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Health Benefits of Gastric Bypass Surgery After 6 Years

Ted D. Adams, PhD, MPH
Lance E. Davidson, PhD
Sheldon E. Litwin, MD
Ronette L. Kolotkin, PhD
Michael J. LaMonte, PhD
Robert C. Pendleton, MD
Michael B. Strong, MD
Russell Vinik, MD
Nathan A. Wanner, MD
Paul N. Hopkins, MD, MSPH
Richard E. Gress, MA
James M. Walker, MD
Tom V. Cloward, MD
R. Tom Nuttall, RRT
Ahmad Hammoud, MD
Jessica L. J. Greenwood, MD, MSPH
Ross D. Crosby, PhD
Rodrick McKinlay, MD
Steven C. Simper, MD
Sherman C. Smith, MD
Steven C. Hunt, PhD

Context Extreme obesity is associated with health and cardiovascular disease risks. Although gastric bypass surgery induces rapid weight loss and ameliorates many of these risks in the short term, long-term outcomes are uncertain.

Objective To examine the association of Roux-en-Y gastric bypass (RYGB) surgery with weight loss, diabetes mellitus, and other health risks 6 years after surgery.

Design, Setting, and Participants A prospective Utah-based study conducted between July 2000 and June 2011 of 1156 severely obese (body mass index [BMI] ≥35) participants aged 18 to 72 years (82% women; mean BMI, 45.9; 95% CI, 31.2-60.6) who sought and received RYGB surgery (n=418), sought but did not have surgery (n=417; control group 1), or who were randomly selected from a population-based sample not seeking weight loss surgery (n=321; control group 2).

Main Outcome Measures Weight loss, diabetes, hypertension, dyslipidemia, and health-related quality of life were compared between participants having RYGB surgery and control participants using propensity score adjustment.

Results Six years after surgery, patients who received RYGB surgery (with 92.6% follow-up) lost 27.7% (95% CI, 26.6%-28.9%) of their initial body weight compared with 0.2% (95% CI, −1.1% to 1.4%) gain in control group 1 and 0% (95% CI, −1.2% to 1.2%) in control group 2. Weight loss maintenance was superior in patients who received RYGB surgery, with 94% (95% CI, 92%-96%) and 76% (95% CI, 72%-81%) of patients receiving RYGB surgery maintaining at least 20% weight loss 2 and 6 years after surgery, respectively. Diabetes remission rates 6 years after surgery were 62% (95% CI, 49%-75%) in the RYGB surgery group, 8% (95% CI, 0%-16%) in control group 1, and 6% (95% CI, 0%-13%) in control group 2, with remission odds ratios (ORs) of 16.5 (95% CI, 4.7-57.6; $P<.001$) vs control group 1 and 21.5 (95% CI, 5.4-85.6; $P<.001$) vs control group 2. The incidence of diabetes throughout the course of the study was reduced after RYGB surgery (2%; 95% CI, 0%-4%; vs 17%; 95% CI, 10%-24%; OR, 0.11; 95% CI, 0.04-0.34 compared with control group 1 and 15%; 95% CI, 9%-21%; OR, 0.21; 95% CI, 0.06-0.67 compared with control group 2; both $P<.001$). The numbers of participants with bariatric surgery–related hospitalizations were 33 (7.9%), 13 (3.9%), and 6 (2.0%) for the RYGB surgery group and 2 control groups, respectively.

Conclusion Among severely obese patients, compared with nonsurgical control patients, the use of RYGB surgery was associated with higher rates of diabetes remission and lower risk of cardiovascular and other health outcomes over 6 years.

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The prevalence of extreme obesity in the United States is increasing at a rate greater than moderate obesity.[1,2] Unfortunately, lifestyle therapy is generally insufficient as a weight management intervention for patients who are extremely obese. To date, effective long-term weight loss through pharmacological therapy has been marginal, leaving bariatric

For editorial comment see p 1160.

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Author Affiliations: Departments of Internal Medicine (Drs Adams, Davidson, Litwin, Pendleton, Strong, Vinik, Wanner, Hopkins, Walker, and Hunt and Mr Gress), Obstetrics and Gynecology (Dr Hammoud), and Family and Preventive Medicine (Dr Greenwood), University of Utah School of Medicine, Salt Lake City; Intermountain Health and Fitness Institute, LDS Hospital (Dr Adams), and Intermountain Sleep Disorders Center (Drs Walker and Cloward and Mr Nuttall), Intermountain Healthcare, Salt Lake City, Utah; Rocky Mountain Associated Physicians Inc, Salt Lake City, Utah (Drs McKinlay, Simper, and Smith); Department of Medicine, Georgia Health Sciences University, Augusta (Dr Litwin); Obesity and Quality of Life Consulting and Department of Community and Family Medicine, Duke University Health System, Durham, North Carolina (Dr Kolotkin); Department of Social and Preventive Medicine, University at Buffalo, Buffalo, New York (Dr LaMonte); and Neuropsychiatric Research Institute, University of North Dakota School of Medicine, Fargo (Dr Crosby).
Corresponding Author: Ted D. Adams, PhD, MPH, Department of Internal Medicine, University of Utah School of Medicine, 420 Chipeta Way, Room 1160, Salt Lake City, UT 84108 (ted.adams@utah.edu).

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surgery as the only reported medical intervention providing substantial, long-term weight loss for most patients who are severely obese.[3] For this high-risk population, however, the number of studies reporting long-term weight loss following bariatric surgery are limited and generally have incomplete follow-up.[4]

This prospective study compared long-term weight loss and cardiometabolic end points in patients who were severely obese receiving Roux-en-Y gastric bypass (RYGB) surgery and in control patients who were severely obese who did not undergo surgery. This study tested the hypothesis that significant weight loss and cardiometabolic health benefits observed 2 years after surgery[5] persist after 6 years.

METHODS

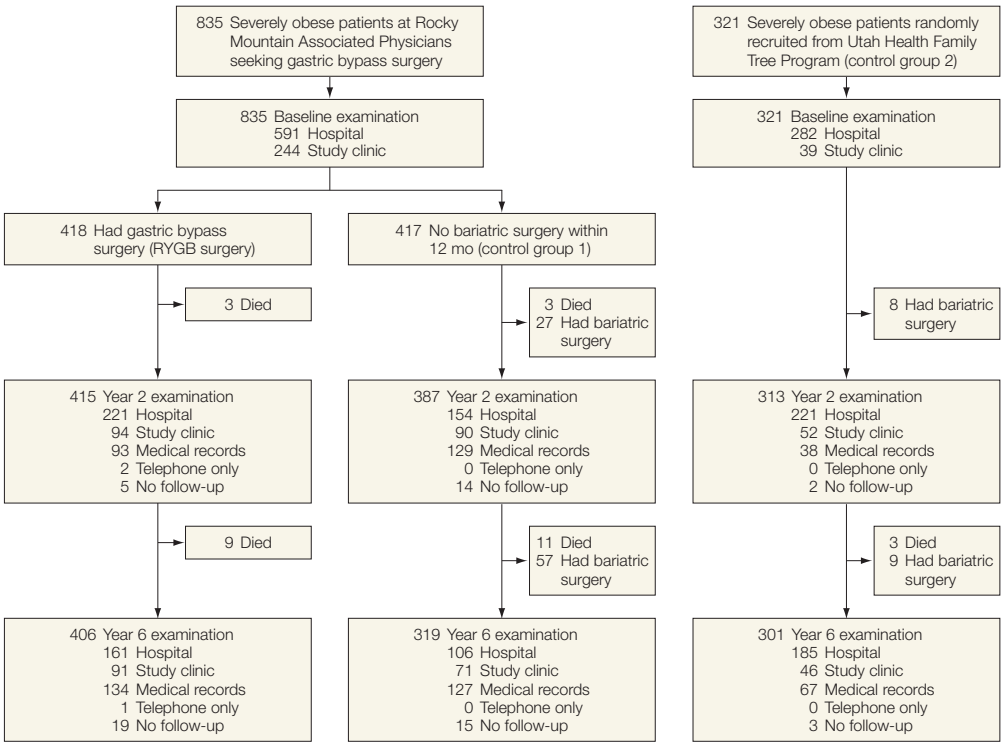
Study Design

This Utah-based study, conducted between July 2000 and June 2011, included 1156 participants aged 18 to 72 years who were severely obese (body mass index [calculated as weight in kilograms divided by height in meters squared] ≥35), among whom patients surgically treated with RYGB surgery (n=418) were compared with 2 nonsurgical, nonintervened severely obese control groups (FIGURE 1). Control group 1 included participants seeking RYGB surgery at the same surgical center as the surgery group (Rocky Mountain Associated Physicians Inc, Salt Lake City, Utah) but who did not have surgery (n=417). Control group 2 was a population-based sample (n=321) of severely obese adults without prior history of bariatric surgery who were recruited at random from a large Utah database (Utah Health Family Tree Program, University of Utah School of Medicine, Salt Lake City, Utah).[6,7] Group assignment and inclusion and exclusion criteria have been previously described,[8] with additional details found in the eMethods (available at http://www.jama.com).

Study protocol was approved by the University of Utah and Intermountain Healthcare institutional review boards, and signed consent was obtained from all participants. No participants from this study were included in our previously published mortality study.[9]

All participants underwent a baseline examination at the University of Utah Center for Clinical and Translational Science or at our center's outpatient clinic as previously described (eMethods).[8] Following this examina-

Figure 1. Utah Obesity Study Flow and Follow-Up Over 6 Years



RYGB indicates Roux-en-Y gastric bypass. Recruitment source and follow-up rates are depicted for the RYGB surgery group and comparative control groups. At year 2 examination (35 control participants) and year 6 examination (66 control participants), 101 total control participants had bariatric surgery subsequent to their baseline examination. Follow-up data were collected on all of the control participants who had postbaseline bariatric surgery, with the exception of 2 participants who were lost to follow-up at year 6 examination.

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tion, patients in the surgical group underwent either an open or laparoscopic RYGB procedure by 1 of 3 surgeons.[10,11] Control groups did not receive any weight-loss intervention but were free to pursue weight-loss therapies if desired.

Type 2 diabetes mellitus was defined as a fasting blood glucose concentration of at least 126 mg/dL (to convert to millimoles per liter, multiply by 0.055), hemoglobin A_{1c} level of at least 6.5%, or use of antidiabetic medication prescribed for diabetes. Hypertension was defined as a resting blood pressure of at least 140/90 mm Hg or if antihypertensive medications had been prescribed for blood pressure control. Dyslipidemia was considered present if fasting low-density lipoprotein cholesterol (LDL-C) was at least 160 mg/dL (to convert to millimoles per liter, multiply by 0.0259), fasting high-density lipoprotein cholesterol (HDL-C) was less than 40 mg/dL (to convert to millimoles per liter, multiply by 0.0259), or fasting triglycerides was at least 200 mg/dL (to convert to millimoles per liter, multiply by 0.0113), or if participants were using lipid-lowering medication. Remission of baseline prevalent disease was defined as normal levels of fasting glucose, hemoglobin A_{1c}, lipids, and resting blood pressure without reported medication use for the respective end point at each examination. Other variables included in this study are described in the eMethods.

Follow-up

All participants were invited to return for examinations at the University of Utah Center for Clinical and Translational Science or outpatient clinic at 2 and 6 years. For participants who could not be contacted or chose not to return for follow-up examinations, clinical and end point data were obtained through home visits, medical chart extraction, or telephone contact (Figure 1). Statewide hospital surgical records (Utah Department of Health) were used to determine if any participants who could not be located had undergone bariatric surgery since baseline and for all participants to identify hospitalizations associated with 138 common postbariatric surgery–related *Current Procedural Terminology* (*CPT*) and *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes (eMethods). Vital status and cause of death were obtained from the National Death Index.[12] Years between the baseline examination and subsequent hospitalization were calculated for each participant.

Statistical Analysis

For each examination, biochemical and blood pressure variables affected by medication were adjusted for medicated participants to their estimated premedication levels (eMethods). Propensity scores, or the probabilities of being in a specific study group at baseline, were created from a logistic regression model regressing baseline group membership on the baseline values of sex, age, body mass index, income, education level, and marital status, once for patients undergoing RYGB surgery vs control group 1 and again for patients undergoing RYGB surgery vs control group 2. Propensity scores adjust for baseline variable distribution differences among study groups. Changes in each outcome variable were compared between groups after adjusting for the baseline level of the outcome variable and the propensity score. Participants were excluded for missing variables on a variable-by-variable basis and control participants who went on to have bariatric surgery were considered lost to follow-up. Sidek multiple comparison adjustments were made to *P* values and confidence intervals (18 multiple comparisons were assumed for continuous variables and 5 comparisons were assumed for dichotomous variables). All analyses used SAS version 9.2 (SAS Institute).

Logistic regression was used to analyze the group differences in incidence and remission of the disease end points (diabetes, dyslipidemia, and hypertension), because disease status was only ascertained at the time of each examination. Those participants with baseline prevalent disease were excluded from analyses of incidence, and only those participants with baseline prevalent disease were used for the remission analyses at examination 2 (year 2) and examination 3 (year 6).

Detailed sensitivity analyses were performed to assess model assumptions. Analyses of the medication-adjusted and propensity score–adjusted data were compared with (1) adjusted data using the covariates included in the propensity score, (2) a data set in which all missing values were imputed using multiple imputation methodology, (3) a medication-adjusted data set limited only to those participants who attended 1 of the 2 study clinics, and (4) a data set in which the postsurgical measurements on control participants who had subsequent bariatric surgery were included in an intention-to-treat design; all participants with missing values had their missing values replaced by carrying the baseline observation forward to examination 3 (eMethods).

RESULTS

Participation Rates

At 6 years, 92.6% (387/418) of the surgical group, 72.9% (304/417) of control group 1, and 96.9% (311/321) of control group 2 had follow-up data (Figure 1). Before examination 3 (6-year examination), 101 participants from the 2 control groups chose to have bariatric surgery and for 99 of these participants, follow-up contact and clinical data were obtained subsequent to their weight-loss surgery and used in the intention-to-treat analysis (eTable 5). After including these 99 examined control participants, overall follow-up rates were 92.6% for the surgical cohort, 92.6% for control group 1, and 98.1% for control group 2. Median (interquartile range) follow-up time was 2.2 (2.0-2.5) years for the year 2 examination and 5.8 (5.3-6.6) years for the year 6 examination.

Clinical Measures

Participant ages ranged between 18 and 72 years (82% women) and 96% of the

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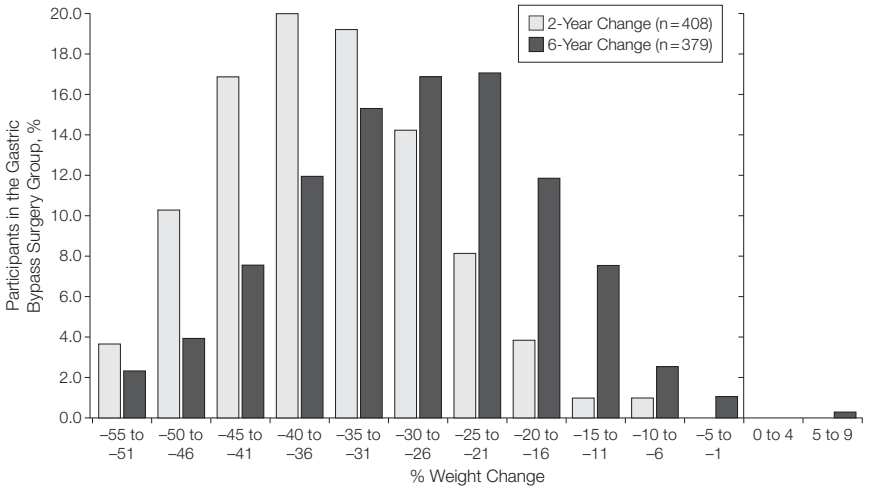
participants were non-Hispanic white; mean body mass index was 45.9 (95% CI, 31.2-60.6). Mean unadjusted weight loss in the surgical group was 34.9% (95% CI, 33.9%-35.8%) from baseline to year 2 and 27.7% (95% CI, 26.6%-28.9%) from baseline to year 6, representing a 7.2% (95% CI, 4.6%-9.8%) regain in weight from years 2 to 6. Weight gain from baseline to year 6 was 0.2% (95% CI, –1.1% to 1.4%) in control group 1 and 0% (95% CI, –1.2% to 1.2%) in control group 2. FIGURE 2 represents the frequency distribution of percentage unadjusted weight change from baseline to years 2 and 6 for the RYGB surgical group. At 2 years, 99% (95% CI, 98%-100%) of surgical patients had maintained more than 10% weight loss from baseline and 94% (95% CI, 92%-96%) had maintained more than 20% weight loss. At 6 years, 96% (95% CI, 94%-98%) of surgical patients had maintained more than 10% weight loss from baseline and 76% (95% CI, 72%-81%) had maintained more than 20% weight loss. Forty-nine percent of the RYGB group had baseline glucose concentrations of at least 100 mg/dL, whereas only 7% of this group had glucose concentrations of at least 100 mg/dL at 2 years, which slightly increased to 11% at 6 years (FIGURE 3).

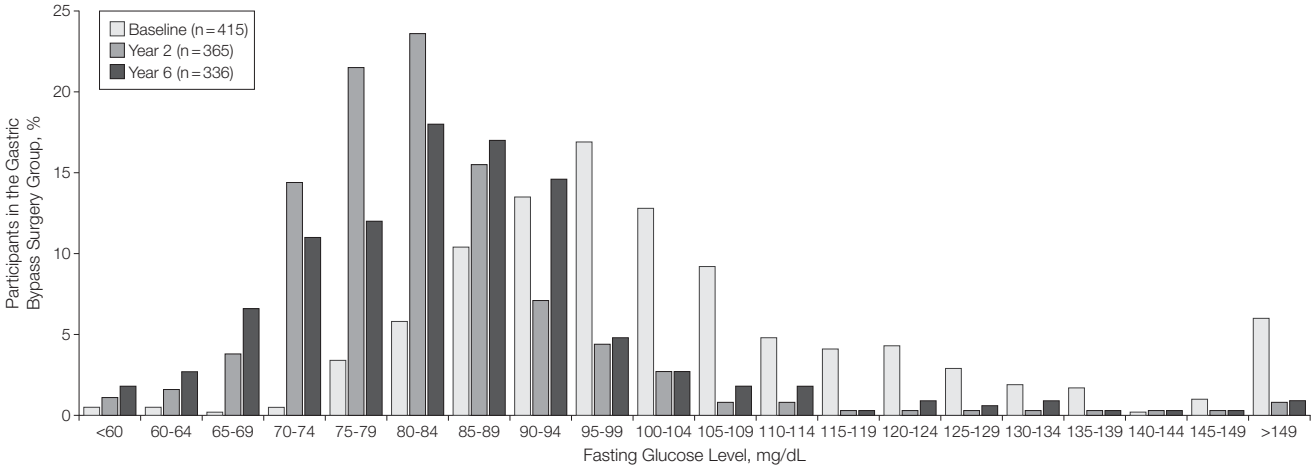
TABLE 1 shows the comparisons of the unadjusted baseline means for each group and eTable 1 shows the baseline means after adjustment for propensity scores, indicating the degree that propensity score adjustment adequately adjusted for the baseline differences between groups. TABLE 2 shows the 6-year change differences between RYGB surgery and control group 1 and RYGB surgery and control group 2, adjusting for the baseline value of the outcome variable and control group–specific propensity scores. Six-year changes did not significantly differ between the 2 control groups for any variable (*P* values not shown in Table 2), despite significant baseline differences between control groups (Table 1). At 6 years, the patients in the RYGB surgery group showed a sustained improvement vs control participants for all propensity score–adjusted and multiple comparison–adjusted variables

Figure 2. Frequency Distribution of Percentage Weight Change From Baseline to 2-Year and 6-Year Follow-up Examinations



The percentages of participants in the gastric bypass surgery group are shown grouped by 5% of unadjusted baseline weight loss intervals at the 2-year and 6-year follow-up examinations.

Figure 3. Frequency Distribution of Fasting Glucose Measured at Baseline and 2-Year and 6-Year Follow-up Examinations



The percentages of participants in the gastric bypass surgery group are shown grouped by unadjusted fasting glucose intervals of 5 mg/dL (to convert to mmol/L, multiply by 0.055) at baseline and 2-year and 6-year follow-up examinations.

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($P<.05$), with the exception of the 36-Item Short Form Health Survey (SF-36) mental component summary score (Table 2). At 6 years, the RYGB surgery group had a decrease in fasting glucose of 23.7 mg/dL (95% CI, 16.0-31.4 mg/dL) relative to control group 1 and a decrease of 19.5 mg/dL (95% CI, 12.5-26.5 mg/dL) relative to control group 2. In addition, the HDL-C level increased by 13.1 mg/dL (95% CI, 9.7-16.5 mg/dL) compared with either control group.

Sensitivity analyses showed that the propensity score–adjusted results (Table 2) were similar to the covariate-adjusted results (eTable 2). Also, all significant variables in Table 2 remained significantly different when analysis was restricted to participants who were examined at both baseline and 6-year visits in either of our 2 standardized clinics (eTable 3) and when imputed values for missing measurements were analyzed (eTable 4). Even the most conservative intention-to-treat analysis with baseline observations carried forward for missing values showed significant improvements in patients in the RYGB surgery group compared with the control groups (eTable 5).

Table 3 shows the incidence and remission of diabetes, hypertension, high LDL-C, low HDL-C, and high triglycerides (prevalence also shown in eTable 6), and **Figure 4** shows the propensity score–adjusted odds ratios (ORs) for these 5 variables. Remission of diabetes for the RYGB surgery group was 75% (95% CI, 63%-87%) at year 2, decreasing to 62% (95% CI, 49%-75%) at year 6. The 6-year RYGB surgery group remission rates were significantly higher than the 2 control groups (62%; 95% CI, 49%-75% for RYGB surgery group; vs 8%; 95% CI, 0%-16% [OR, 16.5; 95% CI, 4.7-57.6; $P<.001$] for control group 1; and 6%; 95% CI, 0%-13% [OR, 21.5; 95% CI, 5.4-85.6; $P<.001$] for control group 2) (Table 3 and Figure 4). At the same time, diabetes incidence following RYGB surgery was significantly lower than the 2 control groups

Table 1. Unadjusted Baseline Results by Study Group[a]

	RYGB Surgery		Control Group 1		Control Group 2	
Propensity Score Covariates	No. of Patients	Mean (SD)	No. of Patients	Mean (SD)	No. of Patients	Mean (SD)
Female sex, %	418	84.4 (0.4)	417	84.4 (0.4)	321	76.0 (0.4)[b]
Age, y	418	42.5 (10.9)	417	43.0 (11.4)	321	49.4 (10.9)[c]
BMI	418	47.3 (7.7)	417	46.3 (7.7)	321	43.8 (6.5)[c]
Income category (scale 1-6)	418	3.6 (1.3)	417	3.2 (1.3)[c]	321	3.6 (1.2)
Education, y	418	14.1 (2.1)	417	13.9 (2.3)	321	13.8 (2.1)
Married, %	418	65.3	417	57.1[d]	321	75.4[b]
Weight, kg	418	133.9 (26.9)	417	129.8 (24.9)[d]	321	124.0 (23.1)[c]
Waist circumference, cm	418	136.0 (17.9)	417	134.6 (17.2)	321	130.9 (15.8)[c]
Body fat, %	416	53.2 (5.1)	416	52.7 (5.4)	310	50.6 (5.8)[c]
SBP, mm Hg	418	126.3 (19.1)	417	125.6 (17.8)	321	128.8 (18.8)
DBP, mm Hg	418	71.9 (11.3)	417	72.0 (10.8)	321	72.3 (10.5)
Glucose, mg/dL	415	101 (30.9)	417	107 (39.1)[d]	321	107 (33.7)[b]
Insulin, μU/mL	416	19.3 (16.4)	414	17.9 (14.4)	321	14.0 (13.1)[c]
HOMA-IR	415	4.9 (4.7)	414	4.8 (4.3)	321	3.7 (3.9)[c]
HbA_{1c}, %	416	5.8 (1.1)	412	6.0 (1.2)[d]	319	6.0 (1.1)
Total cholesterol, mg/dL	417	188 (34.0)	417	185 (37.7)	321	189 (37.8)
LDL-C, mg/dL	417	109 (27.3)	416	107 (27.5)	321	109 (27.6)
HDL-C, mg/dL	417	46.6 (11.5)	416	44.8 (11.0)[d]	321	47.0 (10.9)
VLDL-C, mg/dL	417	34.1 (19.8)	416	35.1 (22.7)	321	34.2 (24.1)
Triglycerides, mg/dL	417	186 (96.9)	416	193 (122.0)[c]	321	186 (184.6)[d]
IWQOL-Lite total score[e]	411	31.4 (16.5)	407	34.9 (18.4)[b]	317	54.5 (19.5)[c]
SF-36 physical component score[f]	401	31.4 (9.3)	400	33.3 (9.7)[b]	314	39.3 (10.2)[c]
SF-36 mental component score[g]	401	41.4 (11.7)	400	40.4 (12.0)	314	47.8 (11.4)[c]

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; DBP, diastolic blood pressure; HbA_{1c}, hemoglobin A_{1c}; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IWQOL, impact of weight quality of life; LDL-C, low-density lipoprotein cholesterol; RYGB, Roux-en-Y gastric bypass; SBP, systolic blood pressure; SF-36, 36-Item Short Form Health Survey; VLDL-C, very low-density lipoprotein cholesterol.

SI conversions: To convert glucose to mmol/L, multiply by 0.055; total cholesterol, LDL-C, HDL-C, and VLDL-C to mmol/L, multiply by 0.0259; and triglycerides to mmol/L, multiply by 0.0113.

[a] Two-sided P values are unadjusted for multiple comparisons. P values are control groups 1 and 2 vs RYGB surgery group. Income categories were grouped according to 1 (<$10 000); 2 ($10 000-$29 999); 3 ($30 000-$49 999); 4 ($50 000-$69 999); 5 ($70 000-$99 999); and 6 (≥$100 000).

[b] $P<.01$.

[c] $P<.001$.

[d] $P<.05$.

[e] Range of scores (0-100, with 100 being best and normative mean of 94.7); a meaningful individual change is considered 7.7 to 12 points depending on baseline severity.[13]

[f] Range of scores (12-69, with 69 being best); meaningful change for either scale is 5 points with a normative mean of 50.[14]

[g] Range of scores (8-73, with 73 being best); meaningful change for either scale is 5 points with a normative mean of 50.[14]

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(2%; 95% CI, 0%-4%; vs 17%; 95% CI, 10%-24% [OR, 0.11; 95% CI, 0.04-0.34; $P<.001$]; and 15%; 95% CI, 9%-21% [OR, 0.21; 95% CI, 0.06-0.67; $P<.001$]; respectively). Remission rates of hypertension at year 6 remained significantly improved in the RYGB surgical group compared with 2 control groups (42%; 95% CI, 32%-52%; vs 18%; 95% CI, 9%-27% [OR, 2.9; 95% CI, 1.4-6.0]; and 9%; 95% CI, 3%-15% [OR, 5.0; 95% CI, 2.1-11.9]; respectively). Low HDL-C remission rates were also significantly improved at year 6 in the RYGB surgery group compared with 2 control groups (67%; 95% CI, 57%-77%; vs 34%; 95% CI, 23%-45% [OR, 3.8; 95% CI, 2.0-7.2]; and 18%; 95% CI, 8%-28% [OR, 6.2; 95% CI, 2.7-14.1]; respectively), with similar remission rates for high LDL-C and triglycerides.

There were 29 deaths in study participants at the end of the 6-year follow-up (12 in participants in the RYGB surgery group [3%], 14 in control group 1 [3%], and 3 in control group 2 [1%]) (eTable 7). None of the deaths in the RYGB surgery group occurred within 30 days following surgery. All 4 sui-

Table 2. Propensity Score–Adjusted 6-Year Change by Study Group and Group Differences[a]

Study Variables	RYGB Surgery		Control Group 1		RYGB Surgery vs Control Group 1 Difference	RYGB Surgery		Control Group 2		RYGB Surgery vs Control Group 2 Difference
	No. of Patients	Mean (95% CI)	No. of Patients	Mean (95% CI)		No. of Patients	Mean (95% CI)	No. of Patients	Mean (95% CI)	
Weight, kg	379	–36.8 (–39.2 to –34.4)	299	–0.4 (–3.1 to 2.3)	–36.4 (–40.1 to –32.7)[b]	379	–37.0 (–39.4 to –34.5)	296	–0.2 (–3.0 to 2.6)	–36.7 (–40.6 to –32.8)[b]
Waist circumference, cm	249	–28.7 (–31.5 to –25.9)	172	0.6 (–2.8 to 4.0)	–29.3 (–33.8 to –24.8)[b]	249	–28.5 (–31.3 to –25.7)	225	0.3 (–2.7 to 3.3)	–28.8 (–33.1 to –24.6)[b]
Body fat, %	244	–5.6 (–6.4 to –4.8)	171	–0.3 (–1.2 to 0.7)	–5.3 (–6.5 to –4.0)[b]	244	–5.5 (–6.3 to –4.6)	209	0.0 (–0.9 to 1.0)	–5.5 (–6.8 to –4.2)[b]
SBP, mm Hg	358	–5.8 (–8.8 to –2.8)	288	3.6 (0.2 to 6.9)	–9.3 (–13.9 to –4.8)[b]	358	–6.0 (–9.0 to –3.1)	293	0.9 (–2.4 to 4.0)	–6.9 (–11.5 to –2.3)[b]
DBP, mm Hg	358	–1.0 (–3.3 to 1.2)	288	4.5 (2.0 to 7.1)	–5.6 (–9.0 to –2.2)[b]	358	–1.3 (–3.5 to 1.0)	293	3.1 (0.6 to 5.6)	–4.4 (–7.9 to –0.9)[c]
Glucose, mg/dL	336	–14.6 (–19.6 to –9.6)	262	9.1 (3.4 to 14.9)	–23.7 (–31.4 to –16.0)[b]	336	–15.0 (–19.5 to –10.5)	281	4.5 (–0.4 to 9.5)	–19.5 (–26.5 to –12.5)[b]
Insulin, μU/mL	256	–11.8 (–13.5 to –10.1)	201	–2.7 (–4.6 to –0.8)	–9.1 (–11.6 to –6.6)[b]	256	–10.0 (–11.7 to –8.4)	248	–2.1 (–3.8 to –0.4)	–7.9 (–10.4 to –5.4)[b]
HOMA-IR	253	–3.1 (–3.7 to –2.6)	201	–0.2 (–0.8 to 0.4)	–2.9 (–3.8 to –2.1)[b]	253	–2.8 (–3.3 to –2.2)	248	–0.2 (–0.7 to 0.4)	–2.6 (–3.4 to –1.8)[b]
HbA_{1c}, %	250	–0.4 (–0.5 to –0.2)	202	0.2 (0.0 to 0.3)	–0.5 (–0.7 to –0.3)[b]	250	–0.3 (–0.5 to –0.2)	245	0.1 (0.0 to 0.3)	–0.5 (–0.7 to –0.2)[b]
Total cholesterol, mg/dL	295	–13.7 (–20.4 to –6.9)	255	16.8 (9.6 to 24.1)	–30.5 (–40.6 to –20.4)[b]	295	–13.2 (–19.9 to –6.6)	271	13.8 (6.9 to 20.8)	–27.1 (–37.1 to –17.0)[b]
LDL-C, mg/dL	291	–9.3 (–15.2 to –3.3)	251	19.4 (13.0 to 25.8)	–28.7 (–37.6 to –19.8)[b]	291	–8.8 (–14.5 to –3.1)	270	19.4 (13.4 to 25.4)	–28.2 (–36.8 to –19.5)[b]
HDL-C, mg/dL	291	11.0 (8.7 to 13.2)	251	–2.1 (–4.6 to 0.3)	13.1 (9.7 to 16.5)[b]	291	10.4 (8.2 to 12.7)	270	–2.7 (–5.0 to –0.3)	13.1 (9.7 to 16.5)[b]
VLDL-C, mg/dL	284	–17.1 (–20.3 to –13.9)	239	–2.9 (–6.4 to 0.5)	–14.2 (–18.9 to –9.4)[b]	284	–16.1 (–19.4 to –12.8)	262	–4.5 (–7.9 to –1.1)	–11.6 (–16.6 to –6.7)[b]
Triglycerides, mg/dL	290	–66.8 (–80.6 to –52.9)	251	0.3 (–14.7 to 15.2)	–67.0 (–87.7 to –46.4)[b]	290	–63.6 (–78.5 to –48.7)	270	–0.7 (–16.2 to –14.8)	–62.9 (–85.3 to –40.4)[b]
IWQOL-Lite total score[d]	241	45.1 (41.6 to 48.6)	168	13.2 (9.0 to 17.4)	31.9 (26.4 to 37.5)[b]	241	42.8 (39.3 to 46.2)	226	8.6 (5.0 to 12.2)	34.2 (28.7 to 39.7)[b]
SF-36 physical component score[d]	230	12.5 (10.5 to 14.5)	167	2.2 (–0.1 to 4.6)	10.2 (7.1 to 13.4)[b]	230	11.6 (9.6 to 13.6)	219	0.4 (–1.7 to 2.4)	11.2 (8.2 to 14.3)[b]
SF-36 mental component score[d]	230	4.2 (2.0 to 6.4)	167	4.7 (2.1 to 7.2)	–0.5 (–3.8 to 2.9)	230	3.4 (1.2 to 5.6)	219	2.7 (0.5 to 5.0)	0.6 (–2.6 to 3.9)

Abbreviations: DBP, diastolic blood pressure; HbA_{1c}, hemoglobin A_{1c}; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IWQOL, impact of weight quality of life; LDL-C, low-density lipoprotein cholesterol; RYGB, Roux-en-Y gastric bypass; SBP, systolic blood pressure; SF-36, 36-Item Short Form Health Survey; VLDL-C, very low-density lipoprotein cholesterol.

SI conversions: To convert glucose to mmol/L, multiply by 0.055; total cholesterol, LDL-C, HDL-C, and VLDL-C to mmol/L, multiply by 0.0259; and triglycerides to mmol/L, multiply by 0.0113.

[a] The sample size of RYGB surgery group and 2 control groups excludes deaths, lost-to-follow-up participants, and control participants who had subsequent bariatric surgery. Because propensity scores were derived separately for each control group vs RYGB surgery group, 2 propensity score–adjusted means are provided for the RYGB surgery group. Group differences are RYGB surgery minus either control group of 6-year changes. Two-sided *P* values and 95% CIs are adjusted for multiple comparisons. *P* values are RYGB surgery group vs the respective control group comparison of 6-year change means.

[b] $P<.001$.

[c] $P<.01$.

[d] See definitions in Table 1.[13,14]

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Table 3. Incidence and Remission Rates for Each Study Group[a]

	Roux-en-Y Gastric Bypass Surgery				Control Group 1				Control Group 2			
	Year 2		Year 6		Year 2		Year 6		Year 2		Year 6	
	Patients, No./Total	% (95% CI)	Patients, No./Total	% (95% CI)	Patients, No./Total	% (95% CI)	Patients, No./Total	% (95% CI)	Patients, No./Total	% (95% CI)	Patients, No./Total	% (95% CI)
						Incidence						
Diabetes	0/299	0 (0-0)	7/290	2 (0-4)	12/255	5 (1-9)	36/207	17 (10-24)	14/213	7 (2-12)	31/207	15 (9-21)
Hypertension	9/234	4 (1-7)	34/220	16 (10-22)	49/219	22 (15-29)	53/169	31 (22-40)	34/147	23 (14-32)	46/141	33 (23-43)
Low HDL-C	8/246	3 (0-6)	11/242	5 (1-9)	57/217	26 (18-34)	58/183	32 (23-41)	65/201	32 (24-40)	73/191	38 (29-47)
High LDL-C	9/334	3 (1-5)	13/328	4 (1-7)	38/321	12 (7-17)	66/265	25 (18-32)	44/248	18 (12-24)	71/237	30 (22-38)
High triglycerides	4/237	2 (0-4)	8/234	3 (0-6)	32/232	14 (8-20)	48/194	25 (17-33)	40/186	22 (14-30)	50/177	28 (19-37)
						Remission						
Diabetes	66/88	75 (63-87)	54/87	62 (49-75)	6/93	7 (0-14)	6/72	8 (0-16)	5/88	6 (0-13)	5/83	6 (0-13)
Hypertension	90/169	53 (43-63)	68/164	42 (32-52)	18/152	12 (5-19)	23/128	18 (9-27)	9/157	6 (1-11)	14/153	9 (3-15)
Low HDL-C	108/165	66 (57-75)	107/161	67 (57-77)	46/170	27 (18-36)	43/126	34 (23-45)	17/111	15 (6-24)	19/108	18 (8-28)
High LDL-C	43/76	57 (42-72)	40/75	53 (38-68)	11/66	17 (5-29)	10/46	22 (6-38)	4/64	6 (0-14)	6/61	10 (0-20)
High triglycerides	119/173	69 (60-78)	120/168	71 (62-80)	45/155	29 (20-38)	38/117	33 (22-44)	36/126	29 (19-39)	40/119	34 (23-45)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
[a] 95% CIs were adjusted for multiple comparisons.

cides and 2 of the 3 poisonings of undetermined intention occurred in the surgical group. Because of the small numbers of events, Fisher exact test was used to analyze the cumulative incidence of suicide, which was significantly higher in patients in the surgical group compared with the combined control groups (Mantel-Haenszel logit OR, 18; 95% CI, 1-385; Fisher exact test, $P = .02$). Suicide incidence between the surgical group and either of the control groups alone was not significantly different. The 30-day RYGB surgery perioperative complication rate was 3%. The numbers of hospitalizations with bariatric surgery–related *ICD-9* and *CPT* codes were 38 (9.1%) for the RYGB surgery group, 15 (4.5%) for control group 1, and 8 (2.6%) for control group 2 (eTable 8). When using numbers of participants rather than number of hospitalizations, the numbers and percentages were 33 (7.9%), 13 (3.9%), and 6 (2.0%), respectively. The majority (61%) of the patients receiving RYGB surgery had their hospitalization occur during the first 2 years after surgery.

COMMENT

Our study reports significant weight loss and 6-year improvements in major cardiovascular and metabolic risk factors in patients receiving RYGB surgery compared with severely obese control participants, including frequent remission and lower incidence of diabetes, dyslipidemia, and hypertension. In contrast, cardiovascular and metabolic status of severely obese control participants generally worsened during the 6-year period.

At 2 years, the surgical group lost 34.9% of their initial weight and at 6 years, their mean weight loss was 27.7%, representing a weight regain of approximately 7%. The Diabetes Prevention Program Outcome study had a 7.5% weight loss at 1 year, with 2.1% weight loss at 4 years of follow-up, and the Action for Health in Diabetes study had an 8.6% weight loss at 1 year, with 6.2% weight loss at 4 years of follow-up, both randomized clinical trials involving intensive lifestyle weight-loss therapies.[15-19] A recently reported randomized clinical trial comparing bariatric surgery and intensive medical therapy demonstrated a mean weight loss of 5.2% for the medical therapy group measured at 1 year.[20] Considering the 5% to 9% weight loss at 1 year with only 2% to 6% weight loss after 4 years of intensive lifestyle-based and medication-based therapy, the weight loss maintenance of 28% from baseline measured at 6 years in our Utah study is quite significant. These findings are similar to the results of the prospective, controlled Swedish Obese Subjects study that also reported a 7% mean weight regain among patients after gastric bypass surgery from 2 years (32% weight loss from baseline) to 10 years (25% weight loss from baseline).[21] The amount of weight loss sustained long term may affect the durability of cardiovascular disease risk factor improvements and explain differential results across bariatric surgical procedures.[21,22]

Although some recurrences of diabetes among patients undergoing RYGB surgery occurred, 62% remission of diabetes was maintained at year 6. Similar findings have been reported by DiGiorgi et al.[23] Although maintenance of diabetes remission at 6 years is somewhat less than the 75% to 80% remission rates reported in studies with shorter follow-up periods,[24-29] the continued protective association of RYGB surgery was underscored by a 5- to 9-fold reduction in the risk of new diabetes in surgical patients compared with nonsurgical control participants. In addition, the dramatic improvement observed in fasting glucose concentrations at year 2 remained at year 6, with only 11% of the RYGB surgery group having a fasting glucose concentra-

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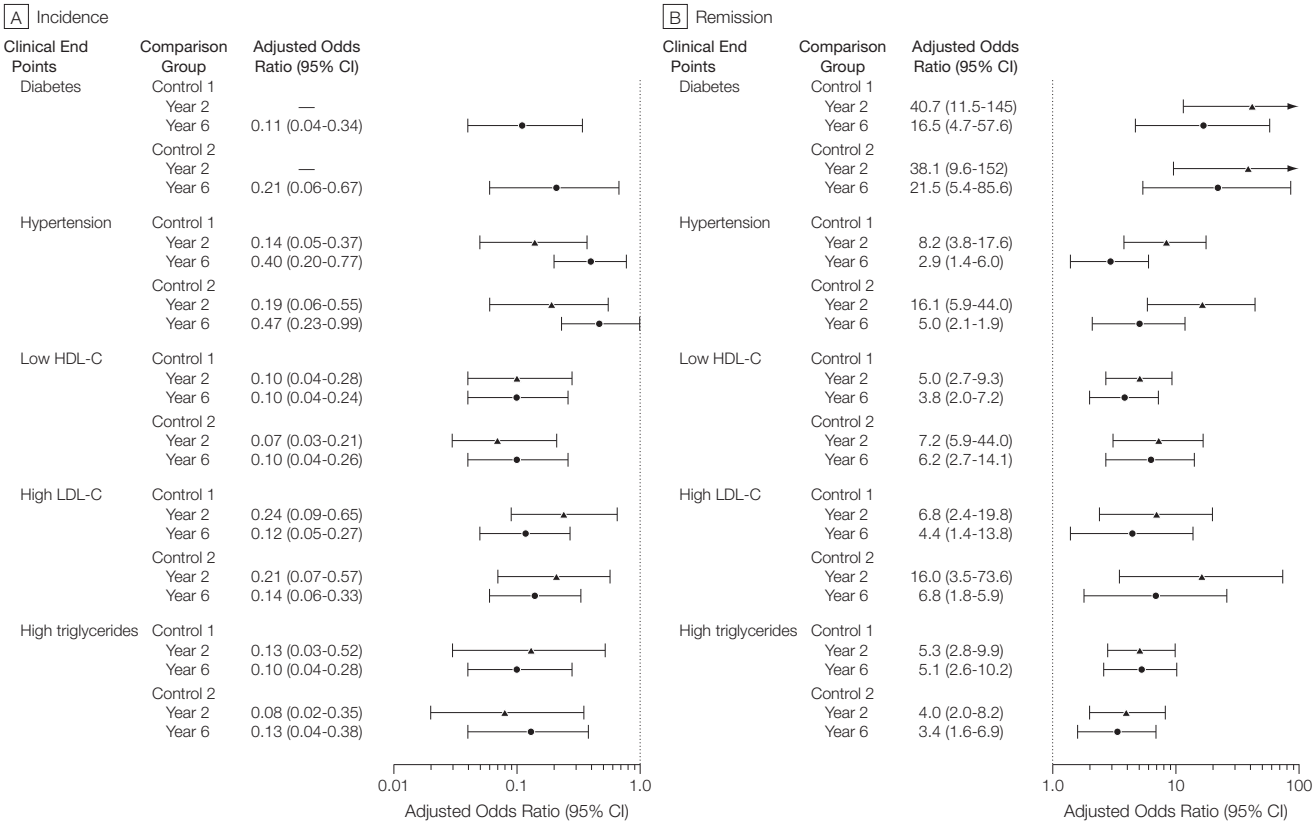
tion of at least 100 mg/dL. To our knowledge, 3 randomized controlled trials[20,29,30] comparing patients with diabetes with bariatric surgical procedures or intensive medical therapy have been reported. Dixon et al[30] reported that 2 years after gastric banding type 2 diabetes remission was 73% compared with 13% after conventional therapy. Using the remission of diabetes definition proposed by Buse et al,[31] Mingrone et al[29] found 75% diabetes remission at 2 years for gastric bypass, 95% for biliopancreatic diversion, and no remission for the conventional medical therapy group. In addition, Schauer et al[20] reported that 42% of gastric bypass, 37% of sleeve-gastrectomy, and 12% of medical therapy groups achieved the primary end point of a glycated hemoglobin level of 6% or less after 1 year. The promising results for diabetes management from these 3 short-term studies are supported by our longer-term follow-up of diabetes remission after bariatric surgery.

Consideration should also be given to the possibility that despite a worsening of diabetes remission rates over time, the years of improved glycemic control following bariatric surgery may have the end result of reduced microvascular disease.[32] Obesity is associated with premature and accelerated coronary atherosclerosis,[33,34] and improvements in coronary risk factors after bariatric surgery have been predicted to lower the 10-year risk of ischemic heart disease events by approximately 50%.[35] Our study demonstrated a sustained improvement in cardiovascular risk factors measured at 6 years. Our prior study showed a significant 2-year increase in HDL-C[5] and, despite a 7% weight regain from year 2 to 6, HDL-C did not decrease in the RYGB surgery group in our current study.

Reasons for the small but significantly increased incidence of suicides in the surgical group compared with the combined control groups ($P = .02$) are not known, but these results are consistent with our previously reported

Figure 4. Propensity Score–Adjusted Odds Ratios Comparing Incidence and Remission Rates of Diabetes, Hypertension, and Dyslipidemia Determined at Years 2 and 6 in RYGB Surgery and Control Groups 1 and 2



RYGB indicates Roux-en-Y gastric bypass. Odds ratios are adjusted for a propensity score composed of age, sex, baseline body mass index, income, education level, and marital status (95% CIs are adjusted for multiple comparisons). Clinical end points for both incidence and remission rates were defined as type 2 diabetes (a fasting concentration of blood glucose ≥126 mg/dL, hemoglobin A_{1c} ≥6.5, or use of antidiabetic medication); hypertension (resting blood pressure ≥140/90 mm Hg or use of antihypertensive medications); and dyslipidemia (a fasting concentration of measured low-density lipoprotein cholesterol [LDL-C] ≥160 mg/dL, high-density lipoprotein cholesterol [HDL-C] <40 mg/dL, or triglycerides ≥200 mg/dL, or use of lipid-lowering medication). No estimate was available for year 2 diabetes incidence (there was no incident diabetes in the RYGB surgery group at 2 years).

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mortality data.[9] The absence of improvement in the SF-36 mental component score in the surgical group during this period was in contrast with the marked improvements in the SF-36 physical component score and the overall quality of life score. Bocchieri et al[36] noted that numerous life changes occur after bariatric surgery that may generate tension and pose special social, psychological, and lifestyle challenges. Preoperative and postoperative psychological assessment of social and emotional status related to postbariatric surgical expectations and the potential risk of self-destructive behavior might be warranted.

A weakness of many bariatric surgery studies has been poor rates of participant retention, introducing a potential bias (ie, patients who regain weight may not return for subsequent screening).[37] Strengths of our study were the high combined 6-year participation and follow-up rate, and thorough sensitivity analysis to confirm that data obtained outside of our primary research centers did not influence study conclusions.

Inclusion of 2 severely obese control groups allowed broad inferences to be made regarding the benefits of gastric bypass surgery. The first control group provided an opportunity to follow severely obese patients who, similar to enrolled surgical cases, sought gastric bypass surgery and were more clinically comparable with study participants who subsequently had gastric bypass surgery.[5] The second control group was older, less severely obese, and reported a higher health-related quality of life. Despite these baseline differences, the 6-year changes were similar between control groups, resulting in the same conclusions when comparing either control group with patients in the RYGB surgery group. Propensity score adjustment for baseline group differences further confirmed this conclusion. The large outcome variable effect sizes after RYGB surgery and associated extremely low *P* values (eTable 4 and eTable 5) suggest that remaining biases would need to be very large to explain the observed results and that baseline differences between groups, sampling errors, or statistical issues did not falsely inflate the beneficial association of surgically-induced weight loss.

In conclusion, significant weight loss was sustained for an average of 6 years in the majority of patients having RYGB surgery. Diabetes remission was also sustained and the incidence of diabetes was much lower during the 6-year follow-up period in patients in the RYGB surgery group compared with the severely obese control participants. Similarly, metabolic and cardiovascular risk profiles during the 6 years of follow-up remained significantly improved after RYGB surgery. These findings are important considering the rapid increase in total numbers of bariatric surgical operations performed in the United States and worldwide,[38,39] and may have significant ramifications for the projected 31 million US individuals meeting criteria for bariatric surgery.[40]

Author Contributions: Drs Adams and Hunt had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Adams, Litwin, Kolotkin, LaMonte, Hopkins, Gress, Walker, Cloward, Hunt.
Acquisition of data: Adams, Davidson, Litwin, Pendleton, Strong, Vinik, Wanner, Gress, Walker, Nuttall, Greenwood, McKinlay, Simper, Smith, Hunt.
Analysis and interpretation of data: Adams, Davidson, Litwin, Kolotkin, LaMonte, Hopkins, Gress, Walker, Cloward, Nuttall, Hammoud, Crosby, Hunt.
Drafting of the manuscript: Adams, Davidson, Litwin, Kolotkin, Hunt.
Critical revision of the manuscript for important intellectual content: Adams, Davidson, Litwin, Kolotkin, LaMonte, Pendleton, Strong, Vinik, Wanner, Hopkins, Gress, Walker, Cloward, Nuttall, Hammoud, Greenwood, Crosby, McKinlay, Simper, Smith, Hunt.
Statistical analysis: Adams, Davidson, Hopkins, Gress, Crosby, Hunt.
Obtained funding: Adams, Litwin, Hunt.
Administrative, technical, or material support: Adams, Gress, Nuttall, Hunt.
Study supervision: Adams, Davidson, Hunt.
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