HEALTH CARE REFORM

Nonsurgical Weight Loss for Extreme Obesity in Primary Care Settings

Results of the Louisiana Obese Subjects Study

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Background: Effective primary care practice (PCP) treatments are needed for extreme obesity. The Louisiana Obese Subjects Study (LOSS) tested whether, with brief training, PCPs could effectively implement weight loss for individuals with a body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) of 40 to 60.

Methods: The LOSS, a 2-year (July 5, 2005, through January 30, 2008) randomized, controlled, “pragmatic clinical trial” trained 7 PCPs and 1 research clinic in obesity management. Primary outcome measure was year-2 percentage change from baseline weight. Volunteers (597) were screened and randomized to intensive medical intervention (IMI) (n=200) or usual care condition (UCC) (n=190). The UCC group had instruction in an Internet weight management program. The IMI group recommendations included a 900-kcal liquid diet for 12 weeks or less, group behavioral counseling, structured diet, and choice of pharmacotherapy (sibutramine hydrochloride, orlistat, or diethylpropion hydrochloride) during months 3 to 7 and continued use of medications and maintenance strategies for months 8 to 24.

Results: The mean age of participants was 47 years; 83% were women, and 75% were white. Retention rates were 51% for the IMI group and 46% for the UCC group (P=.30). After 2 years, the results were as follows: (1) among 390 randomized participants, 31% in the IMI group achieved a 5% or more weight loss and 7% achieved a 20% weight loss or more, compared with 9% and 1% of those in the UCC group. (2) The mean±SEM baseline observation carried forward analysis showed a weight loss of −4.9±0.8% in IMI and −0.2±0.3% in UCC. (3) Last observation carried forward analysis showed a weight loss of −8.3±0.7% for IMI, whereas UCC was −0.0±0.4%. (4) A total of 101 IMI completers lost −9.7±1.3% (−12.7±1.7 kg), whereas 89 UCC completers lost −0.4±0.7% (−0.5±0.9 kg); (P<.001 for all group differences). Many metabolic parameters improved.

Conclusion: Primary care practices can initiate effective medical management for extreme obesity; future efforts must target improving retention and weight loss maintenance.

Trial Registration: clinicaltrials.gov Identifier: NCT00115063

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EXTREME OBESITY (BODY MASS INDEX [BMI], calculated as weight in kilograms divided by height in meters squared, >40) is a criterion for surgery and is remarkably prevalent in the United States, occurring in 2.8% of men and 6.9% of women in 2003 through 2004.1 The number of surgical procedures to treat obesity performed in the United States was reported to be 121 055 in 2004,2 representing only a small fraction of the population with extreme obesity.

Other therapeutic techniques for treating obesity, besides surgery, including diet, exercise, behavior therapy, and pharmacotherapy, might be applied,3 but there are few data on applying them in cases of extreme obesity, despite it being commonly encountered. Furthermore, considerable pessimism exists regarding these persons’ ability to achieve and sustain meaningful weight loss with medical, as opposed to surgical, approaches. Current obesity guidelines from the National Institutes of Health and National Heart, Lung and Blood Institute2 (p1015) state, “Extremely obese persons often do not ben-

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See also pages 121, 126, and 136

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benefit from the more conservative treatments for weight loss and weight maintenance."

We developed the Louisiana Obese Subjects Study (LOSS) to test the hypothesis that primary care physicians could effectively implement intensive medical management to treat patients with extreme obesity, with a goal of weight loss at year 2 significantly better than usual care.

**STUDY DESIGN**

We chose a practical or pragmatic clinical trial (PCT)
approach for the LOSS. A PCT (1) compares clinically relevant alternative interventions, (2) includes a diverse study population, (3) recruits participants from heterogeneous practice settings, and (4) collects data on a broad range of health outcomes. To fulfill these requirements, the LOSS recommended evidence- and guidelines-based and US Food and Drug Administration-approved treatments and mimicked real practice, where physicians and patients could negotiate treatment choices. The LOSS included relatively unselected patients with class III obesity according to the guidelines (265) and used diverse primary care practice (PCP) sites and practitioners.

The Office of Group Benefits (OGB), insurer for more than 100,000 employees of the State of Louisiana and their dependents, approached Pennington Biomedical Research Center (PBRC) to develop treatments that could be delivered in primary care physicians’ offices for class III obesity. The OGB selected 8 population centers (Alexandria, Baton Rouge, Hammond, Lafayette, Lake Charles, Monroe, New Orleans, and Shreveport) and PBRC-identified PCPs. Study coordination was performed by Pennington Management of Clinical Trials (PMCT), which implemented an electronic data capture system and monitored site personnel. The protocol and consent forms were approved by institutional review boards (IRBs) at each of the 8 sites. A data safety monitoring board reviewed and approved the protocol before the start of the study and monitored serious adverse events during the study. The clinical sites provided weight loss management and management of diabetes mellitus (DM) medications during weight loss, but all other medical management was provided by the patients’ primary care physicians.

**TRAINING OF STUDY SITE PERSONNEL AND EVALUATION OF STUDY SITE PERFORMANCE**

Seven sites were primary care clinics and 1 was an academic research facility (PBRC). Study training and procedures were implemented identically at all sites. Pennington Biomedical Research Center trained a principal investigator (PI), study coordinator, interventionist, and business manager from each site in the first 8-hour session. Study investigators and interventionists received instruction in guidelines-based approaches to obesity management, including pharmacotherapy, low-calorie diets, and behavioral intervention. Instructions were given on medication management for participants with DM during weight loss, serious adverse event reporting, and physician signoff. Study coordinators received training on data entry, medical chart construction and regulatory binders, and laboratory procedures, and the business managers were instructed in contracting and payment issues.

A second 6-hour training session focused on the behavioral group therapy procedures using a participant manual and accompanying guide for interventionists. Training included the following: (1) study protocol review, (2) peer-tutored review of earlier behavioral lectures, (3) small group exercises to practice therapeutic skills, and (4) trainees’ observation of the senior interventionist conducting several group sessions. Topics included use of study medication, meal replacements, physical activity, calorie balance, self-monitoring, structured diets, and behavioral approaches (see the description of phase 3 in the subsection titled “Intensive Medical Intervention” in this section), and management of weight loss groups. Certification ensured that clinic staff had clear understanding of the LOSS protocol and manual of procedures and lifestyle manuals. To ensure ongoing quality, PMCT conducted monthly monitoring of each site via conference call or site visit and monthly computerized tracking reports.

**PARTICIPANTS**

The goal was to recruit 480 participants, with at least 40 per site, aged 20 to 60 years, with a BMI of 40 or higher, up to and including 60, who were also enrolled in programs of the Louisiana State Employees Group Benefits Office. Women were required to be nonpregnant and agree to avoid pregnancy during the study through use of approved contraception methods. Entry required hematocrit level, white blood cell count and platelet count, and thyrotropin level that were within reference range, and uric acid level lower than 9.0 mg/dL (to convert uric acid to micromoles per liter, multiply by 59.485). Exclusions included history of major depression, suicidal behavior or eating disorder, hospitalization for mental disorder or substance abuse in the previous year, active cancer, cardiovascular or cerebrovascular disease event in the past year, heart failure, and current use of weight loss medications. Volunteers with systolic blood pressure 160 mm Hg or higher or diastolic blood pressure 100 mm Hg or higher averaged over the first 2 visits were excluded, unless they were treated and rescreened. A Duke Activity Status Index score of 25 or higher was required for entry.

**RETENTION**

Most participants were contacted by letter and telephone to encourage attendance; in Shreveport and Alexandria, the IRBs allowed participant contact only at study visits. A $100 gift card rewarded attendance at the year 2 visit. Figure 1 describes the recruitment, randomization, and retention of participants. The OGB sent a letter to 130 244 enrollees that described the study, height and weight requirements, and major eligibility criteria and invited attendance at informational sessions at 1 of 8 cities. A total of 959 individuals attended information sessions, where they were asked to make an appointment for screening. At screening visit 1, medical history, exclusion and inclusion criteria, and fasting blood samples were obtained. At visit 2, physical examination, electrocardiogram, and questionnaires were obtained. Eligible, consenting participants were randomized using an automated system.

A medical chart marker identified all participants with DM. Sites followed an algorithm for monitoring glycemia and reducing DM medications during weight loss.

**USUAL CARE CONDITION**

At the randomization visit, participants assigned to the usual care condition (UCC) group were instructed in the use of the Mayo Clinic Weight Management Web site (http://mayoclinic.com/health/weightloss/MY00432). The UCC participants were given appointments for annual visits at years 1 and 2.

**INTENSIVE MEDICAL INTERVENTION**

The intensive medical intervention (IMI) group used evidence-based approaches supported by weight management literature...
but delivered in a practical manner. The sites were instructed that the protocols provided general treatment guidelines, and deviations were allowed at the participant’s request and physician’s discretion. The IMI recommended 3 phases.

- Phase 1 began with a low-calorie liquid diet plus 10 g of added fat (choice of 2 teaspoons of vegetable oil or ten 1-g fish oil capsules). The study dispensed, at no cost, powdered HealthOne formula (Health and Nutrition Technology Inc, Carmel, California) and recommended consumption of 5 shakes per day, providing 890 kcal/d, 75 g of protein, 15 g of fat, and 110 g of carbohydrates. Electrocardiograms and electrolytes were obtained every 2 weeks during the liquid diet. Phase 1 could continue for 12 weeks, but if participants could not tolerate the liquid diet, they could progress to phase 2 at any time.

- Phase 2 took place during the next 4 months: a highly structured diet and medication were recommended along with group behavioral therapy. Group sessions were held weekly for 4 weeks and then every 2 weeks for 3 months. Physician visits occurred monthly. The recommended diet consisted of 2 meal replacements (HealthOne, Slim Fast [Unilever, Englewood Cliffs, New Jersey], Glucerna [Abbott Nutrition, Abbott Laboratories, Columbus, Ohio], Boost [Nestle Health Care, Nutrition Inc, Minneapolis, Minnesota], or other commercial product), along with 2 portion-controlled snacks and 1 structured meal each day. This diet was approximately 1200 to 1600 kcal/d. In addition, sibutramine hydrochloride and orlistat were dispensed to aid weight loss and maintenance, but for some patients, we dispensed diethylpropion hydrochloride (intermittent use). Sibutramine was recommended, preferentially, as first-line therapy and was the most commonly dispensed drug from the central pharmacy. For depression, venlafaxine hydrochloride and bupropion hydrochloride were recommended and for DM, metformin, because these drugs do not promote weight gain. Groups consisted of approximately 15 individuals. The 1-hour group sessions followed a common manual, led by an interventionist from the study site. The behavioral intervention allowed flexibility with individually tailored treatment strategies. Participants received education in weight management, physical activity, and behavioral strategies, including self-monitoring, stimulus control, social support, contingency management, problem solving, and relapse prevention. We incorporated physical activity recommendations (walking, water exercise, and weight training) into group sessions, beginning in phase 2 and continuing through phase 3.

- Phase 3 occurred during months 8 to 24. Weight loss medications and 1 daily meal replacement were continued; monthly group sessions were conducted. Phase 3 allowed treatments employed pragmatically as needed, including a repeated low-calorie liquid diet in 4- to 12-week episodes, novel dietary approaches (high-protein/low-carbohydrate diet, the Dietary Approaches to Stop Hypertension [DASH]6 diet, low glycemic load diet), and physical activity.

**MEASUREMENTS**

Height was measured at baseline with a wall-mounted stadiometer graduated in centimeters. Weight was measured twice at every assessment visit by using a calibrated office scale with a digital display. Weight and height were measured in fasting, postvoiding participants wearing light clothing, without shoes. At every contact, weight was measured to monitor therapy but it was recorded only in the database for assessment visits. Blood pressure was obtained at every contact with an appropriately sized cuff using standard mercury sphygmomanometer or electronic blood pressure monitor. Fasting blood samples for complete blood count and chemistry profile were obtained at baseline, year 1, and year 2. Serum electrolytes were measured every 2 weeks during phase 1. All samples were sent to PBRC’s clinical reference laboratory for analysis.

**DATA COLLECTION AND MANAGEMENT**

Pennington Management of Clinical Trials served as the coordinating center to manage randomization and data acquisition using an Internet-based data capture system. Sites were trained in the system and periodically monitored for data collection and protocol compliance and to address issues, concerns, and status of the site.

**STATISTICAL ANALYSIS**

The coordinating center randomly assigned participants to the IMI or UCC groups by applying minimization allocation,7 with stratification by sex, BMI, and age to achieve allocations that were comparable with specified baseline prognostic factors. For the stratification, age and BMI were dichotomized as follows: age (in years) 20 or older but younger than 40, or 40 or older, up to and including 60; and BMI of 40 or higher but less than 45, or 45 or higher, up to and including 60. Enrollment was completed in 8 months.

Categorical variables were summarized as percentages, and χ2 tests were used to test the significance of group differences. Con-
RESULTS

STUDY SITES AND BASELINE POPULATION

Seven of the 8 sites specialized in family medicine, and most physicians had been in practice more than 20 years (Table 1). In 4 of 8 sites, the PI had prior research experience. Four interventionists were dietitians. In August 2005, the New Orleans site was permanently closed owing to Hurricane Katrina, forcing relocation of study staff and participants. Participants were offered treatment in other clinical sites but are censored from this analysis. The site started in Monroe was a newly established clinic and was unable to complete the protocol, providing no observations at year 1 or year 2, and was censored from analysis. Three patients in the UCC group who opted for obesity surgery were also censored from analysis (Figure 1).

Screening, randomization, and retention varied by site (Table 1), with rates of return at year 2 varying from 0% to 72%. Of 597 individuals who were screened at the 8 sites (Figure 1), 465 (78%) met eligibility requirements and were randomized.

Table 1. Characteristics of, and Recruitment and Retention by, Clinical Sites in Louisiana

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Alexandria</th>
<th>Baton Rouge</th>
<th>Hammond</th>
<th>Lafayette</th>
<th>Lake Charles</th>
<th>Monroe</th>
<th>New Orleans</th>
<th>Shreveport</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site PI’s specialty</td>
<td>Family</td>
<td>Family</td>
<td>Internal</td>
<td>Family</td>
<td>Family</td>
<td>Family</td>
<td>Family</td>
<td>Family</td>
</tr>
<tr>
<td>Site PI’s research experience</td>
<td>No</td>
<td>Yes, extensive</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Site PI’s years in practice</td>
<td>6</td>
<td>25</td>
<td>27</td>
<td>8</td>
<td>23</td>
<td>5</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Site PI’s practice type</td>
<td>Group</td>
<td>Group</td>
<td>Group</td>
<td>Group; residency training program</td>
<td>Group; residency training program</td>
<td>Solo</td>
<td>Group</td>
<td>Group</td>
</tr>
<tr>
<td>Site PI’s patient visits/d</td>
<td>20</td>
<td>12</td>
<td>20-25</td>
<td>35</td>
<td>16-24</td>
<td>30</td>
<td>Unknown</td>
<td>30</td>
</tr>
<tr>
<td>Groups formed for intervention delivery, No.</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Credentials of interventionist</td>
<td>RD</td>
<td>RD</td>
<td>LPC</td>
<td>LCSW</td>
<td>LCWS</td>
<td>NA</td>
<td>RD</td>
<td></td>
</tr>
<tr>
<td>Participants screened, No.</td>
<td>106</td>
<td>82</td>
<td>89</td>
<td>75</td>
<td>60</td>
<td>68</td>
<td>45</td>
<td>72</td>
</tr>
<tr>
<td>Participants randomized, No. (%)</td>
<td>76 (75)</td>
<td>68 (71)</td>
<td>76 (85)</td>
<td>60 (80)</td>
<td>54 (90)</td>
<td>49 (72)</td>
<td>23 (NA)</td>
<td>59 (82)</td>
</tr>
<tr>
<td>Year 1 visits, %</td>
<td>41</td>
<td>66</td>
<td>57</td>
<td>60</td>
<td>70</td>
<td>0</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td>Year 2 visits, %</td>
<td>32</td>
<td>63</td>
<td>49</td>
<td>63</td>
<td>72</td>
<td>0</td>
<td>0</td>
<td>15</td>
</tr>
</tbody>
</table>

Abbreviations: LCSW, licensed clinical social worker; LMFT, licensed marriage and family therapist; LPC, licensed professional counselor; NA, not applicable because site closed during randomization; PI, principal investigator; RD, registered dietitian.

Table 2 depicts baseline characteristics of 390 randomized participants. The mean age of the population was 47 years, and they were predominantly white (79%) and female (83%). There were 21% with known type 2 DM, 5.4% who were taking insulin, and 42% with fasting blood glucose levels of 100 mg/dL or higher at study start (to convert glucose levels to millimoles per liter, multiply by 0.0555). There were no group differences in race, sex, age, BMI, and metabolic characteristics at baseline. Attendance at the year 1 visit was greater for the IMI group (60%) than for the UCC group (47%) (P = .01). At the year 2 visit, attendance rates were 51% and 45%, respectively (P = .30).

WEIGHT LOSS

In the IMI group at year 2, the BOCF analysis showed a mean ± SEM weight loss of −4.9% ± 0.8%, whereas in the UCC group it was −0.2% ± 0.3%; LOCF analysis at year 2 for the IMI group was −8.3% ± 0.8% and −0.0% ± 0.4% for the UCC group (Figure 2). At year 2, among the 51% of attending IMI participants, the mean weight loss was −9.7% ± 1.3%, whereas it was −0.4% ± 0.7% among the 46% of attending UCC participants. The group differences were significant (P < .001) at year 2 for BOCF, LOCF, completers, and mixed models analyses. Thus, sensitivity of the different statistical test results to assumptions about missing data mechanisms was verified to be robust in light of resulting F statistics that ranged from 35.60 (mixed model) to 40.18 (completers), with P < .001 for all comparisons. Weight loss trajectory in the IMI group is depicted in Figure 2, showing a nadir of −15.5% ± 0.8% below baseline at 38 weeks for attendees.

The percentage of all randomized individuals (intention to treat) and of completers achieving weight loss of −5%, −10%, −15%, and −20% from baseline is illustrated in Figure 3. At year 2, 31% of 200 people randomized to IMI sustained a weight loss of 5% or more of their initial body weight, 21% sustained a loss of 10% or more, and 7% sustained a loss of 20% or more, compared with 9%, 3%, and 1% of the 190 individuals in the UCC group who met the criteria for these categories (P < .001). In 101 individuals who completed measure-
were not statistically significant (2.4 mg/dL and 6.7 mg/dL, respectively; \( P = .16 \)). The prevalence of fasting plasma glucose levels of 126 mg/dL or higher or 100 to 125 mg/dL showed significant improvements in the IMI group at year 1 but not at year 2. The mean high-density lipoprotein cholesterol (HDL-C) level increased at year 1 by 2.5±0.8 mg/dL in the IMI completers group compared with −1.0±0.9 mg/dL in the UCC group (\( P = .003 \)) (data not shown) (to convert HDL-C to millimoles per liter, multiply by 0.0259). At year 2, those changes were 3.1±0.9 mg/dL and −0.2±0.8 mg/dL (\( P = .01 \)). As seen in Table 3, the percentage change in HDL-C was significant at both years. There was a decrease in serum triglyceride level in the IMI group of −13.2±4.1% at year 1 compared with increases of −1.6%±4.1% and 11.8% in the UCC group (\( P = .002 \)); however, the year 2 results for the IMI group were not significant compared with the results for the UCC group. Uric acid and alanine aminotransferase levels were both improved at year 1 and year 2 in the IMI group compared with those in the UCC group, but the GGT comparison was improved only at year 1 and not at year 2. In contrast, there were no significant group differences in mean values for blood pressure or low-density lipoprotein cholesterol (LDL-C) level at either time point (Table 3).

### SAFETY

There were no problems with electrolyte imbalance during the liquid diet. There were 20 serious adverse events reported in the IMI group and 8 for the UCC group, but none was related to treatment:

#### Intensive Medical Intervention Group
- Hospitalization for deep vein thrombosis
- Hospitalization for coronary stent replacement
- Surgery for cystocele
- Surgical incision and drainage of abscess
- Hospitalization for pneumonia
- Hospitalization for hallucinations, history of mental illness
- Hospitalization for hernia repair
- Hospitalization for arm fracture
- Hospitalization for nephrolithiasis
- Hospitalization for stent placement
- Hospitalization for acute myocardial infarction
- Abdominal hernia repair
- Total knee replacement
- Neov-onset atrial fibrillation

#### Usual Care Condition Group
- Hospitalization for deep vein thrombosis
- Hospitalization for coronary stent replacement
- Surgery for cystocele
- Surgical incision and drainage of abscess
- Hospitalization for pneumonia
- Hospitalization for hallucinations, history of mental illness
- Hospitalization for hernia repair
- Hospitalization for arm fracture
- Hospitalization for nephrolithiasis
- Hospitalization for stent placement
- Hospitalization for acute myocardial infarction
- Abdominal hernia repair
- Total knee replacement
- Neov-onset atrial fibrillation

### METABOLIC PARAMETERS

The mean fasting glucose level decreased by −5.0 mg/dL in the IMI group and increased by 4.6 mg/dL in the UCC group at year 1 (\( P < .001 \)) (Table 3). At year 2, changes in the IMI group and increased by 4.6 mg/dL in the UCC group at year 1 (\( P < .001 \)) (Figure 3).
sion, bipolar disorder, and asthma, who had lost 22.9 kg but was not taking sibutramine or other weight loss medication.

**COMMENT**

Recently, the SOS study demonstrated that surgery for obesity is associated with reduction in mortality. Still, surgery is currently not an option for most patients with extreme obesity because of reimbursement issues and individual preference. In fact, even less costly medical interventions, such as counseling, weight loss medications, and meal replacements are almost never reimbursed for patients with extreme obesity. There is a need for guidance for primary care physicians in more effective management of this commonly encountered condition and a need for evidence to support the effectiveness of medical approaches so that reimbursement might occur. The LOSS used a PCT as a research model to inform real-world medical approaches to extreme obesity. The LOSS’s central hypothesis was that primary care clinics in the real-world setting could implement an approach wherein meaningful weight loss could be achieved and sustained at 2 years. Not all practices were successful; one clinic closed because of a natural disaster and in another, the newly established physician and staff could not perform the study while burdened with the myriad duties of establishing a practice. Certainly, not all patients benefited, but for all those offered the IMI, 31% achieved a loss of 5% or more of their body weight and 21% achieved a loss of 10% or more. This would indicate that physicians with a modicum of training can deliver an intervention with benefit for about a third of those they see.

The issue of poor retention in weight loss studies is well known, and it takes special efforts to produce the excellent retention rates of the Diabetes Prevention Program (92.5% at 1.8-4.6 years) and the Look AHEAD (96% at 1 year) trials and even the POUNDS Lost trial (80% at 2 years). Participant retention in 2-year medication-based weight loss studies ranges from 45% to 52%, similar to the LOSS’s retention rate. In the study by Apfelbaum et al., which had a design like that of the LOSS, the retention rate was 53% at 1 year, if liquid diet dropouts are considered. The lesson for primary care physicians is that only half of those who are offered a weight loss intervention may stay in the pro-

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**Figure 2.** Weight loss (percentage from baseline over 2 years) among participants in the intensive medical intervention (IMI) group of the Louisiana Obese Subjects Study compared with the usual care condition (UCC) group. The 12-week low-calorie liquid diet phase is indicated by a shaded area. The observed weight loss in both conditions is plotted with measured points indicated by circles. Baseline observation carried forward (BOCF) analysis is indicated by a triangle at year 2 (−0.2±0.3% for the UCC group and −4.9±0.8 for the IMI group; \( P < .001 \) for treatment comparison) and last observation carried forward (LOCF) analysis is indicated by a square at year 2 (−0.2±0.4% for UCC and −0.3±0.8 for IMI; \( P < .001 \) for treatment comparison).

**Figure 3.** Percentage of the participants in the Louisiana Obese Subjects Study who met weight loss or gain categories at year 2. The first series is an analysis of all participants who attended the year 2 visit. The second series indicates the prevalence of attaining benchmarks among all enrolled participants. IMI indicates intensive medical intervention; UCC, usual care condition.
Table 3. Metabolic Health Outcomes for Completers in the Intensive Medical Intervention (IMI) Group and Usual Care Condition (UCC) Group

<table>
<thead>
<tr>
<th>Type of Change</th>
<th>IMI Group (n=119)</th>
<th>UCC Group (n=89)</th>
<th>P Valueb</th>
<th>IMI Group (n=10)</th>
<th>UCC Group (n=86)</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>-13.1 (1.2)</td>
<td>-0.9 (0.6)</td>
<td>&lt;.001</td>
<td>-9.7 (1.3)</td>
<td>-0.4 (0.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Weight loss, mean (SE), kg</td>
<td>-17.2 (1.6)</td>
<td>-1.1 (0.8)</td>
<td>&lt;.001</td>
<td>-12.7 (1.7)</td>
<td>-0.5 (0.9)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: ALT, alanine aminotransferase; BP, blood pressure; BUN, blood urea nitrogen; DASI, Duke Activity Status Index; FPG, fasting plasma glucose; GGT, serum γ-glutamyltransferase; LDH, lactate dehydrogenase; TG, triglycerides.

*SI conversion factor: To convert FPG to millimoles per liter, multiply by 0.0555.*

Data are given as mean percentage (SE) except where noted.

*p Values represent comparison between IMI and UCC groups for each year.*

The LOSS does not propose that the IMI replaces the need for bariatric surgery. A meta-analysis of obesity surgery reports weight losses of 20 to 30 kg, durable for 10 years. Furthermore, weight regain with bariatric surgery is not as pronounced as in the LOSS, in which weight gain was demonstrated beginning at year 1. However, for most patients seen in daily practice who do not have access to bariatric surgery, our study suggests that physicians should not be pessimistic about helping them lose weight.

There are only a few studies of nonsurgical weight loss approaches with very heavy patients with which we might compare our results. Andersen et al30 randomized 60 patients to gastropasty or diet. At the end of year 1, the diet group had lost 22 kg, or nearly 20% of their median baseline weight of 115 kg. However, during the next 18 months they regained almost all of the lost weight. In contrast, the LOSS trial demonstrated success at 2 years for a subgroup. In a second trial of diet intervention, patients with a median weight of 129 kg had a median weight loss of 10 kg at 18 months. An observational report32 of 80 patients with a BMI of 40 or higher showed a mean weight loss of 19.7 kg in 79% of patients at their 2-year follow-up. A final comparison of surgery and diet produced a 2-year weight loss of 21.6% in the group treated with surgery and 5.5% in the group treated with diet.33 It is generally accepted that weight losses of 5% or more are associated with improved health outcomes.34 The LOSS was not designed to test the effect of sustained modest weight loss in extreme obesity. In the LOSS, at year 1, the active comparator should make long-term study of intensive approaches to weight management more feasible.
tions. Last, retention in the LOSS probably mimics real-world weight loss behavior, but it was less than desired. Year 2 follow-up rates, although not significantly different at 51% and 45% (P = .30), leave ample room for improvement.

In the United States, physicians should not ignore those patients with class III obesity who cannot undergo bariatric surgery. Research is needed to guide primary care approaches that are safe, efficacious, and cost-effective. The LOSS pragmatic clinical trial demonstrates that this research can be done in the real-world setting, mimicking real-life clinical practices. The issues of retention and weight loss maintenance require further study, for they are not seen only in studies of class III obesity but in many obesity interventions. Finally, less complex and less costly interventions (eg, weight loss medications combined with monthly visits or delivery of counseling by call centers) need to be tested in this population to increase their uptake in PCPs.

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Conflict of Interest for Authors: The following authors receive, have received in the past 5 years, or will receive health insurance from the OGB: Drs Ryan, Johnson, Myers, Rood, Brantley, Bray, Gupta, Broussard, Barootes, Elkins, Savory, and Datz, Ms Prather, and Mssrs Brock and Pothakamuri. The following authors had part of their salary derived from the OGB-sponsored project: Ms Prather, Drs Gaudin, Savory, and Stenlof, and Mssrs Brock and Mr Pothakamuri. Since January 2008, Dr Ryan has refused any remuneration from makers or developers of drugs, devices, or products for obesity or any other health-related uses. She expects to maintain that posture for the foreseeable future. However, prior to that time over the previous 5 years, she received funding for consultation and for services on scientific advisory boards for Abbott Laboratories, Arena, Johnson & Johnson, Merck & Co, NutriSystem, Sanofi-Aventis, Shionogi, and Vivus. Dr Bray has had the following relationships over the past 5 years with makers or developers of drugs, services, or devices for treatment of obesity (he has no stock ownerships or corporate employment): he has been a consultant to Amylin Pharmaceuticals, Orexigen Pharmaceuticals, GlaxoSmithKline, and Merck & Co and has received clinical trial support from Merck & Co and Takeda Pharmaceutical Co. Dr McKnight received financial remuneration within the past 5 years or in the future for services provided to the OGB, a funder of the study. Dr Stenlof was an employee of PMCT when the study was initiated. He has received funding for consultation and for services on scientific advisory boards for Johnson & Johnson, Sanofi-Aventis, Bristol-Myers Squibb, GlaxoSmithKline, AstraZeneca, and Abbott Laboratories. Dr Sjöström has obtained research grants from Hoffmann-La Roche, AstraZeneca, Sanofi-Aventis, and Ethicon, and lecture and consulting fees from AstraZeneca, Biovitrum, BMS, GlaxoSmithKline, Global Health Partners, Johnson & Johnson, Lenimen, Merck & Co, NovoNordisk, Hoffmann La Roche, and Sanofi-Aventis. He holds stocks in Lenimen and Global Health Partners.

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REFERENCES


