Impact of a Weight Management Program on Health-Related Quality of Life in Overweight Adults With Type 2 Diabetes

Donald A. Williamson, PhD; Jack Rejeski, PhD; Wei Lang, PhD; Brent Van Dorsten, PhD; Anthony N. Fabricatore, PhD; Katie Toledo, MS, LPC; for the Look AHEAD Research Group

**Background:** Inconsistent findings have been reported regarding improved health-related quality of life (HRQOL) after weight loss. We tested the efficacy of a weight management program for improving HRQOL in overweight or obese adults diagnosed as having type 2 diabetes mellitus.

**Methods:** We conducted a randomized multisite clinical trial at 16 outpatient research centers with 2 treatment arms and blinded measurements at baseline and the end of year 1. A total of 5145 participants (mean [SD] age, 58.7 [6.9] years; mean [SD] body mass index [calculated as weight in kilograms divided by height in meters squared], 36.0 [5.9]; 59.5% women; 63.1% white) were randomized to an intensive lifestyle intervention (ILI) or to diabetes support and education (DSE). Main outcome measures included the 36-Item Short-Form Health Survey physical component summary (PCS) and mental health component summary (MCS) scores and Beck Depression Inventory II (BDI-II) scores. Baseline mean (SD) scores were 47.9 (7.9) for PCS, 54.0 (8.1) for MCS, and 5.7 (5.0) for BDI-II.

**Results:** Improved HRQOL was demonstrated by the PCS and BDI-II scores ($P < .001$) in the ILI arm compared with the DSE arm. The largest effect was observed for the PCS score (difference, −2.91; 99% confidence interval, −3.44 to −2.37). The greatest HRQOL improvement occurred in participants with the lowest baseline HRQOL levels. Mean (SD) changes in weight (ILI, −8.77 [8.2] kg and DSE, −0.86 [5.0] kg), improved fitness, and improved physical symptoms mediated treatment effects associated with the BDI-II and PCS.

**Conclusions:** Overweight adults diagnosed as having type 2 diabetes experienced significant improvement in HRQOL by enrolling in a weight management program that yielded significant weight loss, improved physical fitness, and reduced physical symptoms.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00017953

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The prevalence of obesity, with its associated medical conditions (eg, type 2 diabetes mellitus), has increased substantially in recent years. Weight loss studies have found that successful weight management is associated with improvements in comorbid medical conditions. A consensus has been reached that sustained weight loss, achieved by healthy diet and physical activity, is a primary goal for improving health in overweight and obese individuals. In recent years, the definition of improved health has expanded to include patient-reported outcomes, most notably health-related quality of life (HRQOL).

An important question in the field of obesity is whether successful weight loss results in improved HRQOL. A related question is whether intensive lifestyle interventions result in improved HRQOL. Investigations of these questions have tested the effects of a variety of weight management strategies on HRQOL. These investigations have defined HRQOL using various self-report questionnaires. In a recent meta-analytic review of this research literature, Maciejewski et al reported that the most frequently used measures of HRQOL were the 36-Item Short-Form Health Survey (SF-36) and the Beck Depression Inventory (BDI). Maciejewski et al concluded that HRQOL was not consistently improved in randomized controlled trials of weight loss.

The Look AHEAD (Action for Health in Diabetes) Trial is a 16-center, randomized controlled trial in overweight and obese individuals with type 2 diabetes mellitus that is designed to evaluate the long-term effects (up to 11.5 years) of an intensive weight loss intervention on the time to incidence of major cardiovascular events. This study provides an opportunity to investigate the impact of a behavioral weight loss program on HRQOL. The present report examines changes in HRQOL after the first year of the Look AHEAD Trial.
AHEAD trial. We hypothesized that HRQOL would be significantly improved in the weight management arm compared with the control arm and that improvement in HRQOL would be mediated by weight loss, improved physical fitness, and reduction of physical symptoms.

**METHODS**

**DESCRIPTION OF THE LOOK AHEAD PROJECT**

The Look AHEAD Trial is a multicenter randomized controlled trial designed to determine whether intentional weight loss reduces cardiovascular morbidity and mortality in overweight individuals with type 2 diabetes mellitus. Participants were randomly assigned to an intensive lifestyle intervention (ILI) or to an enhanced usual-care control condition of diabetes support and education (DSE).

**PARTICIPANTS**

The sample included 5145 overweight or obese persons (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], ≥25 or ≥27 if currently taking insulin) with type 2 diabetes mellitus. It included 2082 men and 3063 women ranging from 45 to 74 years of age. Major exclusions included hemoglobin A1c of more than 11% (to convert to a proportion of 1, multiply by 0.01), blood pressure of more than 160/100 mm Hg, triglyceride levels of more than 600 mg/dL (to convert to millimoles per liter, multiply by 0.0113), inadequate control of comorbid conditions, and underlying diseases likely to limit the life span of the participants or to affect the safety of the interventions. Potential participants were also excluded if they failed to pass a baseline graded exercise stress test. A flow diagram incorporating the Consolidated Standards of Reporting Trials summarizes enrollment of participants into the Look AHEAD (Action for Health in Diabetes) Study.

![Flowchart](image-url)

**Figure 1. Flowchart incorporating the Consolidated Standards of Reporting Trials shows enrollment of participants into the Look AHEAD (Action for Health in Diabetes) Study.**

**ASSESSMENT MEASURES**

**Measures of HRQOL**

Health-related quality of life was assessed with the SF-36 and the Beck Depression Inventory II (BDI-II), the only measures of HRQOL in the Look AHEAD study. The SF-36 is a commonly used measure of health status and HRQOL that consists of the following 2 norm-based composite T scores (mean [SD], 50 [10]): the physical component summary (PCS) and mental health component summary (MCS) scores. Higher scores on the 2 SF-36 component summary scores indicate more favorable quality of life. The SF-36 also provides 8 subscale scores that are described in Table 1. Extensive psychometric data support the reliability and validity of the SF-36.

The BDI-II, a revision of the BDI, is one of the most widely used and well-validated self-report measures of depressive symptoms. Higher scores indicate more severe symptoms of depression. Scores on the BDI-II can be interpreted within the context of the following categories: 0 to 13, minimal depression; 14 to 19, mild depression; 20 to 28, moderate depression; and more than 28, severe depression.

**Demographics**

Self-reported demographic characteristics included age, sex, and race/ethnicity.

**Disease Burden and Fitness**

Self-reported measures of disease burden and fitness included diabetes severity, the number of physical symptoms, and comorbid medical conditions. Body mass index and peak metabolic equivalent capacity were also measured. Physical symptoms were measured by the frequency of 19 different physical symptoms. The number of comorbid medical conditions was based on self-report of arthritis, cardiovascular disease history, hypertension, stroke, and emphysema. Disease severity was defined by the following 3 categories: (1) no use of diabetes-related drugs, (2) use of oral diabetes drugs exclusive of insulin, and (3) use of insulin with or without oral diabetes drugs. Measurements of height and weight to calculate the BMI were obtained by standardized procedures during 1 of the baseline clinical assessments. Maximal metabolic equivalent capacity was estimated from performance on a graded exercise treadmill test (approximately 10 minutes) that included heart rate measurement.

**Procedures**

Informed consent was obtained from all participants before screening. Key components of the Look AHEAD ILI have been described in a recent article. The treatment protocol combined multiple diet and exercise approaches in an effort to maximize the number of participants who met the study’s weight and activity goals. The 2 principal intervention goals were to induce a mean loss of at least 7% of initial weight and to increase participants’ moderately intense physical activity to at least 175 minutes per week. For the first 6 months, participants attended 1 individual and 3 group sessions per month and were encouraged to replace 2 meals and 1 snack each day with liquid shakes and meal bars. From months 7 to 12, they attended 1 individual and 2 group meetings per month.
and continued to replace 1 meal per day. Participants in the ILI arm were instructed to self-monitor energy intake and physical activity, and their body weight was measured at each individual and group counseling session. The DSE control arm involved 3 educational group sessions per year that each focused on 1 of the following 3 topics: nutrition, physical activity, and support. Participants assigned to the DSE arm were not given goals for weight loss or caloric intake, were not instructed to monitor energy intake or physical activity, and were not weighed at group meetings.

STATISTICAL ANALYSES

All analyses were performed using commercially available software (SAS, version 9.1. SAS Institute Inc, Cary, North Carolina). Differences between the ILI and DSE participants in 1-year changes of HRQOL measures were compared using analysis of covariance, with adjustment for baseline values and clinical center, the stratification factor used during randomization. Effect size estimates were summarized using the Glass Δ with the corresponding 99% confidence intervals (CIs). The experiment-wise α level was adjusted through the use of 3 different outcomes in the HRQOL battery via a Bonferroni procedure and resulted in an α level for testing main effects of treatment of P<.017.

Separate linear regression models were fitted to test the moderator effects. The dependent variables were the 1-year changes in PCS, MCS, and BDI-II scores. The independent variables included the clinical center, treatment group, main effect for potential moderator, and interaction effect of treatment by a potential moderator. In addition, in the models testing for the moderator effects (of age, sex, race, BMI, diabetes severity, number of comorbid conditions, and number of physical symptoms), baseline HRQOL score corresponding to the dependent variable was also included as an independent variable. Interpretation of the presence of moderator effects was based on the significance of the treatment × moderator interaction effects (the total numbers of participants in the statistical analyses for treatment and moderator effects were 4772 for the PCS and MCS and 4799 for the BDI-II).

To test whether weight loss, fitness improvement, or changes in physical symptoms during the first year of intervention accounted (fully or partially) for differential treatment effects on the 1-year changes in HRQOL measures, mediator analyses were performed in 3 steps according to the widely used approach of Baron and Kenny. This approach requires the following to be established: (1) that significant relationships exist among the independent variable, treatment group, and dependent variables; (2) that the treatment be related to the potential mediators and the mediators be related to the dependent variables; and (3) that the addition of the mediators to the regression models used in step 1 reduce or remove the significance relationship between treatment and the dependent variables. The Sobel test was used to assess the statistical significance of mediating effects. Mediation analyses were restricted to the participants who had complete data for change in HRQOL measures and changes in weight, fitness, and physical symptoms to assess the changes in regression coefficients. For moderator and mediator analyses, the type I error rate was fixed at 5% (the total numbers of participants in the statistical models testing mediator effects were 4222 for the PCS and MCS and 4223 for the BDI-II).

Intent-to-treat analyses were computed including all randomized participants. Missing 1-year data in the HRQOL measures, weight, fitness, and physical symptoms were imputed using baseline scores. Unless otherwise indicated, data are expressed as mean (SE).

Table 1. Participant Characteristics at Baseline

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of participants</td>
<td>5145</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>58.7 (6.9)</td>
</tr>
<tr>
<td>Female</td>
<td>3063 (59.5)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>African American/black (not Hispanic)</td>
<td>803 (15.6)</td>
</tr>
<tr>
<td>American Indian/Native American/Alaskan Native</td>
<td>258 (5.0)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>50 (1.0)</td>
</tr>
<tr>
<td>White</td>
<td>3246 (63.1)</td>
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<tr>
<td>Hispanic</td>
<td>677 (13.2)</td>
</tr>
<tr>
<td>Other</td>
<td>98 (1.9)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
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<tr>
<td>Never married</td>
<td>386 (7.5)</td>
</tr>
<tr>
<td>Married/marriagelike relationship</td>
<td>3461 (67.3)</td>
</tr>
<tr>
<td>Widowed</td>
<td>359 (7.0)</td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>934 (18.2)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>36.0 (5.9)</td>
</tr>
<tr>
<td>Taking antidepressant medications</td>
<td>848 (16.5)</td>
</tr>
<tr>
<td>Maximal MET value, mean (SD)</td>
<td>7.2 (2.0)</td>
</tr>
<tr>
<td>Maximal MET value (at 80% HR), mean (SD)</td>
<td>5.2 (1.5)</td>
</tr>
<tr>
<td>SF-36 PCS score, mean (SD)</td>
<td>47.9 (7.9)</td>
</tr>
<tr>
<td>SF-36 MCS score, mean (SD)</td>
<td>54.0 (8.1)</td>
</tr>
<tr>
<td>(SD) BDI-II score, mean (SD)</td>
<td>4.2 (1.5)</td>
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<tr>
<td>BDI-II scores &gt;19</td>
<td>94 (1.8)</td>
</tr>
<tr>
<td>SF-36 subscale scores, mean (SD)</td>
<td></td>
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<tr>
<td>Physical functioning</td>
<td>48.5 (7.9)</td>
</tr>
<tr>
<td>Physical role functioning</td>
<td>50.2 (8.1)</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>50.7 (8.8)</td>
</tr>
<tr>
<td>General health</td>
<td>47.2 (8.9)</td>
</tr>
<tr>
<td>Vitality</td>
<td>53.0 (9.0)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>52.2 (7.6)</td>
</tr>
<tr>
<td>Emotional role</td>
<td>51.5 (7.9)</td>
</tr>
<tr>
<td>Mental health</td>
<td>53.7 (8.0)</td>
</tr>
</tbody>
</table>

Abbreviations: BDI-II, Beck Depression Inventory II; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HR, heart rate; MCS, mental health component summary; MET, metabolic equivalent capacity; PCS, physical component summary; SF-36, 36-Item Short-Form Health Survey.

RESULTS

DESCRIPTION OF THE SAMPLE AT BASELINE

The description of the sample has been reported in detail by the Look AHEAD Research Group. Table 1 summarizes the characteristics of the participants at baseline.

EFFECTS OF TREATMENT ASSIGNMENT ON HRQOL

Changes in the SF-36 PCS scores differed as a function of treatment arm (P<.001; difference, −2.91; 99% CI, −3.44 to −2.37). As shown in Figure 2, in addition to treatment arm differences, assignment to ILL was associated with improvement of PCS scores (1.65 [7.94]; P<.001), whereas assignment to DSE was associated with worsening of PCS scores (−1.27 [7.44]; P<.001). The baseline PCS score was associated with change such that greater improvement was associated with lower baseline scores (indicating lower HRQOL related to physical activity, and continued to replace 1 meal per day. Participants in the ILI arm were instructed to self-monitor energy intake and physical activity, and their body weight was measured at each individual and group counseling session. The DSE control arm involved 3 educational group sessions per year that each focused on 1 of the following 3 topics: nutrition, physical activity, and support. Participants assigned to the DSE arm were not given goals for weight loss or caloric intake, were not instructed to monitor energy intake or physical activity, and were not weighed at group meetings.

STATISTICAL ANALYSES

All analyses were performed using commercially available software (SAS, version 9.1. SAS Institute Inc, Cary, North Carolina). Differences between the ILI and DSE participants in 1-year changes of HRQOL measures were compared using analysis of covariance, with adjustment for baseline values and clinical center, the stratification factor used during randomization. Effect size estimates were summarized using the Glass Δ with the corresponding 99% confidence intervals (CIs). The experiment-wise α level was adjusted through the use of 3 different outcomes in the HRQOL battery via a Bonferroni procedure and resulted in an α level for testing main effects of treatment of P<.017.

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To test whether weight loss, fitness improvement, or changes in physical symptoms during the first year of intervention accounted (fully or partially) for differential treatment effects on the 1-year changes in HRQOL measures, mediator analyses were performed in 3 steps according to the widely used approach of Baron and Kenny. This approach requires the following to be established: (1) that significant relationships exist among the independent variable, treatment group, and dependent variables; (2) that the treatment be related to the potential mediators and the mediators be related to the dependent variables; and (3) that the addition of the mediators to the regression models used in step 1 reduce or remove the significance relationship between treatment and the dependent variables. The Sobel test was used to assess the statistical significance of mediating effects. Mediation analyses were restricted to the participants who had complete data for change in HRQOL measures and changes in weight, fitness, and physical symptoms to assess the changes in regression coefficients. For moderator and mediator analyses, the type I error rate was fixed at 5% (the total numbers of participants in the statistical models testing mediator effects were 4222 for the PCS and MCS and 4223 for the BDI-II).

Intent-to-treat analyses were computed including all randomized participants. Missing 1-year data in the HRQOL measures, weight, fitness, and physical symptoms were imputed using baseline scores. Unless otherwise indicated, data are expressed as mean (SE).
health; Spearman \( r = -0.34; P < .001 \). Furthermore, as shown in Figure 3, the effects of treatment were moderated by the baseline PCS score such that participants in the ILI arm with lower baseline PCS scores experienced greater improvement compared with participants in the DSE arm with lower baseline PCS scores. Participants in both treatment arms with relatively high baseline PCS scores did not show improvement after 1 year of the interventions. Baseline BMI also moderated the treatment effects on PCS scores (\( P = .003 \)). This moderator effect is shown in Figure 4. Participants in the ILI arm had increased PCS scores across all BMI ranges, but in the DSE arm, changes in PCS scores were negatively associated with baseline BMI such that participants with very high BMI at baseline (approximately \( \geq 35 \)) did not show improvement. The effect size for the treatment effect related to the PCS score was 0.39.

Average changes in SF-36 MCS scores did not differ as a function of treatment arm (\( P > .05 \); difference, \(-0.46; 99\% CI, -1.04 \) to 0.12). This nonsignificant finding is depicted in Figure 2. The effect size for the treatment arm effect related to the MCS score was quite small (0.08). After 1 year, there were no changes in MCS scores from baseline for the ILI group (0.03 [8.75]; \( P = .21 \)) or the DSE group (\(-0.60 [8.32]; P = .13 \)). As observed for PCS scores, the baseline MCS score was associated with change such that greater improvement was associated with lower baseline scores (Spearman \( r = -0.39; P < .001 \)). As shown in Figure 3, the effect of treatment on MCS scores was moderated by baseline MCS scores (\( P < .001 \)) such that the greatest improvement was observed in ILI participants with the lowest baseline MCS scores.

Change in scores for BDI-II also differed between the 2 treatment arms (\( P < .001 \); difference, 0.55; 99% CI, 0.24-0.86). This treatment arm effect is depicted in Figure 2. The BDI-II scores for the ILI (−0.83 [4.86]; \( P < .001 \)) and DSE arms (−0.23 [4.63]; \( P < .001 \)) decreased from baseline. Correlation analysis indicated that higher scores at baseline were associated with greater reductions in the symptoms of depression (Spearman \( r = -0.45; P < .001 \)). As shown in Figure 3, the treatment effect was moderated by baseline BDI-II scores (\( P = .02 \)). Participants in the ILI arm with higher BDI-II scores at baseline had the greatest reduction in depressive symptoms at the end of the 1-year intervention. The effect size for the treatment arm effect related to changes in BDI-II scores was 0.13.

MODERATING EFFECTS OF COMORBID CONDITIONS, DISEASE SEVERITY, AND PHYSICAL SYMPTOMS

When the baseline number of comorbid medical conditions, disease severity, and physical symptoms were entered into the regression models for the PCS, MCS, and BDI-II to test for moderation of the effects of treatment arm, there were no significant interaction effects between treatment group and comorbid conditions or physical symptoms (for all, \( P > .10 \)). Also, age, sex, and race did not interact with treatment (for all, \( P > .10 \)) and therefore were not interpreted as significant moderators of the treatment effects on measures of HRQOL.

EFFECTS OF TREATMENT ASSIGNMENT ON BODY WEIGHT, FITNESS, AND PHYSICAL SYMPTOMS

The differential effects of treatment arm on weight changes after 1 year of intervention have been described in detail by the Look AHEAD Research Group. The 1-year measurement of outcome was attended by 97.1% of the ILI arm and 95.7% of the DSE arm. Participants in the ILI arm achieved significantly greater reductions in body weight (−8.77 [8.2] kg; mean difference, −8.58% [7.72%]) compared with the DSE arm (−0.86 [5.0] kg; mean difference, −0.81% [4.76%]; \( P < .001 \)). Also, participants in the ILI arm improved fitness (mean difference, 20.72% [29.11%]) to a greater extent than did the participants in the DSE arm (mean difference, 5.83% [22.02%]; \( P < .001 \)). Furthermore, participants in the ILI arm reported a reduction in physical symptoms (mean difference, −0.28 [2.99]) compared with an increase for those in the DSE arm (mean difference, 0.56 [3.06]; \( P < .001 \)).

MEDIATING EFFECTS OF CHANGES IN BODY WEIGHT, FITNESS, AND PHYSICAL SYMPTOMS

Figure 5 provides an illustration of tests for mediation as a companion to Table 2. All of the putative mediators such as changes in body weight (\( P < .001 \)), physical fitness (\( P < .001 \)), and physical symptoms (\( P < .001 \)) differed as a function of treatment arm. Treatment effects for MCS were not observed; thus, mediation effects were not tested for this variable. The direct effects of treatment on the proposed mediators are presented as path A in Table 2. Each of the mediators was significantly related to the PCS and BDI-II; these effects are described under path B in Table 2. Path C, the effects of the treatment on the HRQOL measures, illustrates that the PCS and BDI-II passed this criterion for tests of mediation. To test for mediation of treatment effects on the PCS and BDI-II by changes in weight, fitness, and physical symp-
toms, the putative mediators were entered into the regression models, and the results are summarized in Table 2 as path C. The Sobel test (given as the P value in Table 2) was used to test whether the indirect effect of treatment on the outcome through the mediator was statistically significant. The mediating effects of changes in weight, fitness, and physical symptoms were statistically significant (P < .001) but did not completely attenuate the treatment effects attributable to the ILI for the PCS and BDI-II with the following single exception: weight changes completely mediated the treatment effects on BDI-II scores (as indicated by the nonsignificant treatment effect under path C').

**INTENT-TO-TREAT ANALYSES**

Intent-to-treat analyses were also performed assuming no change during year 1 for participants with missing values for HRQOL changes, weight change, fitness change, and physical symptoms changes. Results were essentially the same as those reported for the patients with no missing values.

The findings of this study support the hypothesis that participation in an intensive lifestyle behavior modification intervention for weight management was associated with significant improvement in HRQOL (relative to the control group), as measured by the PCS score of the SF-36 and the BDI-II score. Assignment to ILI was associated with significant improvements in PCS and BDI-II scores, whereas assignment to DSE was associated with worsening in PCS scores. The overall treatment effect on the PCS score (0.39) was greater than the relatively small effect size (0.13) that was observed for BDI-II score, but it was not sufficiently large to be considered clinically significant. The study also found that individuals with worse HRQOL at baseline derived the greatest benefits from the weight management intervention. Similar results were reported in an uncontrolled study of changes in HRQOL after pharmacologic and lifestyle treatment for obesity. This observation is consistent with a statistical phenomenon called “regression to the mean.” For all 3 measures of HRQOL, the greatest benefits of ILI were observed for participants with base-
The results suggest that the strongest effects of lifestyle modification were on HRQOL related to physical health. Furthermore, the largest changes in HRQOL were observed for participants with the poorest quality of life at baseline. In this context, it is not surprising that the smaller-scale and less well-controlled investigations have yielded conflicting results pertaining to the effect of lifestyle weight management programs on HRQOL.

Given the initial positive findings of the impact of participation in a lifestyle behavior modification program for obesity on HRQOL, it will be very important to observe the stability of improvement in HRQOL for longer study periods. It is highly probable that a substantial portion of the participants in the ILI arm will regain some weight during the 11-year duration of the Look AHEAD trial. Only 1 uncontrolled study has reported on changes in HRQOL associated with weight regain, and that article reported deterioration of improvements in HRQOL after weight regain.

Table 2. Summary of Mediation Analyses Related to Changes in Body Weight, Physical Fitness, and Physical Symptomsa

<table>
<thead>
<tr>
<th>HRQOL Outcome of Interest</th>
<th>Putative Mediators</th>
<th>Path A: Treatment Effect on Mediatorb</th>
<th>Path B: Effect of Mediator on HRQOLb</th>
<th>Path C: Treatment Effect on HRQOL Without Mediationb</th>
<th>Path C': Treatment Effect on HRQOL With Mediation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCS score</td>
<td>Weight change</td>
<td>-0.61 (-17.78 [0.46])</td>
<td>-0.17 (-0.07 [0.01])</td>
<td>0.23 (2.84 [0.21])</td>
<td>0.08 (1.62 [0.24])</td>
</tr>
<tr>
<td></td>
<td>Fitness change</td>
<td>0.30 (0.76 [0.04])</td>
<td>0.12 (0.70 [0.08])</td>
<td>0.08 (0.39 [0.04])</td>
<td>0.19 (2.31 [0.21])</td>
</tr>
<tr>
<td></td>
<td>Physical symptom change</td>
<td>-0.14 (-0.84 [0.09])</td>
<td>-0.20 (-0.45 [0.03])</td>
<td>0.21 (2.47 [0.20])</td>
<td>0.19 (2.31 [0.21])</td>
</tr>
<tr>
<td>BDI-II</td>
<td>Weight change</td>
<td>-0.62 (-17.78 [0.46])</td>
<td>0.07 (0.02 [0.004])</td>
<td>-0.07 (-0.54 [0.12])</td>
<td>-0.01 (-0.12 [0.14])</td>
</tr>
<tr>
<td></td>
<td>Fitness change</td>
<td>0.30 (0.76 [0.04])</td>
<td>-0.07 (-0.27 [0.05])</td>
<td>-0.05 (-0.33 [0.13])</td>
<td>-0.05 (-0.36 [0.12])</td>
</tr>
<tr>
<td></td>
<td>Physical symptom change</td>
<td>-0.14 (-0.84 [0.09])</td>
<td>0.13 (0.21 [0.02])</td>
<td>-0.05 (0.05 [0.002])</td>
<td>-0.05 (0.05 [0.002])</td>
</tr>
</tbody>
</table>

Abbreviations: BDI-II, Beck Depression Inventory II; HRQOL, health-related quality of life; PCS, physical component summary of the 36-Item Short-Form Health Survey.

a Based on models without the interaction effect of treatment group by baseline HRQOL scores. The following statistical models were tested for each putative mediator: Change in PCS (or BDI-II) = Treatment Arm + Baseline PCS (or BDI-II Score) (model 1); Change in Mediator = Treatment Arm (model 2); and Change in PCS (or BDI-II) = Treatment Arm + Baseline PCS (or BDI-II Score) + Mediator (model 3). The designation of paths follows the illustration in Figure 5: path A, treatment arm effect from model 2; path B, mediator effect from model 3; path C, treatment arm effect from model 1; and path C’, treatment arm effect from model 3. The P value from the Sobel test for the significance of the indirect effect AB (ie, the amount of mediation) was < .001 for all comparisons. Results show that changes in weight, fitness, and physical symptoms reduced the effects of treatment on PCS and BDI-II scores as indicated by the reduction in regression parameter estimates from C to C' and Spearman partial correlation coefficients. Changes in weight, fitness, and physical symptoms partially mediated the effects of treatment on PCS and BDI-II scores, with the exception that changes in weight completely mediated treatment effects on BDI-II scores, as evidenced by the nonsignificant treatment effect under path C’.

b Statistical significance of effects, P < .001.
c Statistical significance of effects, P > .05.
d Statistical significance of effects, P < .02.

Line SF-36 scores indicative of poor HRQOL and baseline BDI-II scores indicative of mild to moderate depression (Figure 3).

We conducted secondary analyses on participants with baseline scores indicative of poor HRQOL (SF-36 scores < 40 and BDI-II scores > 13). A significant (P < .001; n = 779) treatment arm effect was found for the PCS score (effect size, 0.56) but not for the MCS (P = .13; n = 325; effect size, 0.17) or for the BDI-II (P = .24; n = 353; effect size, 0.11). The magnitude of this effect size (0.56) for the PCS meets accepted criteria for clinically significant improvement.

We also tested for moderation of treatment effects by baseline BMI, baseline levels of pain symptoms, disease severity, severity of baseline comorbid conditions, age, sex, and race. Baseline BMI moderated the differential effects of the 2 treatment arms on the PCS scores but did not moderate the effects on the MCS or the BDI-II scores.

This study is, to our knowledge, one of the first to evaluate the potential mediation of treatment effects on HRQOL. We tested 3 putative mediators: changes in weight, fitness, and physical symptoms. Mediation analyses (Table 2) indicated that the improvement in PCS associated with participation in the ILI arm was only partially mediated by the improvements in body weight and physical fitness and by the reduction in physical symptoms. Treatment effects related to BDI-II scores were partially mediated by changes in fitness and physical symptoms and completely mediated by changes in body weight. The finding that changes in body weight, physical fitness, and physical symptoms accounted for only a portion of the changes in PCS scores attributed to treatment suggests that other factors (eg, counseling and group support, changes in the social and/or family environment, improved metabolic variables, or improved functional abilities) may be critical variables that account for improved HRQOL that occurs with successful lifestyle modification related to weight management in overweight and obese adults diagnosed as having type 2 diabetes mellitus.

These results significantly inform the medical professions about changes in HRQOL and lifestyle behavior change related to weight management. The research literature on this topic has yielded conflicting findings. This study addresses some of the primary shortcomings of previous studies. First, loss to follow-up for this study was quite low (2.9% for ILI and 4.3% for DSE) relative to earlier studies. Second, the sample size was large. Third, the study assessors were blinded to treatment assignment. Fourth, mediation of changes in HRQOL by changes in body weight, fitness, and physical symptoms was tested. Finally, statistical analyses were adjusted for multiple comparisons.

The results suggest that the strongest effects of lifestyle modification were on HRQOL related to physical health. Furthermore, the largest changes in HRQOL were observed for participants with the poorest quality of life at baseline. In this context, it is not surprising that the smaller-scale and less well-controlled investigations have yielded conflicting results pertaining to the effect of lifestyle weight management programs on HRQOL.

Given the initial positive findings of the impact of participation in a lifestyle behavior modification program for obesity on HRQOL, it will be very important to observe the stability of improvement in HRQOL for longer study periods. It is highly probable that a substantial portion of the participants in the ILI arm will regain some weight during the 11-year duration of the Look AHEAD trial. Only 1 uncontrolled study has reported on changes in HRQOL associated with weight regain, and that article reported deterioration of improvements in HRQOL after weight regain.

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The primary limitations are the relatively brief duration of the study (ie, 1 year) and the focus on a highly selected population of overweight and obese adults who had been diagnosed as having type 2 diabetes mellitus. These findings should not be generalized to other (less highly selected) populations, and future reports on this sample are needed to determine whether these changes in HRQOL persist over much longer periods.

In summary, participation in a 1-year ILI for weight loss improved HRQOL in overweight and obese adult participants with type 2 diabetes mellitus. The greatest effects were observed for improvements in HRQOL related to physical functioning. For all 3 indicators of HRQOL, participants with the lowest quality of life at baseline derived the greatest HRQOL benefit from participation in the ILI. Improvement in HRQOL for physical health (PCS score) was partially mediated by weight loss, improved fitness, and reductions in patient reports of physical problems. It is likely that other factors may account for additional variance in the beneficial changes in HRQOL associated with participation in a weight management program.

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