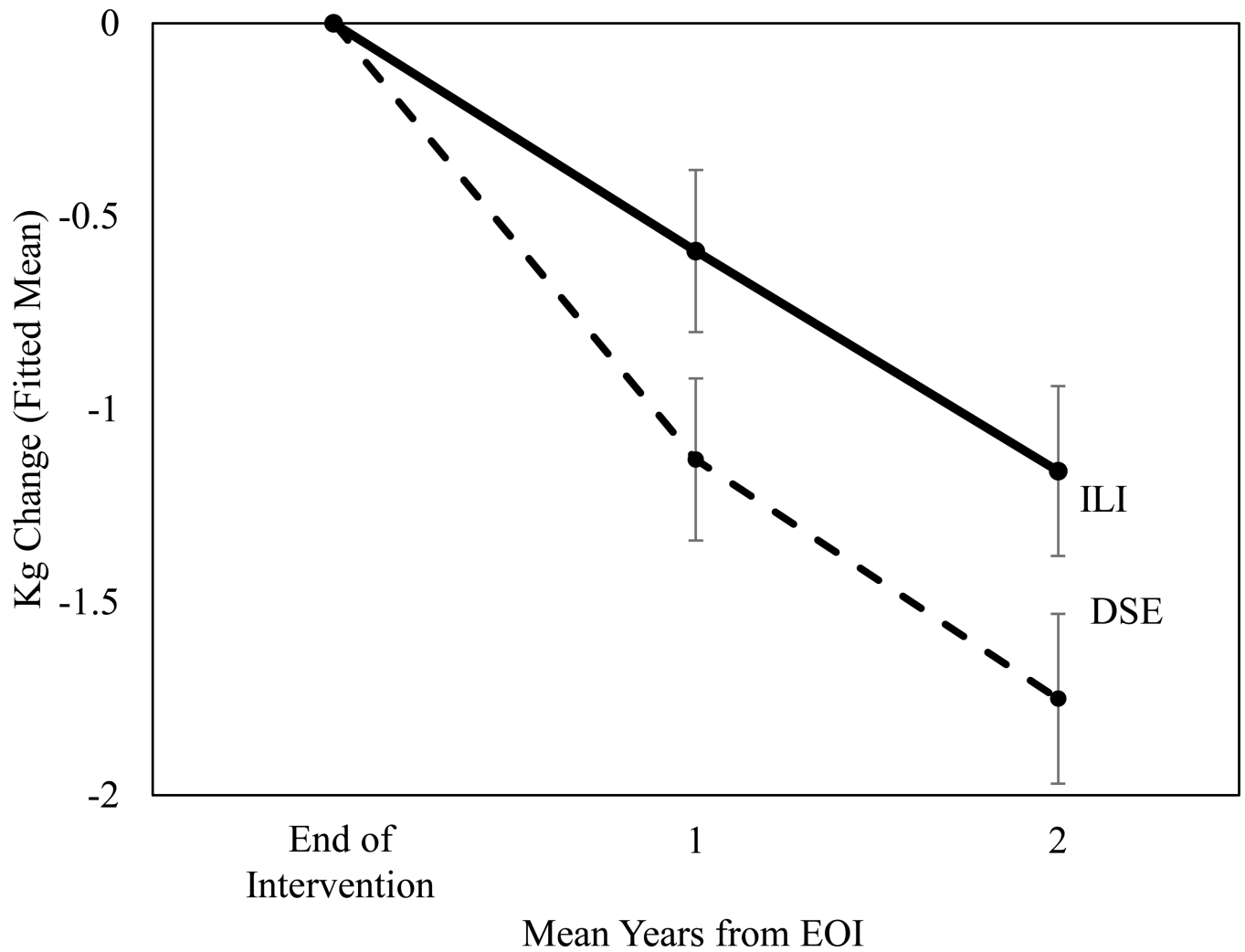
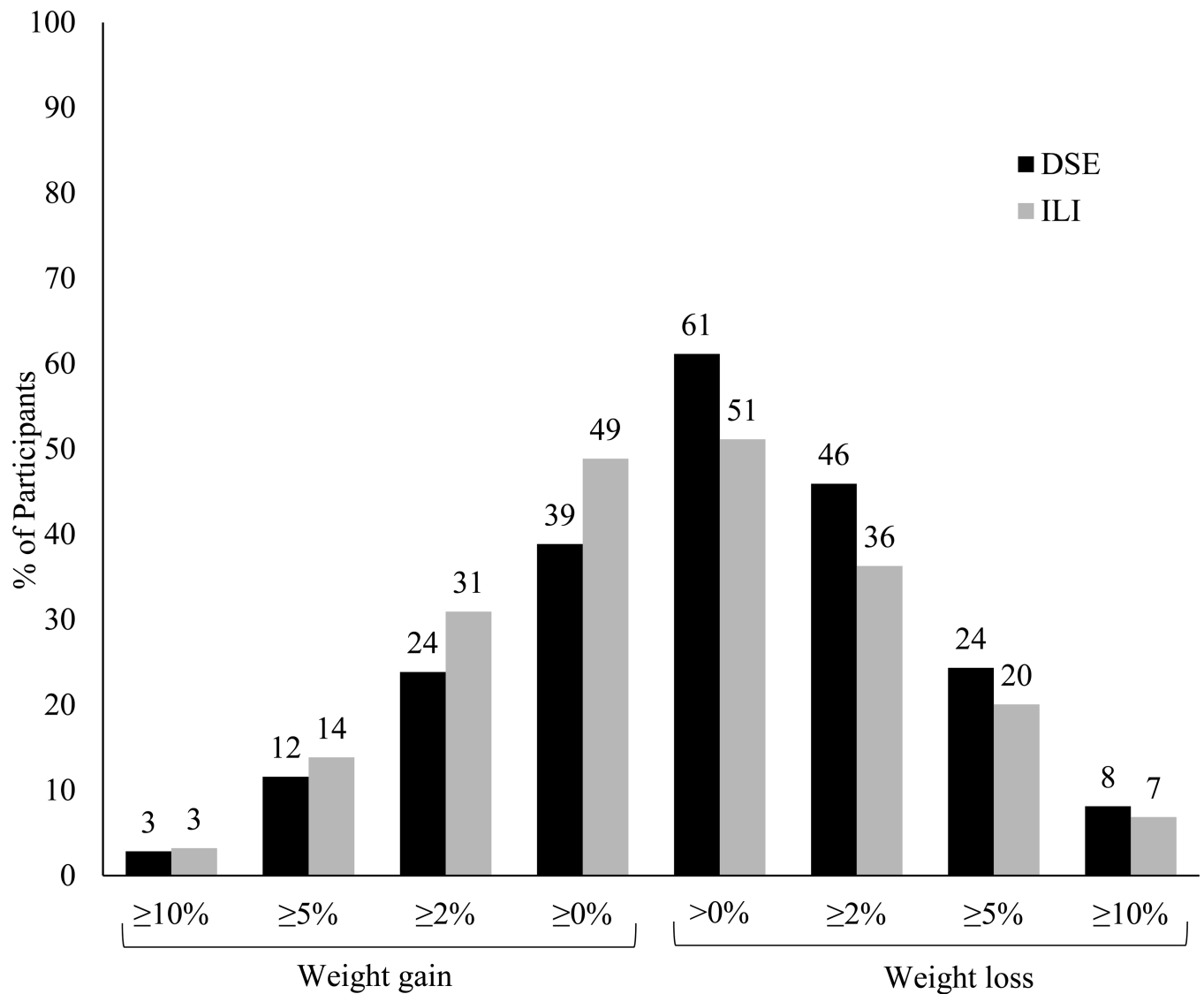


Figure 2:

The figure displays the absolute mean (\pm SE) kg change at the end of intervention (EOI). The fitted means from models are adjusted for race, gender, current age, weight at end of intervention, and repeated measures. ILI = intensive lifestyle intervention; DSE = diabetes support and education.



Weight losses from the end of intervention (EOI) to 2 years after EOI

Figure 3:

The percentage of participants in the ILI and DSE groups who achieved different categorical weight losses from the end of intervention (EOI) to 2 years after EOI. The percentages are cumulative such that the 20.1% of ILI participants, for example, who lost $\geq 5\%$ includes the 6.9% who lost $\geq 10\%$. ILI = intensive lifestyle intervention; DSE = diabetes support and education.

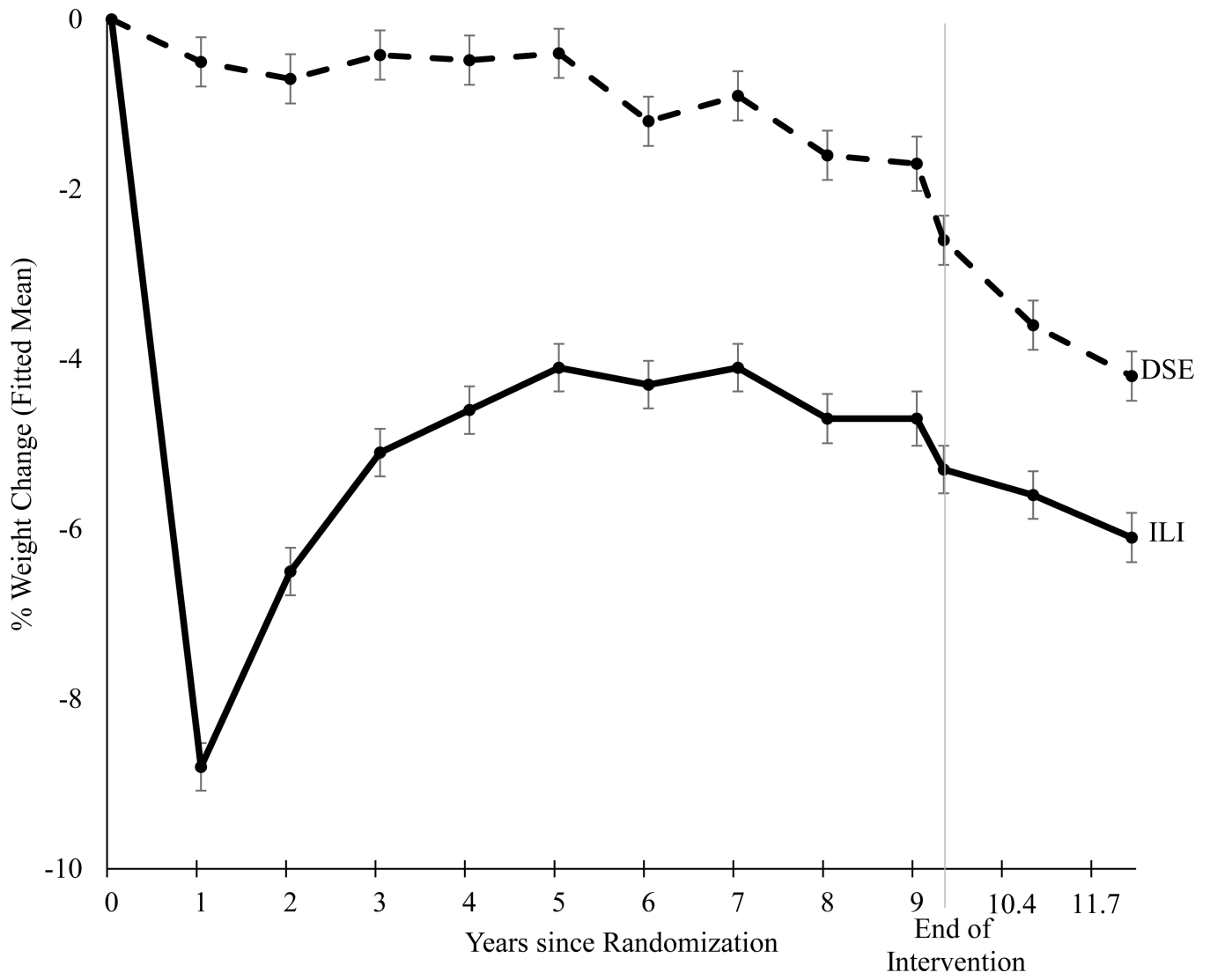


Figure 4:
The figure shows the mean (\pm SE) weight losses from randomization to 2 years after the end of the intervention for participants randomly assigned to an intensive lifestyle intervention (ILI) or diabetes support and education (DSE; usual care group).

Table 1.

Participants' demographic characteristics at randomization, as well as select measures at randomization and at the end of the intervention (N=3739)

	ILI (N=1888)	DSE (N=1851)	P-value
Gender, No. (%)			0.35
Male	773 (40.9%)	730 (39.4%)	
Female	1115 (59.1%)	1121 (60.6%)	
Race, No. (%)			0.90
African American / Black (not Hispanic)	291 (15.4%)	307 (16.6%)	
American Indian / Native American /Alaskan Native	110 (5.8%)	110 (5.9%)	
Asian/Pacific Islander	21 (1.1%)	16 (0.9%)	
White	1176 (62.3%)	1142 (61.7%)	
Hispanic	248 (13.1%)	238 (12.9%)	
Other/Mixed	42 (2.2%)	38 (2.1%)	
Insulin Use, No. (%)			
Randomization			0.92
No	1557 (82.5%)	1526 (82.4%)	
Yes	268 (14.2%)	259 (14.0%)	
Missing	63 (3.3%)	66 (3.6%)	
End of Intervention			0.002
No	1076 (57.0%)	996 (53.8%)	
Yes	586 (31.0%)	671 (36.3%)	
Missing	226 (12.0%)	184 (9.9%)	
Age, mean \pm SD, years			
Randomization	58.3 \pm 6.6	58.6 \pm 6.7	0.11
End of Intervention	68.3 \pm 6.4	68.6 \pm 6.6	0.13
Weight, mean \pm SD, kg			
Randomization	99.6 \pm 19.3	100.0 \pm 18.4	0.52
End of Intervention	94.1 \pm 19.6	97.2 \pm 19.8	<.001
Body Mass Index, mean \pm SD, kg/m ²			
Randomization	35.5 \pm 5.9	35.7 \pm 5.7	0.21
End of Intervention	33.5 \pm 6.0	34.7 \pm 6.1	<0.001
Body Mass Index Group, No. (%)			
Randomization			0.29
<30 kg/m ²	318 (16.8%)	279 (15.1%)	
30-<35 kg/m ²	690 (36.5%)	656 (35.4%)	
35-<40 kg/m ²	497 (26.3%)	521 (28.1%)	
40 kg/m ²	383 (20.3%)	395 (21.3%)	
End of Intervention			<0.001
<30 kg/m ²	587 (31.1%)	422 (22.8%)	
30-<35 kg/m ²	625 (33.1%)	647 (35.0%)	
35-<40 kg/m ²	396 (21.0%)	443 (23.9%)	

	ILI (N=1888)	DSE (N=1851)	P-value
40 kg/m ²	280 (14.8%)	339 (18.3%)	

ILI = intensive lifestyle intervention; DSE = diabetes support and education.

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Table 2.

ILI and DSE participants' reports of their physical activity, and the number of weeks they used strategies related to calorie restriction, and other weight control behaviors during year 8 of intervention and 2 years following EOI

Behavior	Year 8 (n=3322) mean ± SD or n(%)		2 Years after EOI (n=3336) mean ± SD or n(%)		Change from Year 8 to 2 Years after EOI (n=3262) mean (95%CI) or OR(95%CI)		P-value*
	DSE	ILI	DSE	ILI	DSE	ILI	
Paffenbarger: Leisure Time Physical Activity, kcal/wk.	890.4 ± 1309	1088 ± 1604	668.1 ± 1015	792.9 ± 1160	-214.5 (-277.2, -151.9)	-304.5 (-384.6, -225.4)	0.08
Increased exercise, weeks in last year	8.7 ± 15.2	11.4 ± 16.7	8.8 ± 15.9	8.5 ± 15.4	0.2 (-0.7, 1.1)	-3.0 (-4.0, -2.1)	<0.001
Reduced kcal, weeks in last year	11.2 ± 18.0	18.5 ± 20.2	12.2 ± 18.7	14.5 ± 19.6	1.1 (0.0, 2.2)	-4.0 (-5.1, -2.8)	<0.001
Reduced fat, weeks in last year	14.3 ± 20.2	21.3 ± 21.8	13.9 ± 20.2	16.5 ± 21.3	-0.3 (-1.5, 0.9)	-4.5 (-5.7, -3.4)	<0.001
Used meal replacements, weeks in last year	2.4 ± 8.8	19.1 ± 24.3	2.7 ± 9.7	7.7 ± 15.2	0.3 (-0.3, 0.8)	-11.2 (-12.2, -10.2)	<0.001
Daily self-weighting**	245 (15.0%)	594 (35.2%)	289 (17.6%)	461 (27.3%)	1.21 (1.00, 1.45)	0.69 (0.60, 0.80)	<0.001
Weekly self-weighting**	774 (47.4%)	1220 (72.3%)	787 (47.8%)	1071 (63.3%)	1.02(0.89, 1.17)	0.66 (0.57, 0.77)	<0.001

* Student's T-test for mean ± SD, chi-square for n(%)

ILI = intensive lifestyle intervention; DSE = diabetes support and education

** Odds(95%CI) of daily or weekly self-weighting at 2 years after EOI in reference to year 8 within treatment group.

Table 3. Weight control behaviors 2 years following EOI for ILI and DSE participants who gained >2%, gained <2% to lost <2%, and lost >2%

Behavior	DSE				ILI			
	Lost 2%	<2% Gain or Loss	Gain 2%	P-value*	Lost 2%	<2% Gain or Loss	Gain 2%	P-value*
Paffenbarger: Leisure Time Physical Activity, kcal/wk, LSMEAN ± SE	715.8 ± 34.6 ^a	697.2 ± 42.2	558.2 ± 47.8 ^a	0.02	775.4 ± 45.3	852.4 ± 47.3	734.6 ± 48.4	0.21
Increased exercise, weeks in last year, LSMEAN ± SE	10.1 ± 0.6 ^b	8.9 ± 0.7	6.5 ± 0.8 ^b	0.001	9.4 ± 0.6	8.0 ± 0.6	8.2 ± 0.7	0.24
Reduced kcal, weeks in last year, LSMEAN ± SE	13.5 ± 0.7	11.3 ± 0.8	10.9 ± 0.9	0.04	16.1 ± 0.8 ^c	14.4 ± 0.8	12.9 ± 0.8 ^c	0.02
Reduced fat, weeks in last year, LSMEAN ± SE	14.8 ± 0.7	14.2 ± 0.9	11.9 ± 1.0	0.06	18.2 ± 0.8 ^d	17.0 ± 0.8	14.6 ± 0.9 ^d	0.01
Used meal replacements, weeks in last year, LSMEAN ± SE	2.5 ± 0.3	2.7 ± 0.4	2.7 ± 0.5	0.84	7.3 ± 0.6	7.7 ± 0.6	8.0 ± 0.6	0.75
Daily self-weighing, OR(95%CI)	1.25 (0.89,1.76)	REF	0.81 (0.54,1.22)	0.07	1.44 (1.05,1.97)	REF	0.85 (0.61,1.18)	0.004
Weekly self-weighing, OR(95%CI)	1.27 (0.97,1.66)	REF	0.91 (0.66,1.24)	0.05	1.79 (1.34,2.39)	REF	0.91 (0.68,1.21)	<0.001

ILI = intensive lifestyle intervention; DSE = diabetes support and education

* linear regression for continuous measures, logistic regression for binary; adjusted for weight loss at end of intervention and year 8 behavioral strategy use

Bonferroni-adjusted comparison tests^{a-d} with the same super script are significantly different

^a p=0.0241

^b p=0.0006

^c p=0.0138

^d p=0.0091

Table 4.

Partial correlations between weight change in the DSE and ILI from EOI to 2 years afterwards and the change in behaviors from year 8 to 2 years following EOI adjusting for weight loss at EOI and year 8 behavioral strategy use

Behavior	DSE		ILI	
	r	P-value*	r	P-value*
Paffenbarger: Leisure Time Physical Activity, kcal/wk, mean ± SD	-0.07	0.01	-0.02	0.54
Increased exercise, weeks in last year, mean ± SD	-0.10	<0.001	-0.03	0.22
Reduced kcal, weeks in last year, mean ± SD	-0.07	0.005	-0.06	0.01
Reduced fat, weeks in last year, mean ± SD	-0.05	0.04	-0.06	0.02
Used meal replacements, weeks in last year, mean ± SD	0.04	0.11	0.02	0.53
Daily self-weighing, n (%)	-0.08	<0.001	-0.08	0.001
Weekly self-weighing, n (%)	-0.08	<0.001	-0.13	<0.001

ILI = intensive lifestyle intervention; DSE = diabetes support and education

* Pearson correlations for continuous, Spearman non-parametric correlation for binary