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Comparison of the Performance of Common Measures of Weight Regain After Bariatric Surgery for Association With Clinical Outcomes

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IMPORTANCE Estimates of weight regain following bariatric surgery vary widely.

OBJECTIVE To describe weight regain after reaching nadir weight following Roux-en-Y gastric bypass (RYGB) surgery and compare weight regain measures for association with outcomes.

DESIGN, SETTING, AND PARTICIPANTS Prospective cohort study of 2458 adults who underwent bariatric surgery at 10 hospitals in 6 US cities between March 2006 and April 2009. Assessments were conducted within 30 days' presurgery, at 6 months' postsurgery, and then annually until January 2015. Of the 1703 participants who underwent RYGB surgery, 1406 (83%) were followed up for 5 years or longer and had 5 or more weight measurements (excluding those who died or underwent surgical reversal).

EXPOSURES Weight regain assessed by 5 continuous measures (weight in kilograms, body mass index [BMI], percentage of presurgery weight, percentage of nadir weight, and percentage of maximum weight lost) and 8 dichotomous measures (per established thresholds) were compared in relation to clinical outcomes based on statistical significance, magnitude of association, and model fit.

MAIN OUTCOMES AND MEASURES Progression of diabetes, hyperlipidemia, and hypertension and declines in physical and mental health–related quality of life and satisfaction with surgery.

RESULTS Among the 1406 participants who underwent RYGB surgery, the median age was 47 years (25th-75th percentile, 38-55 years) and the median BMI was 46.3 (25th-75th percentile, 42.3-51.8) prior to surgery. Most participants were female (80.3%) and white (85.6%). The median follow-up was 6.6 years (25th-75th percentile, 5.9-7.0 years). The median percentage of maximum weight loss was 37.4% (25th-75th percentile, 31.6%-43.3%) of presurgery weight and occurred a median of 2.0 years after RYGB surgery (25th-75th percentile, 1.0-3.2 years). The rate of weight regain was highest during the first year after reaching nadir weight, but weight regain continued to increase throughout follow-up (range, a median of 9.5% of maximum weight lost [25th-75th percentile, 4.7%-17.2%] to 26.8% of maximum weight lost [25th-75th percentile, 16.7%-41.5%] 1 to 5 years after reaching nadir weight). The percentage of participants who regained weight depended on threshold (eg, 5 years after nadir weight, 43.6% regained ≥5 BMI points; 50.2% regained ≥15% of nadir weight; and 67.3% regained ≥20% of maximum weight lost). Compared with other continuous weight regain measures, the percentage of maximum weight lost had the strongest association and best model fit for all outcomes except hyperlipidemia, which had a slightly stronger association with BMI. Of the dichotomous measures, 20% or greater of maximum weight lost performed better or similarly with most of the outcomes, and was the second best measure for hyperlipidemia (after ≥10 kg of weight) and hypertension (after ≥10% of maximum weight lost).

CONCLUSIONS AND RELEVANCE Among a large cohort of adults who underwent RYGB surgery, weight regain quantified as percentage of maximum weight lost performed better for association with most clinical outcomes than the alternatives examined. These findings may inform standardizing the measurement of weight regain in studies of bariatric surgery.

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Although weight loss patterns vary, bariatric surgery results in substantial and durable weight reduction for the majority of patients, making it the most effective treatment for severe obesity.[1-3] Still, similar to all weight loss interventions, weight regain, which may have deleterious effects on weight-related comorbidities,[1,4,5] health-related quality of life,[6-8] patient satisfaction with surgery,[7] and health care costs,[9] is a concern following surgical treatment of obesity.[10,11]

Numerous studies have been conducted to understand the extent of weight regain following bariatric surgery. However, reported weight regain varies widely across studies.[10,11] Small sample sizes and lack of generalizability for case series, use of clinical records or patient recall to estimate nadir weight, loss to follow-up, and variable follow-up times likely contribute to the inconsistency in the literature,[10,11] as does the lack of a standard measure of weight regain.[7,11,12] For example, weight regain has been calculated as absolute change in weight or body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), and as a percentage of presurgery weight, nadir weight, or maximum weight lost.[7,10,11] Furthermore, thresholds are commonly used to indicate clinically meaningful weight regain (eg, ≥10%, ≥20%, and ≥25% of maximum weight lost) without demonstrating the biological relevance or function of the specified threshold used.[7,11,12]

The purpose of this study was to inform standardizing the measurement of weight regain in studies of bariatric surgery by (1) describing weight regain after participants reached nadir weight assessed by 5 continuous and 8 dichotomous measures in a large geographically diverse cohort of adults who underwent Roux-en-Y gastric bypass (RYGB) surgery and who were followed up for 5 to 7 years[1] and (2) comparing the performance of these weight regain measures for association with 6 clinical outcomes (concurrent progression of diabetes, hyperlipidemia, and hypertension, and declines in physical health-related quality of life, mental health-related quality of life, and satisfaction with surgery).

Key Points

Question Are there approaches to measuring weight regain following bariatric surgery that are more predictive of clinical outcomes than others?

Findings In this prospective cohort study of 1406 adults who underwent Roux-en-Y gastric bypass with a median follow-up of 6.6 years, weight regain measured as the percentage of maximum weight lost (vs weight in kilograms, body mass index, percentage of presurgery weight, or percentage of nadir weight) had the strongest associations with and best fits of the models for declines in mental health, satisfaction with surgery, and most physical health measures.

Meaning These findings may inform standardizing the measurement of weight regain in studies of bariatric surgery.

Methods

Design and Subjects

The Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) was a prospective cohort study of 2458 adults aged 18 years or older undergoing a first bariatric surgical procedure between March 2006 and April 2009 performed by a participating surgeon at 10 hospitals in 6 cities (Fargo, North Dakota; Greenville, North Carolina; New York, New York; Pittsburgh, Pennsylvania; Portland, Oregon; and Seattle, Washington) throughout the United States (eFigure 1 in the Supplement).[13] The institutional review board at each clinical center approved the protocol[14] and participants gave written informed consent.

Standardized assessments were conducted by research investigators and their staff within 30 days prior to surgery, at 6 months after surgery, and annually for 6 or 7 years through January 2015. Assessments were primarily conducted in person. However, the 6-month and 6-year assessments were completed by telephone or mail and were brief. Depending on when participants underwent bariatric surgery, they had a maximum of 8 or 9 assessments over 6 or 7 years. This analysis included participants (N = 1406; eFigure 1 in the Supplement) who underwent RYGB surgery, those who did not die, and those who did not undergo a reversal or revision to a new bariatric procedure within 5 years, and met the criteria for nadir weight determination (described below).

Weight Assessment

During in-person assessments, weight was measured using a standard scale (Tanita Body Composition Analyzer, model TBF-310). If this per-protocol weight was not obtained, weight was measured by research or medical personnel. If neither was available, a participant's self-report of current weight obtained via use of any scale was used. In a prior LABS-2 study, the validity of self-reported weights collected during a telephone call (occurred ≤30 days prior to weight measured in person) were evaluated.[15] The mean difference between measured and self-reported weights in this cohort was 1 kg and did not differ significantly by measured BMI or degree of postoperative weight change.[15]

Determination of Nadir Weight

The lowest weight among participants whose weight was measured at 5 or more assessments, at least 1 of which occurred during or after the 5-year assessment, was classified as the nadir weight if the weight assessment was not missing at the assessments due immediately prior to and immediately following the assessment with the lowest weight. If the lowest weight was measured during the final year of data collection, only the weight at the assessment immediately prior to the final assessment was required.

Weight Loss and Weight Regain

Weights assessments collected during or within 6 months following a pregnancy were excluded. Weight loss from surgery was calculated in weight as kilograms, BMI, and percentage of presurgery weight.[16] Weight regain from nadir weight was calculated as weight in kilograms,[17] BMI,[18] percentage of presurgery weight,[19] percentage of nadir weight,[20-23] and percentage of maximum weight lost.[24,25] Formulas for these measurements appear in eAppendix 1 in the Supplement. In addition,

8 common thresholds for clinically meaningful weight regain (ie, ≥10 kg[11]; ≥5 BMI points[11]; ≥10% of presurgery weight[19]; ≥10%[20] and ≥15%[26] of nadir weight; and ≥10%,[27] ≥20%,[24] and ≥25%[28] of maximum weight lost) were applied. Some previously reported weight regain thresholds (eg, any weight regain, regain to a BMI >35 after successful weight loss) were not used due to their lack of plausible biological relevance.[7,16]

Clinical Outcomes of Bariatric Surgery

Using laboratory tests, physical measures, and questionnaires (described below), 6 outcomes were calculated for each assessment after nadir weight was reached, with status at nadir weight as the reference. Outcome definitions were developed a priori specifically for this analysis after the completion of the LABS-2 study using standard thresholds when available to determine progression of disease or minimal clinically important decline.

Levels of glycated hemoglobin (hemoglobin A_{1c}) and low-density lipoprotein cholesterol were measured by a central laboratory. Blood pressure was measured by research staff. These data were not collected at the 6-year assessment. Medication use was self-reported. Health-related quality of life was measured using the Medical Outcomes Study 36-item Short-Form Health Survey.

The Physical Component Summary and the Mental Component Summary scores from the 36-item Short-Form Health Survey are commonly used in reports of bariatric surgery and are sensitive to weight loss and weight gain.[29] Using norm-based methods, the scores transform to a mean (SD) of 50 (10) in the general US population (score range, 0-100).[30] Lower scores imply more disability or worse function. In January 2010, an item was added to the annual assessment to assess participants' satisfaction with the results of their first bariatric surgery on a 7-point scale from 1 (very satisfied) to 7 (very dissatisfied).

Progression of diabetes was defined as (1) a change from not taking a diabetes medication to taking a diabetes medication, (2) a change from not taking insulin to taking insulin, or (3) an increase in hemoglobin A_{1c} level by at least 0.5% to 5.7% or greater.[31,32] Among women who reported having polycystic ovarian syndrome, the first criteria required use of a diabetes medication other than metformin.

Progression of hyperlipidemia was defined as (1) a change from not taking a lipid-lowering medication to taking a lipid-lowering medication, or (2) an increase in low-density lipoprotein cholesterol level by at least 10 mg/dL to at least 100 mg/dL.[33] Progression of hypertension was defined as (1) a change from not taking a hypertension medication to taking a hypertension medication, (2) an increase in systolic blood pressure by at least 5 mm Hg to at least 120 mm Hg, or (3) an increase in diastolic blood pressure by at least 5 mm Hg to at least 80 mm Hg or greater.[34]

A clinically important decline in physical and mental health-related quality of life was defined as a decrease of 5 points or greater in the Physical Component Summary and the Mental Component Summary scores, respectively.[35] A clinically important decline in satisfaction with surgery was defined as an increase by at least 1 point to a rating of at least 3 (ie, from somewhat satisfied to very dissatisfied with surgery).

Sociodemographic Factors

Sociodemographics were self-reported. Participants were asked whether they were married or living as married. Race was set to missing for participants who did not self-report their race as 1 or more of the investigator-defined categories (ie, white/Caucasian, black/African-American, Asian, American Indian/Alaskan Native, Native Hawaiian/other Pacific Islander). Race was reported as a descriptor of the sample.

Statistical Analysis

The statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc). All reported P values are 2-sided; $P < .05$ is considered to be statistically significant. Data were assumed to be missing at random. Mixed models, described below, controlled for factors related to missing follow-up data (study site, presurgery age, and presurgery smoking status[1]) as fixed effects. The assumption of data missing at random for weight, comorbidity, and 36-item Short-Form Health Survey response was evaluated and there was no indication that data were not missing at random.[1,36]

Descriptive statistics were used to summarize the participant characteristics prior to surgery. The frequencies and percentages are reported for categorical data. Medians and 25th and 75th percentiles are reported for continuous data.

The Pearson χ^2 test and the Fisher exact test for categorical variables, the Cochran-Armitage test for ordinal variables, and the Wilcoxon rank sum test for continuous variables were used to assess differences in the distributions of participant characteristics prior to surgery between those who were included in the analysis sample vs those who were excluded due to missing data. A between-group difference in weight lost, which was measured as a percentage of presurgery weight, was assessed using a linear mixed model that was fit using the maximum likelihood with a person-level random intercept, a group indicator (ie, included or excluded) as a discrete fixed effect, and time since surgery as a continuous fixed effect.

Descriptive statistics were used to summarize weight loss and weight regain from nadir weight. One hundred twenty participants were excluded from the evaluation of weight regain (119 reached nadir weight during the final year of data collection; 1 was pregnant at the only assessment after reaching nadir weight).

Linear mixed models with a person-level random intercept were used to model continuous weight regain measures by time since reaching nadir weight and to test associations with the continuous fixed effect of time since reaching nadir weight. Similarly, Poisson mixed models with robust error variance were used to model dichotomous weight regain measures by time since reaching nadir weight. Both linear mixed model and Poisson mixed model linear and quadratic terms for time since reaching nadir weight were considered; the quadratic term was retained if significant.

A series of Poisson mixed models with robust error variance were used to test and estimate associations between each weight regain measure with the following 6 outcomes: progression of diabetes, progression of hyperlipidemia, progression of hypertension, decline in physical health–related quality of life, decline in mental health–related quality of life, and decline in satisfaction with surgery. The relevant

corresponding measures (ie, hemoglobin A_{1c} level, low-density lipoprotein cholesterol level, systolic blood pressure, diastolic blood pressure, Short-Form 36 Physical or Mental Component Summary score, or satisfaction rating for surgery) at time of reaching nadir weight and time since reaching nadir weight were entered as continuous fixed effects.

The adjusted relative risk (RR) with 95% CI, statistical significance, and the Bayesian information criteria from each model are reported. Because the magnitude of an RR estimate for a continuous variable varies by the unit selected for presentation, a standard unit (eg, the median weight regain of the study sample calculated from all of the assessments after reaching nadir weight) was applied.

Comparing the Performance of Weight Regain Measures

The significance of the *P* values was compared to evaluate the significance of the associations. The RR estimates were compared to evaluate the magnitude of the associations. The Bayesian information criteria were compared to evaluate the model fits. All 3 of these were compared among continuous weight regain measures. Next, all 3 were compared among dichotomous measures. Given the models for each outcome were identical except for the weight regain measure, a difference of greater than 2 for the Bayesian information criterion was considered to be good evidence that the weight regain measure with the lower Bayesian information criterion fit better.[37] Weight regain measures were considered to perform similarly if the difference in the Bayesian information criteria was 2 or less, or if the model fit was better with one measure but the magnitude of the significant associations was larger with another measure.

The significance of the *P* values and the Bayesian information criteria also was compared between each continuous weight regain measure and its dichotomous counterpart for indication of a dose response or threshold effect. In addition, for each outcome, the Bayesian information criteria of the best continuous measure and the best dichotomous measure were compared to determine which had the better fit. The RR estimates of continuous vs dichotomous measures were not compared because the RR for a continuous variable differs by the selected unit.

Sensitivity Analysis

Although the likelihood-based approaches used to analyze the data produced consistent estimates of RRs and other parameters among the analysis sample, the extent of the missing data was not trivial. Therefore, a sensitivity analysis using multiple imputation was conducted to address the potential effect of excluding participants from the analysis sample due to inadequate weight measurement.

For the 1703 eligible participants (eFigure 1 in the Supplement), 20 imputed data sets were generated in which missing weights, missing data components of the other clinical outcomes (eg, hemoglobin A_{1c} level and diabetes medication use) and select missing variables measured prior to surgery (race, diabetes status, and smoking status) were imputed based on full conditional specification (also known as the chained equation or sequential regression approach). Satisfaction with surgery was excluded from the sensitivity analysis because this measure was missing at all assessments prior to 2010 when it was added to the study protocol.

For the imputation of binary variables, logistic regression with logit link was used; for categorical variables, logistic regression with generalized logit link was used; and for continuous variables, linear regression models were used. Time points at which the observations were not expected by design (eg, hemoglobin A_{1c} level was not collected at the 6-year assessment) were not imputed. Details of the models used for imputation appear in eAppendix 2 in the Supplement.

For each imputed data set, the same analyses were conducted to report weight regain by time since reaching nadir weight and to obtain the RRs and corresponding standard errors for each weight regain measure and clinical outcome. Of 1703 eligible participants, a minimum of 137 and a maximum of 158 participants who reached nadir weight during the final year of data collection were excluded from the 20 imputed data sets. The estimates were averaged over the 20 imputations and the standard errors were adjusted using the formula by Rubin[38] to produce a Wald-type 95% CI for the RRs after multiple imputation.

Results

The requirements for nadir weight determination were met by 1406 of 1703 participants (82.6%) who underwent RYGB surgery, who did not undergo a reversal or revision to another bariatric procedure, or who did not die prior to the 5-year assessment (eFigure 1 in the Supplement). Among the 1406 participants, the median age was 47 years (25th-75th percentile, 38-55 years), 1129 were female (80.3%), 1193 were white (85.6%), and the median BMI was 46.3 (25th-75th percentile, 42.3-51.8). Additional characteristics of the full analysis sample prior to surgery and in the weight regain subsample appear in **Table 1**.

Those who were excluded from the analysis sample due to missing data were younger compared with those who were included (median age, 39 vs 47 years, respectively; $P < .001$) and more likely to smoke (60 of 295 [20.3%] vs 183 of 1404 [13.0%]; $P = .001$). A full comparison of characteristics prior to surgery between those included vs excluded from the analysis sample appears in eTable 1 in the Supplement. There was not a significant between-group difference in weight loss throughout follow-up (eTable 2 in the Supplement).

Weight Assessment

After participants underwent RYGB surgery, the median follow-up was 6.6 years (25th-75th percentile, 5.9-7.0 years). Reflecting the strict inclusion criteria, weight was obtained at each follow-up assessment in almost all surviving participants who were not pregnant. Specifically, weight was obtained in 1375 of 1403 participants (98.0%) at the 6-month assessment, 1376 of 1399 (98.4%) at the 1-year assessment, 1361 of 1383 (98.4%) at the 2-year assessment, 1341 of 1392 (96.3%) at the 3-year assessment, 1327 of 1387 (95.7%) at the 4-year assessment, 1337 of 1394 (95.9%) at the 5-year assessment,

Table 1. Demographic and Clinical Characteristics Prior to Surgery

	Full Analysis Sample (N = 1406)	Weight Regain Subsample (n = 1286)[a]
Age, median (25th-75th percentile), y	47 (38-55)	46 (38-55)
Female, No. (%)	1129 (80.3)	1030 (80.1)
Race, No./total No. (%)		
White	1193/1394 (85.6)	1092/1276 (85.6)
Black	150/1394 (10.8)	137/1276 (10.7)
Asian	3/1394 (0.2)	3/1276 (0.2)
American Indian/Alaskan Native	14/1394 (1.0)	13/1276 (1.0)
Native Hawaiian/other Pacific Islander	3/1394 (0.2)	3/1276 (0.2)
Mixed (≥2 races)	31/1394 (2.2)	28/1276 (2.2)
Hispanic or Latino ethnicity, No. (%)	61 (4.3)	58 (4.5)
Married or living as married, No. (%)	818 (58.2)	751 (58.4)
Education, No./total No. (%)		
≤High school degree	305/1307 (23.3)	277/1196 (23.2)
Some college	559/1307 (42.8)	517/1196 (43.2)
College degree	443/1307 (33.9)	402/1196 (33.6)
Unemployed, No. (%)	50 (3.6)	46 (3.6)
Household income, No./total No. (%)		
<$25 000	243/1271 (19.1)	212/1166 (18.2)
$25 000-$49 999	358/1271 (28.2)	333/1166 (28.6)
$50 000-$74 999	300/1271 (23.6)	277/1166 (23.8)
$75 000-$99 999	194/1271 (15.3)	181/1166 (15.5)
≥$100 000	176/1271 (13.8)	163/1166 (14.0)
Current or recent smoker, No./total No. (%)	183/1404 (13.0)	156/1284 (12.1)
Weight, median (25th-75th percentile), kg	129.7 (116.1-148.8)	129.3 (116.1-147.4)
Body mass index, median (25th-75th percentile)[b]	46.3 (42.3-51.8)	46.2 (42.2-51.7)
Diabetes, No./total No. (%)	502/1383 (36.3)	438/1221 (35.9)
Hyperlipidemia, No./total No. (%)	525/1219 (43.1)	399/1035 (38.6)
Hypertension, No./total No. (%)	972/1383 (70.3)	869/1244 (69.9)
SF-36 score, median (25th-75th percentile)[c]		
Physical Component Summary	35.1 (26.7-43.9)	35.3 (27.0-44.2)
Mental Component Summary	51.6 (42.8-57.2)	52.0 (43.4-57.4)

Abbreviation: SF-36, 36-item Short-Form Health Survey.

[a] The subsample size is 1286 because 120 patients were excluded from the evaluation of weight regain (119 reached nadir weight during the final year of data collection; 1 was pregnant at the only assessment after reaching nadir weight).

[b] Calculated as weight in kilograms divided by height in meters squared.

[c] Lower scores imply more disability or worse function. There were missing data for 119 patients in the full analysis sample and 103 patients in the subsample for this variable. Norm-based methods transform the score to a mean (SD) of 50 (10) in the general US population (range, 0-100).

1313 of 1390 (94.5%) at the 6-year assessment, and 875 of 945 (92.6%) at the 7-year assessment. The denominator for the 7-year assessment excludes participants who were due for the 7-year assessment after data collection ended. Of 11 711 weight measures for all assessments, 8022 (68.5%) were measured per protocol, 808 (6.9%) were determined by research or medical personnel using a nonstudy scale, and 2881 (24.6%) were self-reported.

Weight Loss

The median time to reaching nadir weight was 2.0 years after RYGB surgery (25th-75th percentile, 1.0-3.2 years); however, 119 participants (8.5%) achieved nadir weight during the final year of follow-up (ie, at 6- or 7-year assessment). The cumulative incidence of time to maximum weight loss appears in eFigure 2 in the Supplement. The median percentage of maximum weight loss was 37.4% (25th-75th percentile, 31.6%-43.3%) of presurgery weight. The median nadir BMI was 28.8 (25th-75th percentile, 25.7-33.1). By the last assessment, the median percentage of weight loss was 28.0% (25th-75th percentile, 20.6%-35.6%) and the median BMI was 33.2 (25th-75th percentile, 29.7-38.5). Additional measures of maximum weight loss and weight loss at each participant's last assessment (≥5 years) appear in eTable 3 in the Supplement.

Weight Regain After Reaching Nadir Weight

Weight regain was a quadratic function of time since reaching nadir weight ($P < .001$ in all weight regain models) such that the rate of weight regain was largest during the first year after reaching nadir weight and decreased over time, but continued throughout follow-up (eAppendix 3 and eTable 4 in the Supplement). The median rate of weight regain was 9.5% of the maximum weight lost (25th-75th percentile, 4.7%-17.2%) 1 year after reaching nadir weight, 22.5% (25th-75th percentile, 12.9%-34.5%) 3 years after reaching nadir weight, and 26.8% (25th-75th percentile, 16.7%-41.5%) 5 years after reaching nadir weight. Additional weight regain measures by time since reaching nadir weight appear in **Table 2**.

At each time point, the upper quartile of participants gained at least 2.5 times more than the bottom quartile for all continuous weight regain measures, indicating substantial variability in the magnitude of weight regain. The percentages of

Table 2. Observed Weight Regain by Time Since Reaching Nadir Weight

	Time Since Reaching Nadir Weight				
	1 y	2 y	3 y	4 y	5 y
Weight measured, No. (%)	1265 (100)	1133 (93)	1057 (92)	966 (90)	771 (78)
Weight measurement missing, No. (%)	0	78 (7)	85 (8)	101 (10)	166 (12)
Reasons ineligible for weight assessment, No.					
Pregnant at time point	21	10	14	14	10
Died prior to time point	0	4	5	7	12
Data collection ended prior to time point	0	61	125	198	327
Time since initial surgery, median (25th-75th percentile), y	3.0 (2.1-3.9)	3.8 (3.1-4.3)	4.6 (4.0-5.2)	5.3 (5.0-6.0)	6.0 (5.8-6.6)
Weight Regain Measures, Median (25th-75th Percentile)					
Weight, kg	4.5 (2.3-8.2)	8.2 (5.0-13.2)	10.4 (5.9-16.3)	11.8 (7.3-18.6)	12.7 (7.3-19.5)
Body mass index[a]	1.6 (0.8-2.8)	3.0 (1.7-4.6)	3.7 (2.2-5.8)	4.2 (2.6-6.7)	4.5 (2.7-6.8)
Percentage of presurgery weight	3.5 (1.7-6.1)	6.5 (3.8-9.7)	8.3 (4.8-12.2)	8.9 (5.7-14.0)	9.7 (6.0-14.4)
Percentage of nadir weight	5.7 (2.7-9.6)	10.1 (6.0-16.1)	12.9 (7.5-19.4)	14.2 (8.6-22.3)	15.0 (9.2-23.2)
Percentage of maximum weight lost	9.5 (4.7-17.2)	17.8 (10.2-27.3)	22.5 (12.9-34.5)	24.6 (16.1-39.4)	26.8 (16.7-41.5)
Clinically Important Weight Regain, No. (%)[b]					
≥10 kg	205 (16.2)	441 (38.9)	542 (51.3)	551 (57.0)	474 (61.5)
≥5 body mass index points[a]	95 (7.5)	235 (20.7)	354 (33.5)	379 (39.2)	336 (43.6)
≥10% of presurgery weight	100 (7.9)	267 (23.6)	392 (37.1)	420 (43.5)	376 (48.8)
≥10% of nadir weight	297 (23.5)	576 (50.8)	676 (64.0)	669 (69.3)	559 (72.5)
≥15% of nadir weight	125 (9.9)	325 (28.7)	422 (39.9)	453 (46.9)	387 (50.2)
≥10% of maximum weight lost	604 (47.8)	859 (75.8)	880 (83.3)	839 (86.9)	667 (86.5)
≥20% of maximum weight lost	235 (18.6)	492 (43.4)	599 (56.7)	612 (63.4)	519 (67.3)
≥25% of maximum weight lost	148 (11.7)	340 (30.0)	465 (44.0)	476 (49.3)	427 (55.4)

[a] Calculated as weight in kilograms divided by height in meters squared.

[b] Based on how defined in the scientific literature.[11,19,20,24,26-28]

participants with clinically meaningful weight regain varied by measure. For example, 5 years after reaching nadir weight, 336 participants (43.6%) regained 5 BMI points or greater, 387 (50.2%) regained 15% or greater of nadir weight, and 667 (86.5%) regained 10% or greater of the maximum weight lost (Table 2). Weight regain was similar in the sensitivity analysis among the larger sample for RYGB surgery using multiple imputation; for example, 432 (45.6%) regained 5 BMI points or greater, 495 (52.3%) regained 15% or greater of nadir weight, and 826 (87.3%) regained 10% or greater of the maximum weight lost (eTable 5 in the Supplement).

Progression of Comorbidities and Declines in Health-Related Quality of Life and Satisfaction With Surgery

During the first year after reaching nadir weight, 55 of 555 participants (9.9%) experienced progression of diabetes, 107 of 414 (25.8%) experienced progression of hyperlipidemia, and 380 of 822 (46.2%) experienced progression of hypertension. There were clinically important declines in physical health-related quality of life in 144 of 712 participants (20.2%), in mental health-related quality of life in 197 of 712 (27.7%), and in satisfaction with surgery in 27 of 218 (12.4%). The prevalence of clinical outcomes increased linearly with time since reaching nadir weight (ie, the linear term but not the quadratic term for time was significant in all models; eTable 6 in the Supplement). Five years after reaching nadir weight, the prevalence of diabetes was 35.3% (54 of 153 participants); hyperlipidemia, 68.4% (78 of 114); and hypertension, 71.5% (188 of 263). There were declines in physical health-related quality of life in 73 of 174 participants (42.0%), in mental health-related quality of life in 57 of 174 (32.8%), and in satisfaction with surgery in 8 of 29 (27.6%).

Comparing the Performance of Weight Regain Measures

Table 3 provides the RR, statistical significance, and model fit (Bayesian information criteria) for each measure of weight regain for progression of diabetes and for declines in physical and mental health-related quality of life and satisfaction with surgery. The measures for progression of hyperlipidemia and hypertension appear in eTable 7 in the Supplement.

All 5 continuous weight regain measures were significantly related to progression of diabetes, progression of hypertension, decline in the physical health-related quality of life, and decline in satisfaction with surgery. For these outcomes, the percentage of maximum weight lost had the highest point estimates (RRs) for weight regain and the lowest Bayesian information criterion, although model fits with weight in kilograms and percentage of presurgery weight were similar (ie, Bayesian information criteria within 2) to percentage of maximum weight lost and satisfaction with surgery. Based on the RRs and Bayesian information criterion, percentage of maximum weight lost also was better than or similar to other weight regain measures for decline in the mental health-related quality of life (along with percentage of presurgery

Table 3. Associations Between Common Measures of Weight Regain and Concurrent Declines in Health Outcomes Among Adults Who Underwent Roux-en-Y Gastric Bypass Surgery

	Progression of Diabetes (n = 689)[a]			Clinically Important Decline								
				Physical Health–Related Quality of Life (n = 903)[b]			Mental Health–Related Quality of Life (n = 903)[b]			Satisfaction With Surgery (n = 272)[c]		
	Adjusted RR (95% CI)[d]	*P* Value	BIC[e]	Adjusted RR (95% CI)[d]	*P* Value	BIC[e]	Adjusted RR (95% CI)[d]	*P* Value	BIC[e]	Adjusted RR (95% CI)[d]	*P* Value	BIC[e]
Weight Regain Measures												
Weight per 9.1 kg	1.40 (1.18-1.67)	<.001	1543.2	1.21 (1.12-1.31)	<.001	3541.9	1.08 (1.00-1.17)	.05	3739.2	1.41 (1.14-1.74)	.002	584.4
BMI per 3.2 points[f]	1.41 (1.19-1.68)	<.001	1543.2	1.21 (1.12-1.31)	<.001	3542.8	1.09 (1.01-1.18)	.03	3738.5	1.44 (1.16-1.78)	<.001	583.3
Percentage of presurgery weight per 6.9%	1.45 (1.22-1.73)	<.001	1541.9	1.22 (1.12-1.32)	<.001	3544.1	1.11 (1.02-1.20)	.02	3737.7	1.45 (1.12-1.87)	.005	585.5
Percentage of nadir weight per 11.0%	1.36 (1.15-1.60)	<.001	1545.5	1.16 (1.07-1.25)	<.001	3551.2	1.08 (1.00-1.17)	.04	3738.8	1.35 (1.07-1.70)	.01	586.9
Percentage of maximum weight lost per 18.9%	1.51 (1.27-1.78)	<.001	1535.8	1.28 (1.18-1.38)	<.001	3532.8	1.11 (1.02-1.20)	.02	3737.6	1.56 (1.19-2.04)	.001	582.6
Clinically Important Weight Regain[g]												
≥10 kg	1.56 (1.15-2.11)	.004	1549.4	1.39 (1.19-1.63)	<.001	3548.0	1.12 (0.96-1.30)	.15	3741.9	1.91 (1.21-3.01)	.006	584.3
≥5 BMI points[f]	1.66 (1.19-2.30)	.002	1548.6	1.40 (1.18-1.65)	<.001	3550.2	1.23 (1.04-1.45)	.01	3737.3	1.84 (1.13-3.01)	.02	586.9
≥10% of presurgery weight	1.63 (1.19-2.25)	.003	1549.5	1.45 (1.23-1.71)	<.001	3544.4	1.17 (1.00-1.38)	.05	3739.6	1.73 (1.05-2.84)	.03	587.1
≥10% of nadir weight	1.37 (1.02-1.84)	.03	1553.2	1.36 (1.15-1.59)	<.001	3552.0	1.11 (0.95-1.29)	.19	3741.0	1.82 (1.14-2.91)	.01	586.5
≥15% of nadir weight	1.41 (1.03-1.92)	.03	1554.0	1.36 (1.16-1.59)	<.001	3550.3	1.19 (1.01-1.39)	.03	3739.6	1.51 (0.93-2.46)	.09	589.8
≥10% of maximum weight lost	1.42 (1.02-1.98)	.04	1554.0	1.42 (1.17-1.72)	<.001	3550.4	1.09 (0.92-1.29)	.31	3742.2	2.54 (1.34-4.82)	.005	582.9
≥20% of maximum weight lost	1.64 (1.22-2.19)	<.001	1547.2	1.55 (1.33-1.82)	<.001	3535.5	1.23 (1.06-1.43)	.008	3735.8	2.33 (1.50-3.63)	<.001	579.4
≥25% of maximum weight lost	1.64 (1.21-2.20)	.001	1547.3	1.43 (1.22-1.68)	<.001	3546.5	1.16 (0.99-1.36)	.06	3739.9	2.22 (1.44-3.42)	<.001	575.9

Abbreviations: BIC, Bayesian information criteria; BMI, body mass index; RR, relative risk.

[a] Defined as (1) a change from not taking a diabetes medication to taking a diabetes medication, (2) a change from not taking insulin to taking insulin, or (3) an increase in hemoglobin A_{1c} level by at least 0.5% to 5.7% or greater.

[b] A decrease of 5 points or greater for the 36-item Short-Form Health Survey Physical and Mental Component Summary scores.

[c] An increase of 1 or greater on a 7-point scale (ranging from 1 "very satisfied" to 7 "very dissatisfied") to a rating of at least 3 (ie, "somewhat satisfied with surgery").

[d] Reported per median weight regain across time points. Adjusted for factors prior to surgery related to missing data (ie, site, age, and smoking status), and either hemoglobin A_{1c} level, Physical Health Summary score, Mental Health Summary score, or satisfaction with surgery at time of reaching nadir weight, and time since reaching nadir weight (only linear term retained) as fixed effects. The sample size for each model is based on 1286 participants minus those with missing outcome data.

[e] A difference of more than 2 is good evidence that the model with the lower BIC has better fit.

[f] Calculated as weight in kilograms divided by height in meters squared.

[g] Based on how defined in the scientific literature.[11,19,20,24,26-28]

weight). Only 2 continuous weight regain measures (increase in weight in kilograms and BMI) were significantly associated with progression of hyperlipidemia.

Of dichotomous weight regain measures, 20% or greater of maximum weight lost had the highest RR point estimate and best model fit with decline in physical health-related quality of life. This measure (≥20% of maximum weight lost) also performed better or similarly to other dichotomous weight regain measures as determined by RR point estimates and Bayesian information criterion for progression of diabetes (along with ≥5 BMI points and ≥25% of maximum weight loss), decline in the mental health-related quality of life (along with ≥5 BMI points), and decline in satisfaction with surgery (along with ≥10% of maximum weight loss and ≥25% of maximum weight loss). In addition, 20% or greater of maximum weight lost was the second best measure for hyperlipidemia (after ≥10 kg of weight) and hypertension (after ≥10% of maximum weight lost).

In the sensitivity analysis using multiple imputation, RR point estimates were the same or higher than values from the primary analysis and the 95% CIs from the sensitivity vs primary analysis overlapped (eTable 8 in the Supplement). In addition, with the exception of progression of hyperlipidemia, the ordering of regain measures by RR point estimates in the sensitivity analysis was similar to the primary analysis. Compared with other regain measures, the highest RR values for continuous measures were found for percentage of maximum weight loss; and for dichotomous measures, 20% or greater for maximum weight loss (eTable 8 in the Supplement).

In general, dichotomous measures of weight regain did not perform as well as their continuous counterparts, as indicated by their lack of statistical significance with outcomes (eg, ≥5 BMI points with progression of hyperlipidemia) or inferior model fit with outcomes (eg, all 8 dichotomous measures with progression of diabetes) (Table 3 and eTable 7 in the Supplement). Of 48 comparisons, a dichotomous weight regain measure only resulted in a better model fit than its continuous counterpart in 3 comparisons (≥20% of maximum weight lost for hyperlipidemia; ≥20% and ≥25% of maximum weight lost for satisfaction with surgery), whereas continuous weight regain measures resulted in better model fits in 30 comparisons (eTable 9 in the Supplement).

When the best continuous measure was compared with the best dichotomous measure for each outcome (percentage of maximum weight lost vs a dichotomous counterpart for all outcomes except hyperlipidemia), the continuous weight regain measure resulted in better model fits for 3 outcomes (diabetes, hypertension, and Physical Component Summary score), a similar model fit for 2 outcomes (hyperlipidemia and Mental Component Summary score) and a worse model fit for 1 outcome (satisfaction with surgery) (eTable 9 in the Supplement).

Discussion

Among a large geographically diverse cohort of adults who underwent RYGB surgery, a comparison of the relative performance of common weight regain measures in relation to several important outcomes of bariatric surgery demonstrated that weight regain measured as percentage of maximum weight lost generally performed better than the alternatives examined. These findings may inform standardizing the measurement of weight regain in studies of bariatric surgery.

All continuous and most dichotomous measures of weight regain were associated with progression of diabetes and hypertension, and declines in physical health-related quality of life and satisfaction with surgery. Some weight regain measures were weakly associated with progression of hyperlipidemia and decline in mental health-related quality of life. Even though the relative performance of weight regain measures varied by the clinical outcomes, percentage of maximum weight lost performed best (ie, had the strongest associations and best model fits with clinical outcomes) in general of all continuous measures examined and 20% or greater of maximum weight lost performed best among all dichotomous measures.

For diabetes, hypertension, and physical health-related quality of life, the model with percentage of maximum weight lost fit better than the model with the best dichotomous measure, likely reflecting that information is lost when applying a threshold compared with a continuous measure that allows dose-repose assessment across the entire distribution. However, the weight regain measure of 20% or greater of maximum weight lost had a similar model fit to the best continuous measure in relation to hyperlipidemia and mental health-related quality of life and had a better model fit for satisfaction with surgery, indicating there may be a threshold effect for at least some outcomes.

Although a few studies have reported weight regain using multiple measures,[22,27,39] only 1 prior study has compared weight regain measures in a sample of adults who have undergone bariatric surgery. Lauti et al[7] reported weight regain in 55 patients 5 years after gastric sleeve surgery using a variety of measures, and evaluated associations between weight regain measures with satisfaction with surgery, and the Bariatric Analysis Reporting Outcome System (BAROS) score, which incorporates weight loss, changes in medical conditions, health-related quality of life, and reoperations. The 2 definitions of clinically meaningful weight regain (>5 BMI points and >25% of excess weight loss), but not a third definition (>10 kg) were associated with a lower odds of satisfaction with surgery.[7] In addition, all 3 dichotomous weight regain measures were inversely associated with the BAROS score. However, several continuous measures of weight regain (ie, BMI, percentage of presurgery weight, percentage of excess BMI, and percentage of excess weight loss) explained more of the variance in the BAROS score than the dichotomous measures, suggesting a dose-response relationship with weight regain.

Lauti et al[7] did not evaluate the percentage of maximum weight lost, whereas Jirapinyo et al[6] recently reported the percentage of maximum weight lost was negatively and linearly associated with the Bariatric Quality of Life Index score ($\beta = -0.56$; $P = .001$). Thus, the current study's findings, as well as those reported by Lauti et al[7] and Jirapinyo et al,[6] support a dose-response relationship (ie, the less weight regained the better) for at least some clinical outcomes (eg, diabetes, hypertension, and physical health-related quality of life).

The median timing of nadir weight in the current study (ie, 2 years) was similar to the mean time reported in samples from 3 other RYGB surgical studies.[22,26,39] However, there was substantial variation in the timing of nadir weight within the LABS-2 cohort, with approximately 20% continuing to lose weight after their 4-year assessment, possibly due to complications (eg, ulcer) or other problems. Likewise, there was substantial variability in the magnitude of weight regain, suggesting that patient-level factors play an important role in weight loss maintenance. Given the detrimental effects of weight regain on progression of comorbidities, and decline in physical health-related quality of life and satisfaction with surgery, coupled with the fact that the rate of weight regain is highest during the first year after reaching nadir weight, early detection and treatment of weight regain may be important for maximizing the long-term benefits of RYGB surgery. Future work is needed to develop tools for patients and clinicians to more easily recognize and understand the effect of weight regain (eAppendix 3 in the Supplement).

Unlike previous studies in the bariatric literature, which generally report weight regain at 1 time point since surgery, this study reported weight regain over time as a function of time since reaching nadir weight. This was helpful for (1) highlighting the substantial effect that timing may have on estimates of weight regain and (2) suggesting that the rate of weight regain may be highest during the first year after reaching nadir weight but may continue at a diminishing rate over time. However, the difference in time scales across studies (ie, time since surgery vs time since reaching nadir weight) makes it difficult to compare weight regain in the RYGB surgery sample of this LABS-2 study with previous studies.

Given the LABS-2 study had standard data collection with relatively frequent weight measurement and high retention among a large, geographically diverse sample, the weight regain statistics from this study may be more generalizable to clinical practice in the United States than prior studies.[7,10,20-27,39] Even though 17% of the RYGB surgery cohort was excluded from the primary analysis due to missing weight data, a sensitivity analysis using multiple imputation support that the primary results are representative of the larger RYGB surgery cohort.

Limitations

This study has several limitations. First, this study did not include the gastric sleeve procedure, which was relatively uncommon at the time study participants underwent surgery (2006-2009), but is now the most common procedure in the United States.[40] However, RYGB surgery remains a common primary procedure, as well as a common revisional procedure for weight regain after failure of the gastric sleeve procedure. A second limitation is that nadir weight could have been reached between research assessments. However, using research assessments with standardized weight measurement at 6 months and annually after surgery to estimate nadir weight is likely superior to patient recall years after reaching nadir weight, or clinical records, which often have large time lapses after the first postoperative year. Third, comorbidities were not assessed at the 6-year minimal research assessment, which limited the sample size for analyses evaluating progression of diabetes, hyperlipidemia, and hypertension during weight regain. Likewise, patient satisfaction with surgery was not assessed during the first few years of data collection, resulting in a smaller sample size for this outcome. Fourth, this study's evaluation of weight regain measures did not include interpretation and ease of use by patients and clinicians.

Conclusions

Among a large cohort of adults who underwent RYGB surgery, weight regain quantified as percentage of maximum weight lost performed better for association with most clinical outcomes than the alternatives examined. These findings may inform standardizing the measurement of weight regain in studies of bariatric surgery.

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