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%±0.79% 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.

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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 Institute[3(p1015)] state, "Extremely obese persons often do not ben-

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efit 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.

METHODS

STUDY DESIGN

We chose a practical or pragmatic clinical trial (PCT)[4] 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[3(p545)] 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[3] 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 sign-off. 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, toolbox 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[5] 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, inclusion and exclusion 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

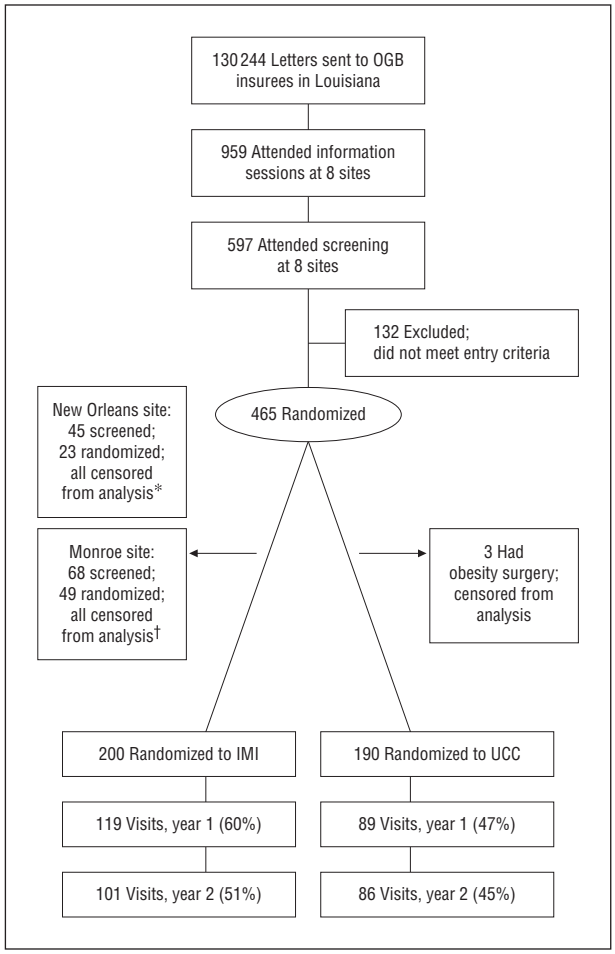

Figure 1. Profile of the Louisiana Obese Subjects Study recruitment and retention. IMI indicates intensive medical intervention; OGB, Office of Group Benefits; UCC, usual care condition. *The New Orleans clinic closed 3 weeks after initiating screening due to Hurricane Katrina. †The Monroe site was censored because of inability to fulfill the treatment and research requirements. There were no participant visits obtained at year 1 or 2. See the subsection titled "Study Sites and Baseline Population" in the "Results" section.

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 [Nestlé 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 χ^2 tests were used to test the significance of group differences. Con-

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

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

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.

tinuous variables were summarized as means and standard errors (SEs). Significance of weight loss from baseline to 2 years was evaluated using 1-sample *t* test of the hypothesis that the mean percentage change at 2 years was zero.[8] Assessment was performed separately within the 2 groups using only data from participants who completed their 2-year visit, for analysis of data for completers. Analogous tests were used to analyze metabolic parameters. For missing data, baseline observations were carried to 2 years for baseline observation carried forward (BOCF) analysis, and last assessment data were carried forward for last observation carried forward (LOCF) analysis. A 2-sample *t* test or an equivalent *F* test was used to compare the 2 groups with respect to mean percentage change for completers, BOCF, and LOCF at 2 years. Finally, a mixed model analysis was performed using restricted maximum likelihood using all available data. These different tests require different assumptions about the mechanisms that led to the missing data so a sensitivity analysis was performed to compare the consistency of test results. Tests resulting in $P \leq .05$ were considered statistically significant. Data were analyzed using the SAS System for Windows, (version 9.1; SAS Institute, Cary, North Carolina).

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 2 depicts baseline characteristics of 390 randomized participants. The mean age of the population was 47 years, and they were predominantly white (75%) 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-

Table 2. Baseline Characteristics

Characteristic	Intensive Medical Intervention (n=200)	Usual Care Condition (n=190)	*P* Value
Male, total, No. (%)	33 (16.5)	31 (16.3)	.80
White	29 (14.5)	26 (13.7)	
Black	4 (2.0)	5 (2.2)	
Female, total, No. (%)	167 (83.5)	159 (83.7)	.66
White	120 (60.0)	121 (63.7)	
Black	46 (23.0)	38 (20.0)	
Hispanic	1 (0.5)	0 (0.0)	
Presence of DM, No. (%)	42 (26.0)	38 (20.0)	.79
Use of insulin, No. (%)	11 (6.0)	10 (4.7)	.99
Weight, median (IQR), kg	126.2 (23.2)	128.4 (28.6)	.54
BMI, median (IQR)	45.6 (7.9)	46.6 (8.5)	.31
Male	44.9 (7.2)	46.4 (9.6)	.22
Female	45.7 (8.0)	46.8 (8.4)	.74
Age, mean (SE), y	47.2 (0.6)	47.1 (0.6)	.90
BP, mean (SE), mm Hg			
Systolic	131.4 (1.0)	132.3 (1.2)	.55
Diastolic	79.6 (0.7)	80.3 (0.7)	.46
Heart rate, mean (SE), BPM	75.1 (0.7)	73.4 (0.7)	.46
Glucose level, mean (SE), mg/dL	107.0 (2.5)	105.6 (2.5)	.57
ALT, mean (SE), U/L	25.9 (1.0)	26.5 (1.3)	.73
GGT, mean (SE), U/L	31.4 (1.7)	32.8 (2.0)	.59
Total cholesterol level, mean (SE), mg/dL	202.1 (2.8)	198.7 (2.7)	.38
HDL-C level, mean (SE), mg/dL	52.4 (1.0)	50.6 (0.9)	.18
Male	44.1 (2.1)	41.7 (1.9)	.42
Female	54.0 (1.1)	52.4 (1.0)	.26
LDL-C level, mean (SE), mg/dL	118.6 (2.3)	116.0 (2.3)	.44
Triglycerides level, mean (SE), mg/dL	158.1 (6.1)	163.0 (6.3)	.58
Uric acid, mean (SE), mg/dL	5.8 (0.1)	6.0 (0.1)	.31
LDH, mean (SE)	165.1 (2.4)	164.3 (2.3)	.80
BUN, mean (SE), mg/dL	14.0 (0.3)	13.8 (0.3)	.70
Creatinine, mean (SE), mg/dL	0.9 (0.0)	0.9 (0.0)	.58

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BUN, blood urea nitrogen; DM, diabetes mellitus; GGT, serum γ-glutamyltransferase; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDH, lactate hydrogenase; LDL-C, low-density lipoprotein cholesterol.

SI conversion factors: To convert ALT and LDH to microkatals per liter, multiply by 0.0167 and 0.0167, respectively; to convert BUN to millimoles per liter, multiply by 0.357; to convert creatinine to micromoles per liter, multiply by 88.4; to convert GGT to microkatals per liter, multiply by 0.01667; to convert glucose to millimoles per liter, multiply by 0.0555; to convert total cholesterol, HDL-C, and LDL-C to millimoles per liter, multiply by 0.0259; to convert triglycerides and uric acid to millimoles per liter, multiply by 0.0113 and 59.485, respectively.

ments at year 2, 61%, 41%, and 14% of the IMI group achieved losses of 5% or more, 10% or more, and 20% or more, respectively, compared with 20%, 6%, and 1%, respectively, of the 86 participants in the UCC group who met the criteria for these categories ($P<.001$) (Figure 3).

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 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 cystocoele
- 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 asthma and bronchitis
- Chest heaviness and referral to cardiologist
- Elevated blood pressure and mood swings
- Chest pain and angiography; negative workup
- Hospitalization for chest pain; diagnosis dehydration
- Cervical disk surgery
- Bleeding duodenal ulcer
- Death due to myocardial infarction
- Abdominal hernia repair
- Total knee replacement
- New-onset atrial fibrillation

Usual Care Condition Group
- Hospitalization for acute myocardial infarction
- Pacemaker insertion
- Hospitalization for back surgery
- Hospitalization for hypokalemia
- Hospitalization for stent placement
- Total knee replacement
- Hysterectomy
- Breast cancer

There was 1 death from a myocardial infarction in a 48-year-old male patient who had a history of hyperten-

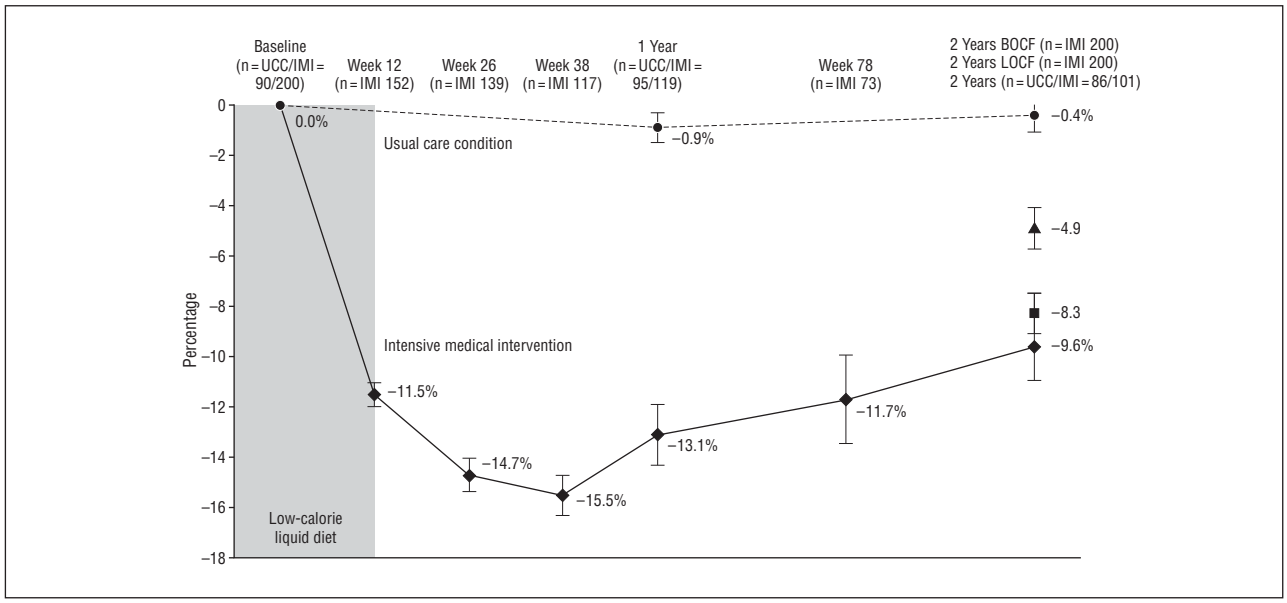

Figure 2. Weight loss (percentage from baseline over 2 years) among participants in the intensive medical intervention (IMI) group of the Louisiana Obese Subjects Study compared with the usual care condition (UCC) group. The 12-week low-calorie liquid diet phase is indicated by a shaded area. The observed 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 (−0.0±0.4% for UCC and −0.3±0.8 for IMI; $P<.001$ for treatment comparison).

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[9] 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[4] 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,[10] and it takes special efforts to produce the excellent retention rates of the Diabetes Prevention Program [11]

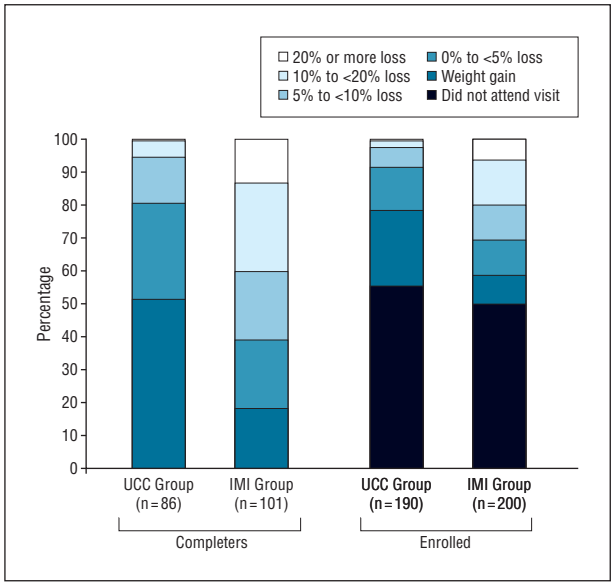

Figure 3. Percentage of the participants in the Louisiana Obese Subjects Study who met weight loss or gain categories at year 2. The first series is an analysis of all participants who attended the year 2 visit. The second series indicates the prevalence of attaining benchmarks among all enrolled participants. IMI indicates intensive medical intervention; UCC, usual care condition.

(92.5% at 1.8-4.6 years) and the Look AHEAD[11] (96% at 1 year) trials and even the POUNDS Lost[12] trial (80% at 2 years). Participant retention in 2-year medication-based weight loss studies ranges from 45% to 52%,[13-17] similar to the LOSS's retention rate. In the study by Apfelbaum et al,[18] 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-

Table 3. Metabolic Health Outcomes for Completers in the Intensive Medical Intervention (IMI) Group and Usual Care Condition (UCC) Group[a]

Type of Change	Year 1			Year 2		
	IMI Group (n=119)	UCC Group (n=89)	*P* Value[b]	IMI Group (n=10)	UCC Group (n=86)	*P* Value[b]
Weight loss	−13.1 (1.2)	−0.9 (0.6)	<.001	−9.7 (1.3)	−0.4 (0.7)	<.001
Weight loss, mean (SE), kg	−17.2 (1.6)	−1.1 (0.8)	<.001	−12.7 (1.7)	−0.5 (0.9)	<.001
Change						
In FPG level, mean (SE), mg/dL	−5.0 (1.8)	4.6 (1.6)	.001	2.4 (2.1)	6.7 (2.1)	.16
% With FPG level of 100-125 mg/dL	9.9	22.9	.01	11.1	22.6	.04
% With FPG level >125 mg/dL	7.1	16.9	.03	16.2	21.2	.38
In systolic BP, mean (SE), mm Hg	−9.7 (1.5)	−8.7 (2.1)	.67	−14.7 (2.4)	−8.6 (2.6)	.09
In diastolic BP, % (SE), mm Hg	−2.9 (1.0)	−4.6 (1.2)	.28	−4.4 (1.8)	−3.2 (1.5)	.60
In LDL-C level	1.9 (2.1)	1.5 (1.7)	.87	1.8 (2.4)	0.7 (2.4)	.73
In HDL-C level	6.8 (1.5)	−0.1 (1.7)	.004	7.9 (1.8)	1.5 (1.8)	.01
In TG level	−13.2 (4.1)	−1.6 (4.1)	.05	−9.2 (3.5)	−4.8 (4.3)	.42
In ALT level	−11.9 (2.8)	5.1 (5.0)	.003	−4.3 (5.2)	11.8 (6.7)	.06
In GGT level	−17.2 (4.2)	−4.6 (3.2)	.02	13.0 (14.2)	3.7 (9.8)	.59
In uric acid level	−7.0 (2.0)	2.9 (1.4)	.001	−3.0 (2.4)	3.1 (1.8)	.05
In LDH level	−5.4 (1.4)	1.3 (1.5)	.001	−1.5 (1.7)	−1.7 (2.4)	.48
In BUN level	15.1 (2.6)	20.0 (3.9)	.31	19.1 (3.4)	20.2 (4.2)	.85
In creatinine level	7.3 (1.3)	9.9 (1.6)	.20	10.4 (1.4)	11.1 (2.1)	.76
Mean change in DASI score, U	0.8 (1.3)	−7.8 (1.9)	.001	−2.1 (1.7)	−11.6 (2.0)	.001

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 hydrogenase; TG, triglycerides.

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

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

[b] *P* values represent comparison between IMI and UCC groups for each year.

gram. However, the results for those who do may be quite encouraging. For those in the IMI group who were seen at year 2, perhaps spurred by a gift card, 61% and 41% achieved weight losses of 5% or more and 10% or more, respectively. This would indicate that roughly 3 in 5 who are active in such a program will achieve clinically significant benefit.

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.[19] 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 al[20] randomized 60 patients to gastroplasty 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[21] of diet intervention, patients with a median weight of 129 kg had a median weight loss of 10 kg at 18 months. An observational report[22] 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.[23]

It is generally accepted that weight losses of 5% or more are associated with improved health outcomes.[24] The LOSS was not designed to test the effect of sustained modest weight loss in extreme obesity. In the LOSS, at year 1, improvements were mostly demonstrable, but at year 2, many were no longer evident. This almost certainly represents the impact of weight regain. At neither year was there improvement in LDL-C level, which requires a larger amount of weight loss.[25]

Weight regain is of concern in the LOSS. This is common in long-term obesity trials, whether they use lifestyle intervention or medications. Recently, strategies to promote maintenance with lifestyle and behavioral approaches have been explored, using telephone and Internet methods to improve counselor contacts, with modest success.[26] The longest reported trial with medication, the Xenical in the Prevention of Diabetes in Obese Subjects (XENDOS) study,[27] used orlistat over 4 years. For those receiving orlistat, 52% completed year 4, and their average weight was −6.9 kg below their baseline compared with a loss of −4.1 kg and a 34% completion rate for the placebo-treated group ($P<.001$). The XENDOS study demonstrates that long-term weight loss studies are possible. An active comparator should make long-term study of intensive approaches to weight management more feasible.

There are several caveats about the LOSS. The treatment paradigm did not always mimic medical practices. Medications and liquid formula diets were *dispensed* by the primary care clinics. The weight loss program was delivered by the physicians and their staff who were managing obesity as a referral model. The treatment program was devised by physicians and scientists experienced in obesity treatment and research, and the treatment strategy was based on well-established behavioral programs[10,28,29] and on experience with obesity medica-

tions.[30-32] Last, retention in the LOSS probably mimics real-world weight loss behavior, but it was less than desired.[33] 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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