Health Benefits of Gastric Bypass Surgery After 6 Years

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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.

JAMA. 2012;308(11):1122-1131

For editorial comment see p 1160.

Author Video Interview available at www.jama.com.
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 surgery5 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-

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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 A1c 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 medication. That participants with lipid-lowering medication were adjusted for medications 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...
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.
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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

<table>
<thead>
<tr>
<th>Propensity Score Covariates</th>
<th>RYGB Surgery</th>
<th>Control Group 1</th>
<th>Control Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
<td>Mean (SD)</td>
<td>No. of Patients</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>418 84.4 (0.4)</td>
<td>417 84.4 (0.4)</td>
<td>321 76.0 (0.4)</td>
</tr>
<tr>
<td>Age, y</td>
<td>418 42.5 (10.9)</td>
<td>417 43.0 (11.4)</td>
<td>321 49.4 (10.9)</td>
</tr>
<tr>
<td>BMI</td>
<td>418 47.3 (7.7)</td>
<td>417 46.3 (7.7)</td>
<td>321 43.8 (6.5)</td>
</tr>
<tr>
<td>Income category (scale 1-6)</td>
<td>418 3.6 (1.3)</td>
<td>417 3.2 (1.3)</td>
<td>321 3.6 (1.2)</td>
</tr>
<tr>
<td>Education, y</td>
<td>418 14.1 (2.1)</td>
<td>417 13.9 (2.3)</td>
<td>321 13.8 (2.1)</td>
</tr>
<tr>
<td>Married, %</td>
<td>418 65.3</td>
<td>417 57.1</td>
<td>321 75.4</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>418 133.9 (26.9)</td>
<td>417 129.8 (24.9)</td>
<td>321 124.0 (23.1)</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>418 136.0 (17.9)</td>
<td>417 134.6 (17.2)</td>
<td>321 130.9 (15.8)</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>416 53.2 (5.1)</td>
<td>417 52.7 (5.4)</td>
<td>321 50.6 (5.8)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>418 126.3 (19.1)</td>
<td>417 125.6 (17.8)</td>
<td>321 128.8 (18.8)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>418 71.9 (11.3)</td>
<td>417 72.0 (10.8)</td>
<td>321 72.3 (10.5)</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>415 101 (30.9)</td>
<td>417 107 (39.1)</td>
<td>321 102 (37.7)</td>
</tr>
<tr>
<td>Insulin, µU/mL</td>
<td>416 19.3 (16.4)</td>
<td>414 17.9 (14.4)</td>
<td>321 14.0 (13.1)</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>415 4.9 (4.7)</td>
<td>414 4.8 (4.3)</td>
<td>321 3.7 (3.9)</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>416 5.8 (1.1)</td>
<td>412 6.0 (1.2)</td>
<td>319 6.0 (1.1)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>417 188 (34.0)</td>
<td>417 185 (37.7)</td>
<td>321 189 (37.8)</td>
</tr>
<tr>
<td>LDL-C, mg/dL</td>
<td>417 109 (27.3)</td>
<td>417 107 (27.5)</td>
<td>321 107 (26.9)</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>417 46.6 (11.5)</td>
<td>416 44.8 (11.0)</td>
<td>321 47.0 (10.9)</td>
</tr>
<tr>
<td>VLDL-C, mg/dL</td>
<td>417 34.1 (19.8)</td>
<td>416 35.1 (22.7)</td>
<td>321 34.2 (24.1)</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>417 186 (96.9)</td>
<td>416 193 (122.0)</td>
<td>321 186 (184.6)</td>
</tr>
<tr>
<td>IWQOL-Lite total score</td>
<td>411 31.4 (16.5)</td>
<td>407 34.9 (18.4)</td>
<td>317 54.5 (19.5)</td>
</tr>
<tr>
<td>SF-36 physical component score</td>
<td>401 31.4 (9.3)</td>
<td>400 33.3 (9.7)</td>
<td>314 39.3 (10.2)</td>
</tr>
<tr>
<td>SF-36 mental component score</td>
<td>401 41.4 (11.7)</td>
<td>400 40.4 (12.0)</td>
<td>314 47.8 (11.4)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IWQOL-Lite, 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.

*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-$299 999).

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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

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>No. of Patients</th>
<th>Mean (95% CI)</th>
<th>No. of Patients</th>
<th>Mean (95% CI)</th>
<th>Differences</th>
<th>P</th>
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<td>Weight, kg</td>
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<td>299</td>
<td>−0.4</td>
<td>−36.4</td>
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<tr>
<td>Waist circumference, cm</td>
<td>249</td>
<td>−28.7</td>
<td>172</td>
<td>0.6</td>
<td>−29.3</td>
<td>0.0113 b</td>
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<td>Body fat, %</td>
<td>244</td>
<td>−5.6</td>
<td>171</td>
<td>−0.3</td>
<td>−5.3</td>
<td>.001 c</td>
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<tr>
<td>SBP, mm Hg</td>
<td>358</td>
<td>−5.8</td>
<td>286</td>
<td>0.3</td>
<td>−5.5</td>
<td>.001 c</td>
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<tr>
<td>Glucose, mg/dL</td>
<td>336</td>
<td>−14.6</td>
<td>262</td>
<td>9.1</td>
<td>−23.7</td>
<td>.001 c</td>
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<td>Insulin, µU/mL</td>
<td>256</td>
<td>−11.8</td>
<td>201</td>
<td>−2.7</td>
<td>−9.1</td>
<td>.001 c</td>
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<td>HOMA-IR</td>
<td>253</td>
<td>−3.3</td>
<td>201</td>
<td>−0.8</td>
<td>−2.9</td>
<td>.001 c</td>
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<tr>
<td>HbA1c, %</td>
<td>253</td>
<td>−0.4</td>
<td>202</td>
<td>0.0</td>
<td>−0.5</td>
<td>.001 c</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>295</td>
<td>−13.7</td>
<td>255</td>
<td>16.8</td>
<td>−30.5</td>
<td>.001 c</td>
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<tr>
<td>LDL-C, mg/dL</td>
<td>291</td>
<td>−9.3</td>
<td>251</td>
<td>19.4</td>
<td>−28.7</td>
<td>.001 c</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>291</td>
<td>11.0</td>
<td>251</td>
<td>21.9</td>
<td>−32.8</td>
<td>.001 c</td>
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<tr>
<td>VLDL-C, mg/dL</td>
<td>284</td>
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<td>239</td>
<td>−6.4</td>
<td>−11.1</td>
<td>.001 c</td>
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<tr>
<td>Triglycerides, mg/dL</td>
<td>290</td>
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<td>251</td>
<td>0.3</td>
<td>−67.1</td>
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<td>SF-36 physical component score</td>
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<td>10.3</td>
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<td>SF-36 mental component score</td>
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<td>4.2</td>
<td>147</td>
<td>2.0</td>
<td>2.2</td>
<td>.001 c</td>
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</table>

Abbreviations: DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; WQOL-Lite, 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.

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.

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Table 3. Incidence and Remission Rates for Each Study Group

<table>
<thead>
<tr>
<th>No./Total</th>
<th>% (95% CI)</th>
<th>No./Total</th>
<th>% (95% CI)</th>
<th>No./Total</th>
<th>% (95% CI)</th>
<th>No./Total</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td></td>
<td>Remission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>0/299</td>
<td>0 (0-0)</td>
<td>2 (0-4)</td>
<td>12/255</td>
<td>5 (1-9)</td>
<td>36/207</td>
<td>17 (10-24)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9/234</td>
<td>4 (1-7)</td>
<td>13/220</td>
<td>6 (1-10)</td>
<td>34/197</td>
<td>22 (15-29)</td>
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<tr>
<td>Low HDL-C</td>
<td>8/248</td>
<td>3 (0-6)</td>
<td>11/242</td>
<td>5 (1-9)</td>
<td>57/171</td>
<td>26 (18-34)</td>
<td></td>
</tr>
<tr>
<td>High LDL-C</td>
<td>9/334</td>
<td>3 (1-5)</td>
<td>13/328</td>
<td>4 (1-7)</td>
<td>38/321</td>
<td>12 (7-17)</td>
<td></td>
</tr>
<tr>
<td>High triglycerides</td>
<td>4/237</td>
<td>2 (0-4)</td>
<td>8/234</td>
<td>3 (0-6)</td>
<td>32/232</td>
<td>14 (8-20)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

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. 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. 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). 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.

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. 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, 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 concentration...
tion of at least 100 mg/dL. To our knowledge, 3 randomized controlled trials\(^{10,20,30}\) 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\(^{32}\) 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\(^{2}\) 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...
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 al10 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, Litwinc, Kolotkin, LaMonte, Hopkins, Gress, Walker, Cloward, Hunt.

Acquisition of data: Adams, Davidson, Litwin, Pendleton, Strong, Vink, Wanner, Gress, Walker, Nuttall, Greenwood, McKinlay, Simper, Smith, Hunt.

Analysis and interpretation of data: Adams, Davidson, Litwin, Kolotkin, LaMonte, Hopkins, Gress, Walker, Cloward, Nuttall, Hammond, 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, Vink, Wanner, Gress, Walker, Cloward, Nuttall, Hammond, Crosby, Hunt.

Obtained funding: Adams, Litwin, Hunt.

Administrative, technical, or material support: Adams, Gress, Hunt.

Study supervision: Adams, Davidson, Hunt.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Kolotkin reported receiving royalties for use of the IWQOL-Lite from Duke University, being a consultant for Vivus, Orexigen, and GlaxoSmithKline. Dr Crosby reported receiving consulting honorarium from Health Outcome Solutions. Dr Simper reported receiving consulting honorarium from Ethicon EndoSurgical. No other authors reported any disclosure.

Funding/Support: This work was supported by grant DK-59506 from the National Institutes of Health/ The National Institute of Diabetes and Digestive and Kidney Diseases and Public Health Service research grant 1MD01-RR00064 from the National Center for Research Resources.

Role of the Sponsor: The National Institutes of Health had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Online-Only Material: eMethods, eTables 1 through 8, and eAuthor Video. Interview are available at http://www.jama.com.

Additional Contributions: We thank R.C. Halverson, MD, Charles B. Edwards, MD, Gerald N. Goodman, MD, and the late David K. Miller, MD (bariatric surgeons with Rocky Mountain Associated Physicians Inc, Salt Lake City, Utah). Acknowledgments are also expressed for clinical and technical support from the staff of the Cardiovascular Genetics Division who assisted with recruitment and clinical testing (including Sara Frogley, Loni Gardner, and Sawsan Ibrahim), the Huntsman Center for Clinical and Translational Science and their very capable staff, and the Cardiology Division, University of Utah School of Medicine. No financial compensation was given to the surgeons but salary support was received by the above-named staff members.

REFERENCES


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HEALTH BENEFITS OF GASTRIC BYPASS SURGERY AFTER 6 YEARS


