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Change in Predicted 10-year and Lifetime Cardiovascular Disease Risk After Roux-en-Y Gastric Bypass

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Abstract

Objective—To report sex-specific changes in CVD risk following Roux-en-Y gastric bypass surgery (RYGB).

Background: Long-term changes in cardiovascular disease (CVD) risk following bariatric surgery are not well characterized.

Methods: Between 2006–2009 1770 adults enrolled in a prospective cohort study underwent Roux-en-Y gastric bypass (RYGB) at 1 of 10 U.S. hospitals. Research assessments were conducted pre-surgery and annually post-surgery over 7 years. Sex-specific predicted 10-year and lifetime CVD risk were calculated using the Framingham-lipid, Framingham-body mass index (BMI) and Atherosclerotic (ASCVD) scoring algorithms among participants with no history of CVD. Of 1566 eligible participants, 1234 (75.9%) with CVD risk determination pre- and post-surgery were included (1013 females, 221 males).

Results: Based on the Framingham-lipid, the percentage of females with predicted high (>20%) 10-year CVD risk declined from pre-surgery (6.5% [95% CI:6.7–7.5]) to 1 year post-surgery (1.0% [95% CI:0.8–1.2]; p<0.001), then increased 1 to 7 years post-surgery (to 2.8% [95% CI:1.6–3.3]; p=0.003), but was lower 7 years post-surgery versus pre-surgery (p<0.001). Time trends for percentage of high-risk participants and mean CVD risk scores were similar for both sexes and other evaluated CVD risk scores. For example, among males mean lifetime ASCVD score declined from pre-surgery to 1 year post-surgery, then increased 1 to 7 years post-surgery. However, there was a net decline from pre-surgery (p<0.001).

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Conflicts of interest statement

Authors have no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work other than the following: Dr. Couroulas reports grant from Allurion Inc.,

Conclusion: Among both females and males, predicted 10-year and lifetime CVD risk was substantially lower 7 years post-RYGB than pre-surgery, suggesting RYGB surgery can lead to sustained improvements in short- and long-term CVD risk.

Keywords

bariatric surgery; gastric bypass; severe obesity; cardiovascular disease

Introduction

As body mass index (BMI) increases, the risk of developing cardiovascular disease (CVD) also increases[1]. The association is thought to be primarily a function of an increase in CVD risk factors (i.e., hypertension, dyslipidemia, and insulin resistance[2]) related to increasing BMI[3]. Obesity also directly increases risk of CVD by impacting cardiovascular structure and function. For example, obesity increases the risk of left ventricular structural abnormalities which may lead to remodeling and left ventricle hypertrophy, left atrial enlargement, and impairment of systolic and diastolic function[4]. Those with severe obesity (BMI ≥ 40 kg/m^2) are an especially high risk population for specific types of CVD including coronary artery disease, myocardial infarction and heart arrhythmias, compared to those with less severe obesity[5].

Roux-en-Y gastric bypass (RYGB) surgery, which was the most common modern-day bariatric surgical procedure prior to 2013 and is currently the second most common procedure[6,7], is an effective treatment for severe obesity[8]. Surgical changes to the gastrointestinal tract result in substantial weight loss and impact metabolic disorders including the remission of Type 2 diabetes (T2D)[9]. There is also evidence that CVD risk and CVD-related mortality decline in the first few years following RYGB surgery[10–12]. However, associations between post-surgery weight regain with worsening of T2D, hyperlipidemia, and hypertension[13], suggest initial improvements in CVD risk may diminish over time. Studies of currently performed bariatric surgical procedures with repeated measures over long-term follow-up are needed to evaluate the sustainability of the reduction in CVD risk[12,14]. Furthermore, given evidence that biological sex may moderate the effect of interventions on CVD risk (i.e., due to general biological differences, as well as differences in environment, lifestyle and attitudes that can affect CVD risk and CVD outcomes)[15,16], there is a need to evaluate sex-specific changes in CVD[17,18].

Since CVD events (e.g. stroke, heart attack, angina) usually occur later in life, risk assessment for future CVD events is critical to monitoring health status[19]. This can be done by evaluating individual risk factors (e.g. systolic pressure, T2D, treatment for hypertension), or with CVD risk scores, which use an array of CVD risk factors to estimate the likelihood of an individual having a CVD event within a specified time frame (i.e. 10-years or lifetime)[20,21].

The primary aim of this study was to report sex-specific changes in CVD risk following RYGB in a large multisite prospective cohort study with long-term follow-up. Changes from pre-surgery to 7 years post-surgery in predicted 10-year and lifetime CVD risk (based on the Framingham Risk Score (FRS)[22] and the Atherosclerotic CVD (ASCVD)[21] risk score), as

well as individual CVD risk factors, were evaluated. Secondary aims were to evaluate changes in predicted CVD risk in relation to post-surgery weight regain, as well as to report short- and long-term rates of post-surgery non-fatal CVD events and CVD-related mortality.

Materials and Methods

Design and Participants

The Longitudinal Assessment of Bariatric Surgery (LABS)-2 was a prospective cohort study of 2,458 adults who were at least age 18 at time of enrollment[23]. Participants who underwent their first bariatric surgery between April 2006 and April 2009 were recruited between February 2005 and February 2009 at one of ten hospitals at six clinical centers throughout the United States. Research assessments are described in Supplementary Appendix 1.

Participants were eligible for evaluation of the secondary aim of CVD event reporting if they underwent RYGB (N=1770) regardless of CVD status at pre-surgery assessment. Per recommended exclusion criteria[19,21,22], CVD risk scores were not calculated for participants with a history of CVD (n=204. For the primary aim of reporting change in CVD risk after RYGB, all data components to calculate CVD risk scores at the pre-surgery assessment and at least one follow-up assessment were required for participants to be included in the analysis of CVD risk (n=1234 of 1566 without a history of CVD prior to the first post-surgery assessment, 78.7%) (Supplementary Figure 1).

Measures

Assessment of sociodemographics, anthropometrics and individual CVD risk score components has been described previously[13] and is provided in Supplementary Appendix 1.

CVD risk scores

The Framingham and the ASCVD 10-year and lifetime CVD risk scores were calculated using published algorithms[19,21,22]. All four scores utilize age, sex, total cholesterol, systolic blood pressure, blood pressure treatment, smoking status, and T2D and hyperlipidemia treatment. Race is also used in ASCVD scoring algorithms. Both risk scores both predict coronary heart disease (CHD) death, nonfatal myocardial infarction (MI) and stroke, but the Framingham also predicts coronary insufficiency, transient ischemic attack, intermittent claudication, heart failure and angina pectoris. Alternative versions of the Framingham 10-year and lifetime risk scores (hereafter referred to as “Framingham-lipid”) replace lipid variables (total cholesterol and hyperlipidemia treatment) with BMI[22] which allows for calculation of risk with less clinical data (hereafter referred to as “Framingham-BMI”). Pre-surgery age was used to calculate risk scores at all assessments to eliminate the effect of aging on change in risk[24]. CVD scores were not calculated for participants following a CVD event[19,21,22].

To describe CVD risk and to help guide statin therapy decisions in the clinical setting, both the Framingham and ASCVD 10-year risk scores are categorized[25,26]. The Framingham 10-year risk categories are defined as: low (score <10%), intermediate (10–20%), and high (>20% or more) 10-year risk[27]. The ASCVD 10-year categories are defined as low (score

<7.5%) and high (≥7.5%) 10-year risk[28]. The Framingham 10-year intermediate and high risk categories[29] and the ASCVD high risk category indicate it may be appropriate to initiate statin therapy[30]. Lifetime scores are intended to motivate patients to make lifestyle changes rather than to guide pharmacological interventions[19]. The Framingham-lipid, Framingham-BMI and ASCVD lifetime scores utilize the same cut point to indicate low (<39%) and high (≥39%) lifetime CVD risk.

CVD events

A LABS-certified clinical researcher used medical records, physical examination, and patient interviews to determine history of CVD prior to surgery, and CVD events annually post-surgery[23]. CVD-related mortality was determined using the annual study follow-up and the National Death Index[31] through December 31, 2014. For this study, CVD was defined as having a nonfatal myocardial infarction (MI), stroke, ischemic heart disease, congestive heart failure, angina, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) or death attributed to CVD. Additional information on CVD assessment and identification of CVD-related mortality is available in Supplementary Appendix 1.

To be able to compare the observed CVD-related mortality in the 7 years following RYGB to the CVD-related mortality rate in the general population matched on participants' sex, age and race, and calendar year, sex-, age-, race-, and year-specific crude mortality rates from the U.S. general population for each calendar year from 2006–2014 were downloaded from the death certificate database collected by the Centers for Disease Control and Prevention (CDC) Wonder Underlying Cause of Death[32].

Statistical analysis

Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). All reported p values are two-sided; p values less than 0.05 are reported to guide interpretation of findings. All further analyses were stratified by sex. Descriptive statistics were used to summarize participant characteristics. The observed CVD risk scores, as well as individual CVD risk components [i.e., systolic blood pressure/diastolic blood pressure/treatment for hypertension, total cholesterol /treatment for hypercholesterolemia, high-density lipoproteins (HDL-C), T2D and current cigarette smoking], were reported by time point in relation to surgery through 7 years of follow-up. Both continuous and categorical versions of the risk scores and components are reported. Because the Framingham 10-year intermediate and high risk categories[29] can both be used to initiate statin therapies, these groups were combined for some analyses, while the three category version (i.e., low, intermediate and high) was used to describe the more detailed change in risk score category over time.

Binary mixed models were used for dichotomous CVD risk categories and CVD risk score components, and mixed-effects ordinal logistic regression models were used for three-level Framingham 10-year CVD risk categories. Likewise, linear mixed models were used to estimate the mean of continuous CVD risk scores and CVD risk score components by time point. Mixed models used all available data via maximum likelihood, with a person-level random intercept, and controlled for pre-surgery factors related to missing data (i.e., site, age and pre-surgery smoking status), with time since surgery entered as a discrete fixed effect.

Pairwise comparisons were made between pre-surgery and year 1 (to assess short-term change), pre-surgery and 7 years (to assess long-term change), as well as year 1 and 7 years (to assess the durability of the short-term change). P values were adjusted by simulation for multiple comparisons[33]. The modeling was repeated for estimating the distributions of categorical risk groups and the mean of continuous CVD risk scores in relation to weight regain, with time since participants' lowest recorded weight entered as a discrete fixed effect.

Event rates were calculated for non-fatal CVD events and CVD-related mortality by dividing the number of events by the person-years of observation per 1000 person-years, overall and by short (<5 year) and long-term follow-up (≥ 5 years)[34]. The matched mortality rate in the general population was calculated by multiplying the sex-, age-, race-, and year-specific crude mortality rate per 1,000 from the general population by the number of LABS-2 RYGB participants with each characteristic. Standardized mortality ratios (SMRs) were calculated as the ratio of observed mortality rate in the RYGB sample to the calculated mortality rate in the matched-general population. The 95% confidence intervals (CI) for the event rates and the SMRs were constructed using the Poisson distribution.

Results

Within the CVD risk score sample (1013 females, 221 males), the median age of females was 45 years (IQR: 36–53), 84.9% were white, and median BMI was 46.1 kg/m^2 (42.2–51.3). Among males, the median age was 47 years (IQR: 38–55), 92.3% were white, and median BMI was 47.4 kg/m^2 (IQR: 43.2–53.0). Additional characteristics by sex are reported in Table 1.

Data completeness of CVD scores among the sex-specific analysis samples by time period is provided in supplemental material (Supplementary Table 1). Across follow-up, 64.1% of potential CVD risk scores were determined among females and 60.9% among males.

CVD risk.

Figure 1 shows the modeled percentages (95% CI) of females and males categorized as intermediate/high or high risk of having a CVD event within 10-years or lifetime based on the Framingham-lipid, Framingham-BMI and ASCVD scores. The estimated percentage of females and males with predicted intermediate/high or high 10-year risk was lower 1 year post-surgery vs pre-surgery (p for all <0.001), then appeared to increase from 1 year to 7 years post-surgery (p for both Framinghams <0.01; for ASCVD females p=0.14, males p=0.08). Still, the percentage with predicted intermediate/high or high 10-year risk was lower at 7 years compared to pre-surgery (p for all <0.001). Similar to the 10-year results, both Framinghams and ASCVD categorized fewer female and male participants with high lifetime risk at 1 year post-surgery compared to pre-surgery (p for all <0.001, Figure 1; values provided in Supplementary Table 2). Though the percentage of females and males with high risk increased from 1 year to 7 years post-surgery (p for all ≤0.01 with exception of female Framingham-lipid, p=0.12), the percentage with high risk was lower at 7 years compared to pre-surgery (p for all <0.001). A comparison of the modeled means of the 10-

year and lifetime CVD risk scores by time point revealed similar time trends (Supplementary Table 3, Supplementary Figure 2).

Although time trends were similar across 10-year and lifetime CVD risk scores for both sexes, the percentage identified as high risk varied by score and sex (e.g., among females, the percentage with high 10-year CVD risk, was highest with the Framingham-BMI and lowest with the ASCVD; the percentage with predicted high lifetime CVD risk was highest with ASCVD and lowest with Framingham-lipid). Likewise, the magnitude of change over time varied by score and sex (e.g., among males, there was a greater absolute and relative decrease in the percentage with predicted high lifetime risk 1 year and 7 years post-surgery based on the Framingham-lipid vs. the Framingham-BMI or ASCVD).

CVD risk score components.

Figure 2 shows the modeled values of CVD risk score components (i.e. total cholesterol, HDL-C, systolic blood pressure, blood pressure treatment, smoking prevalence, T2D and BMI) by time in relation to RYGB among females. Although most CVD risk score components were different (i.e. worse) in year 7 compared year 1 (Figure 2, values provided in Supplementary Table 4), both year 1 and year 7 values were different (i.e. better) compared pre-surgery (p for all <.01). An exception was smoking, the prevalence of which was higher (i.e., worse) 1 year and 7 years post-surgery vs pre-surgery (p for both <.001). Time comparisons were similar among males compared to females (i.e. worse at year 7 compared to year 1 but better at year 7 compared to pre-surgery) (Supplementary Figure 3, Supplementary Table 4).

Changes in CVD risk in relation to weight regain.

From the CVD risk sample of 1234 participants, 1102 (911 females and 191 males; Supplementary Figure 1) had CVD risk determination following their lowest recorded weight (median time since surgery=4.4 [IQR=1.6–7.5] years; median follow-up after lowest weight=2.7 [IQR=0.4–6.5] years). The percentage of participants with predicted intermediate/high or high 10-year and lifetime risk increased across time as a linear function of weight regain for both females and males (p for all ≤0.01) except for the ASCVD 10-year, which showed a similar trend in males (p=0.06) but did not appear to increase among females (p=0.92) (Figure 3).

CVD events.

The frequency and the rates of non-fatal CVD events and CVD mortality are reported in Table 2 among all participants who underwent RYGB (N=1770); the frequency of these outcomes by time in relation to RYGB is available in supplemental material (Supplementary Table 5). For both females and males, atherosclerotic cardiovascular disease was the most common ICD-10 coded CVD-related mortality (Supplementary table 6).

Among females, there were 499 non-fatal CVD events and 8 CVD deaths within 7 years following RYGB, corresponding to a non-fatal event rate of 50.4 (95% CI:41.6–61.2) per 1000 person-years and CVD mortality rate of 0.9 (95% CI:0.5–1.9) per 1000 person-years.The SMR for females was 1.18 (95% CI:0.51, 2.32; p=0.74). The non-fatal event rate

was higher during long-term versus short-term follow-up (61.1 [95% CI:48.5–77.0] vs 42.5 [33.8–53.3] per 1000 person-year; p<0.001). The mortality rate appeared higher during the long-term versus short term follow-up but given the low frequency of the outcome, statistical power to evaluate this comparison was limited (1.2 [95% CI:0.5–3.3] vs 0.8 [95% CI:0.3–2.1] per 1000 person-years; p=0.52).

Among males, there were 179 non-fatal CVD events within 7 years following RYGB, corresponding to an event rate of 71.6 (95% CI:53.7–95.5) per 1000 person-years and CVD mortality rate of 4.3 (95% CI:2.3–8.2) per 1000 person-years. The SMR for males was 1.96 (95% CI:0.89, 3.71; p=0.09). There was not clear evidence that the non-fatal event rates among males differed during long-term versus short-term follow-up (65.4 [95% CI:45.7–93.6] vs 76.3 [95% CI:53.9–108.1] per 1000 person-year; p=0.47). The mortality rate was higher during the long-term versus short term follow-up (8.8 [95% CI:4.2–18.3] vs 1.6 [95% CI:0.4–6.2] per 1000 person-years; p=0.03).

Discussion

Among a large cohort of adults with severe obesity, discounting age, predicted 10-year and lifetime CVD risk was lower throughout 7 years following RYGB surgery versus pre-surgery whether assessed with the Framingham-lipid, the Framingham-BMI or the ASCVD scoring algorithm. This was true whether considering the percentage of participants with elevated risk or the sample's mean risk. Although the magnitude of improvement in CVD risk varied by score and timeframe, improvement was substantially larger 1 through 7 years following RYGB than what is typically achieved from diet, exercise or lifestyle interventions aimed at weight loss or CVD risk reduction in overweight and obese adults[35–37]. For example, 1 year post-RYGB, the percentage of participants with high CVD risk decreased by 85% in females and 89% in males with the Framingham-lipid algorithm, or by 73% in females and 61% in males with the ASCVD algorithm. Seven years post-RYGB these values were still striking, with 57% and 79% decreases in females and males, respectively, with the Framingham-lipid algorithm, or 61% and 38% decreases in females and males, respectively, with the ASCVD algorithm.

While there is limited data on long-term changes in CVD risk with multiple assessments following bariatric surgery[12], the reductions in overall CVD risk found in this study are supported by a retrospective cohort study with 1724 RYGB participants and 1724 matched non-surgical controls which reported 63 CVD events (e.g. myocardial infarction, congestive heart failure, or stroke) in the RYGB group versus 110 in the control group across 12 years of follow-up[14]. In addition, the findings of this study support the durability of effect reported in studies with short-term follow-up[12].

Multiple short term (10-year) and long-term (lifetime) CVD risk scores were employed due to the difference between the usage of the scores in clinical care and lack of a consensus on which CVD risk score is best for the bariatric surgery population. The selected CVD risk scores were chosen due to the ability of each score to be used in younger populations in which CVD events are less likely to occur. Additionally, the 2008 Framingham score was chosen due to its prevalence, recognizability, and high external validity. However, the

Framingham was developed among only Caucasians, and includes CVD outcomes without proven statin therapy benefit (e.g. heart failure). Thus, the ASCVD risk score, which addresses these limitations and is recommended by the American College of Cardiology/ American Heart Association (ACC/AHA)[21], was also used.

While both Framingham scores and the ASCVD score showed similar trends of change in 10-year and lifetime CVD risk over time, the scores differed in the percentage of participants identified as having high 10-year and lifetime CVD risk. For example, the Framingham-BMI 10-year algorithm categorized more participants as high risk across follow-up compared to the lipid version. This difference in categorization may be due to the high levels of obesity among bariatric surgery patients both before and after surgery, compared to the general population in which the scores were developed. Compared to the ASCVD score, both Framingham scores identified more women and men as having intermediate or high 10-year risk, perhaps because the Framingham predicts more outcomes. Given these risk designations can be used for the initiation of statin therapy, and the lifetime risk scores can be used to motivate patients to make behavioral changes, score selection has important clinical implications. For example, more females and males would be identified as potential candidates for initiation of statins if the Framingham-BMI was used versus the Framingham-lipid, or either Framingham versus the ASCVD.

Similar to a previous study showing select CVD risk factors (i.e. increases in SBP, HDL-C) increased as a function of weight regain[38], the current study demonstrated that the percentage of participants with predicted intermediate/high or high for 10-year and lifetime CVD risk (with the exception of the 10-year ASCVD in women) increased as a function of time since lowest weight. Future work should investigate additional factors that contribute to change in CVD risk over time among adults who undergo bariatric surgery and interventions that may mitigate weight regain and associated CVD risk factor changes.

The non-fatal CVD event rates within the current study revealed females had a higher rate of non-fatal CVD events in the long-term (i.e., 5 or more years) versus short-term (i.e., fewer than 5 years) post-surgery. In contrast, the short- vs. long-term non-fatal CVD event rates were similar among males (and similar to the female long-term rate). There are several reasons why females, but not males, may have lower rates in the short-term. Females may be physically healthier prior to surgery. Specifically, men undergoing bariatric surgery tend to be older, have higher BMI, and more obesity-related comorbidities compared to women[39]. Additionally, women develop CVD, on average, 7 to 10 years after men. Thus, the higher rate among women 5 years after surgery may be a reflection of aging[40].

Our post-RYGB sample had a SMR higher than 1 (females: 1.18; males: 1.96), indicating a higher mortality rate compared to the general population, adjusted for age, sex and race. This could reflect that despite improvements in weight and comorbidities following surgery, post-surgical patients still have higher levels of obesity and other comorbidities including T2D, respiratory disorders and non-alcoholic fatty liver disease[41]. However, the 95% CI of these SMR included 1. Thus, additional research is needed to determine whether these findings reflect low power to detect a difference or no actual difference.

Strengths and limitations

Major strengths of this study were the longer-term follow-up, which allowed for continued measurement of CVD risk through maximum weight loss and several years of weight regain in adults undergoing RYGB, and the large geographically diverse cohort. Additionally, multiple common CVD risk algorithms were compared.

Several limitations should be considered when interpreting the data, including the lack of representation of the gastric sleeve procedure which was uncommon during the study's time period (2006–2009), but has surpassed RYGB as the most common procedure performed in the United States[42]. Also, this study lacked a non-surgical comparison group. Thus, the impact surgery had on reductions in risk, events and mortality cannot be commented on directly. Similarly, because CVD risk was calculated independent of age (i.e. participant age at pre-surgery was used for all CVD risk score calculations), the impact of age on CVD risk is lost. Additionally, our cohort was 86% Caucasian. While the Framingham scoring algorithm was developed among a largely Caucasian sample, and the ASCVD scoring algorithm takes race into account, applying the findings of this study to other racial groups may not be appropriate. Finally, due to the lack of CVD events in our cohort, there was a lack of statistical power for some short-term versus long-term comparisons and for a precise SMR estimate.

Conclusions

Among a large cohort of adults who underwent RYGB surgery, predicted 10-year and lifetime CVD risk improved after surgery. In general, discounting age, CVD risk declined from pre-surgery to 1 year, then increased between 1 and 7 years post-surgery. However, after 7 years, CVD risk was substantially lower among both females and males compared to pre-surgery. While similar time trends were evident using all three CVD risk scores, the percentage of patients identified as having high 10-year and lifetime CVD risk and the magnitude of change over time, differed by score and sex. These findings help inform sex-specific short and long-term improvements in CVD risk after RYGB surgery and demonstrate that CVD risk score selection has important clinical implications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Sex-specific predicted 10-year and lifetime cardiovascular disease (CVD) risk were calculated using the Framingham-lipid, Framingham-body mass index (BMI) and Atherosclerotic (ASCVD) scoring algorithms among participants with no history of CVD.
- The percentage of patients identified as having high 10-year and lifetime CVD risk pre- and post-surgery, and the magnitude of change over time, differed by score and sex.
- The mean improvement in short- and long-term CVD risk was substantially larger 1 through 7 years following RYGB than what is typically achieved from diet, exercise or lifestyle interventions aimed at weight loss or CVD risk reduction in overweight and obese adults.

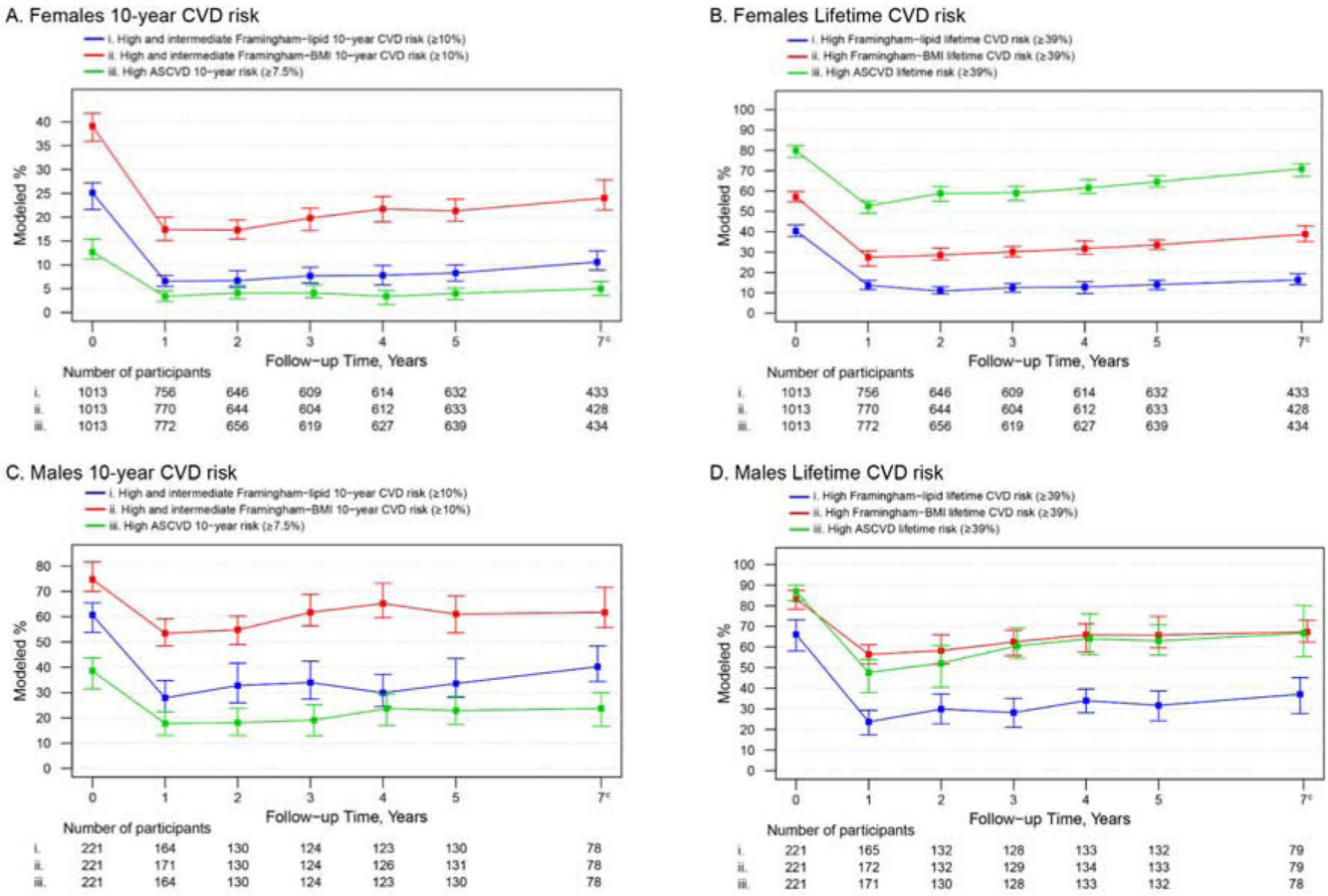

Figure 1.

Modeled[a] percentage and 95% confidence intervals of adults categorized as intermediate/high[b] or high CVD risk by time in relation to Roux-en-Y gastric bypass, stratified by sex. Abbreviations: ASCVD, Atherosclerotic cardiovascular disease; BMI, Body Mass Index (kg/m2); CVD, cardiovascular disease.

[a] Adjusted for factors related to missing follow-up data (i.e. site, age and current smoking status at pre-surgery). All pairwise comparison tests (for pre-surgery vs 1 year, 1 year vs 7 years and pre-surgery vs 7 years) were significant ($p \leq 0.01$) with the exception of 1 year vs 7 years 10-year ASCVD ($p=0.14$) and lifetime Framingham-lipids ($p=0.12$) in females, and the 10-year ASCVD in males ($p=0.08$).

[b] Because the Framingham intermediate risk category can be used to initiate statin therapy, the Framingham intermediate and high risk groups were combined.

[c] Data collection ended before the 7 year assessment of 316 females and 71 males.

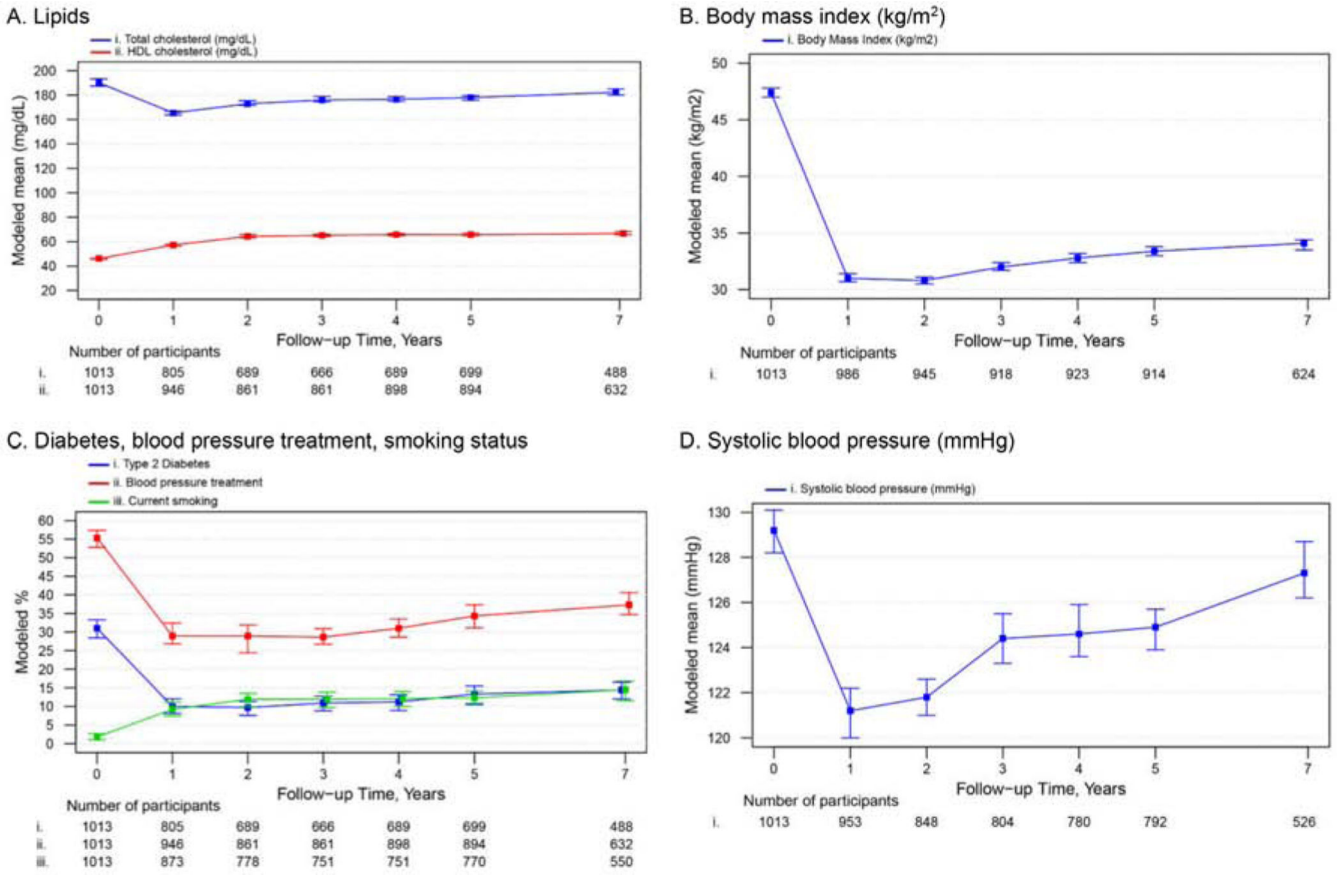

Figure 2.

Modeled[a] mean or percentage and 95% confidence intervals of CVD risk components among females by timepoint in relation to Roux-en-Y gastric bypass.

Abbreviations: HDL, high-density lipoprotein.

[a] Adjusted for factors related to missing follow-up data (i.e. site, age and current smoking status at pre-surgery). All pairwise comparison tests (for pre-surgery vs 1 year, 1 year vs 7 years and pre-surgery vs 7 years) were significant ($p \leq 0.01$).

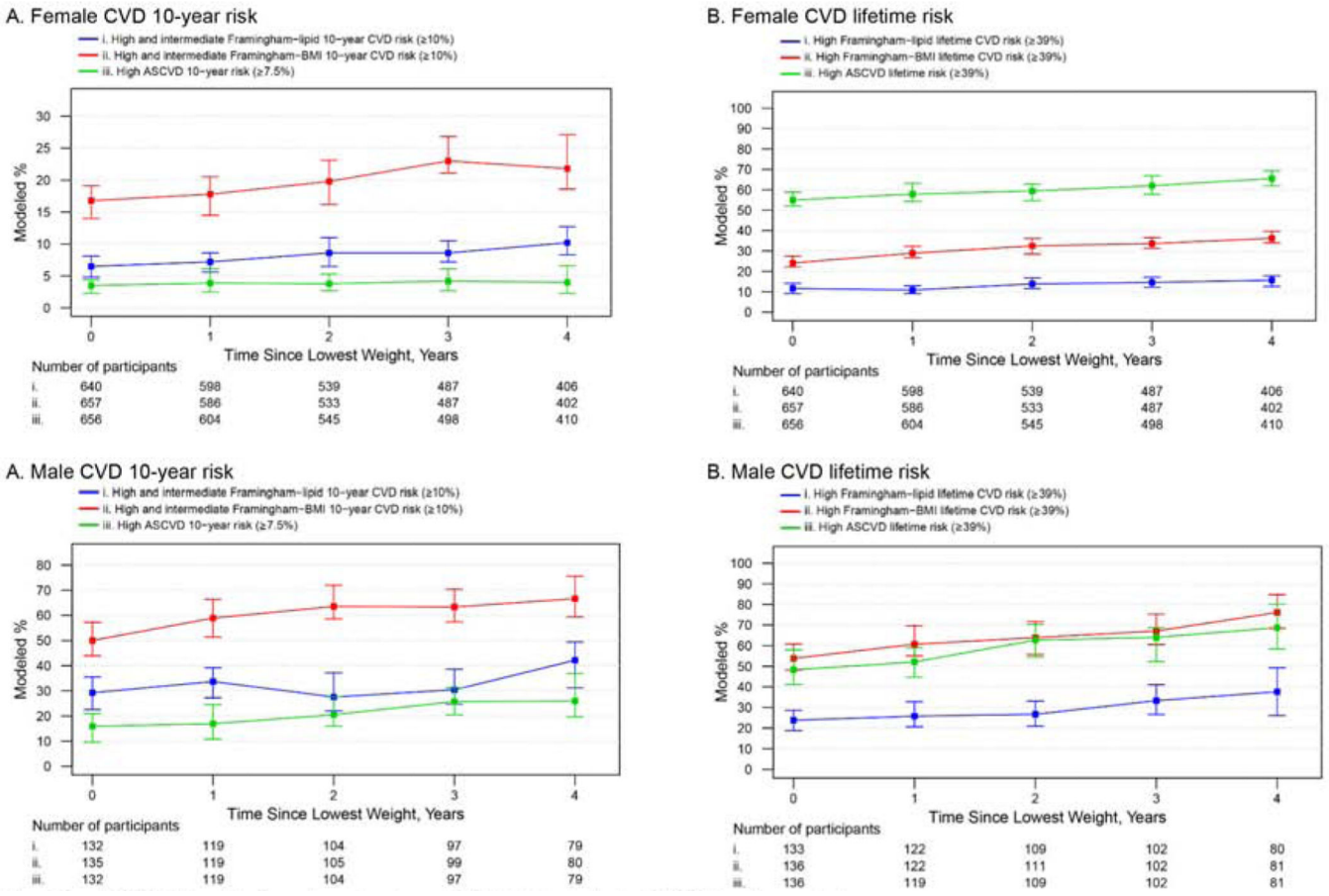

Figure 3.

Modeled[a] percentage and 95% confidence intervals of participants categorized as intermediate/high[b] or high CVD risk by time since lowest weight, stratified by sex.

Abbreviations: ASCVD, Atherosclerotic cardiovascular disease; BMI, Body Mass Index (kg/m2); CVD, cardiovascular disease.

[a] Adjusted for factors related to missing follow-up data (i.e. site, age and current smoking status at pre-surgery). All pairwise comparison tests (for pre-surgery vs 1 year, 1 year vs 7 years and pre-surgery vs 7 years) were significant ($p \leq 0.01$) with the exception of 1 year vs 7 years.

[b] Because the Framingham intermediate risk category can be used to initiate statin therapy, the Framingham intermediate and high risk groups were combined.

[c] A linear term for time since lowest weight recorded was significant ($p \leq 0.05$) for all CVD scores with the exception of 10-year ASCVD in females ($p=0.92$) and males ($p=0.06$).

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Table 1.

Characteristics of adults prior to undergoing Roux-en-Y gastric bypass in the CVD risk score sample and CVD event sample, stratified by sex.

	CVD risk score sample (N=12345)[a] No. (%)[b]		CVD event sample (N=1770) No. (%)[b]	
	Female (N=1013)	**Male (N=221)**	**Female (N=1413)**	**Male (N=357)**
Age, years				
Median (25th −75th %-ile)	45 (36, 53)	47 (38, 55)	45 (36, 53)	47 (39, 56)
Range	19–70	19–75	19–73	19–75
Race			N=1397	N=354
White	860 (84.9)	204 (92.3)	1177 (84.3)	317 (89.5)
Black	115 (11.4)	14 (6.3)	168 (12.0)	28 (7.9)
Other	38 (3.8)	3 (1.4)	52 (3.7)	9 (2.5)
Ethnicity				N=356
Hispanic	39 (3.8)	7 (3.2)	72 (5.1)	15 (4.2)
Non-Hispanic	974 (96.2)	214 (96.8)	1341 (94.9)	341 (95.8)
Married or living as married[c]	788/1302 (60.6)	231/332 (69.6)	788/1301 (60.6)	231/332 69.6
Education	N=970	N=209	N=1303	N=332
High school or less	231 (23.8)	45 (21.5)	312 (23.9)	73 (22.0)
Some college	419 (43.2)	87 (41.6)	559 (42.9)	141 (42.5)
College degree	320 (33.0)	77 (36.8)	432 (33.2)	118 (35.5)
Employed for pay[c]	680/967 (70.3)	150/206 (72.8)	894/1298 (68.9)	231/328 (70.4)
Household income, US $	N=939	N=205	N=1263	N=326
Less than 25,000	181 (19.3)	29 (14.2)	262 (20.7)	54 (16.6)
25,000–49,999	278 (29.6)	58 (28.3)	368 (29.1)	79 (24.2)
50,000–74,999	216 (23.0)	42 (20.5)	299 (23.7)	79 (24.2)
75,000–99,999	141 (15.0)	30 (14.6)	188 (14.9)	49 (15.0)
>100,000	123 (13.1)	46 (22.4)	146 (11.6)	65 (19.9)
Current smoker	18 (1.8)	5 (2.3)	32 (2.3)	11 (3.1)
	N=1011		N=1410	N=356
Body mass index, kg/m^2				
Median (25th −75th %-ile)	46.1 (42.2, 51.3)	47.4 (43.2, 53.0)	46.3 (42.1, 51.5)	47.8 (43.4, 53.3)

	CVD risk score sample (N=12345)[a] No. (%)[b]		CVD event sample (N=1770) No. (%)[b]	
	Female (N=1013)	**Male (N=221)**	**Female (N=1413)**	**Male (N=357)**
Range	34.1–81.0	33.7–76.0	33.8–81.0	33.7–76.0
Hypertension medication[c]	560 (55.3)	140 (63.3)	777/1394 (55.7)	239/353 (67.7)
Hyperlipidemia medication[c]	266/1007 (26.4)	75/221 (33.9)	380/1379 (27.6)	147/352 (41.8)
Total cholesterol (mg/dl)			N=1357	N=344
Median (25th −75th %-ile)	189.0 (162.0, 215.0)	175.0 (153.0, 198.0)	188.0 (162.0, 215.0)	170.5 (148.0, 197.0)
Range	84.0–384.0	96.0–298.0	84.0–384.0	96.0–469.0
High-density lipoproteins (mg/dl)			N=1357	N=344
Median (25th −75th %-ile)	44.0 (38.0, 53.0)	37.0 (32.0, 43.0)	44.0 (38.0, 52.0)	36.0 (31.0, 42.0)
Range	21.0–107.0	21.0–83.0	21.0–107.0	15.0–83.0
Low-density lipoprotein (mg/dl)	N=866	N=192	N=1160	N=299
Median (25th −75th %-ile)	112.0 (89.0, 134.0)	105.0 (82.0, 124.0)	112.0 (89.0, 134.0)	101.0 (78.0, 124.0)
Range	27.0–308.0	23.0–223.0	27.0–308.0	23.0–223.0
Triglycerides (mg/dl)	N=863	N=192	N=1155	N=299
Median (25th −75th %-ile)	137.0 (101.0, 191.0)	141.0 (106.0, 199.5)	138.0 (100.0, 193.0)	142.0 (107.0, 208.0)
Range	37.0–1584.0	43.0–675.0	30.0–1584.0	43.0–1677.0
Systolic blood pressure (mmHg)			N=1383	N=354
Median (25th −75th %-ile)	129.0 (120.0, 138.0)	133.0 (120.0, 142.0)	128.0 (119.0, 138.0)	130.0 (120.0, 142.0)
Range	83.0–189.0	90.0–186.0	83.0–189.0	90.0–192.0
Type 2 Diabetes	314 (31.0)	90 (40.7)	455/1385 (32.9)	160/352 (45.5)
Hypertension	667 (65.8)	164 (74.2)	926/1387 (66.8)	281/353 (79.6)

Abbreviations: CVD, cardiovascular disease.

[a] Participants free of pre-surgery history of cardiovascular disease and have cardiovascular disease risk score at pre-surgery and at least one follow-up assessment.

[b] Denominator shifts between variables due to missing data. Data are reported as No. (%) unless otherwise indicated.

[c] No./total (%).

Table 2.

CVD event rates following Roux-en-Y Gastric Bypass, stratified by sex (N=1770 [a]).

	Total Events, No.	Total Person-Years	Event rate per 1000 person-year			p-value[b]
			Overall (≤7 years)	Short-term (<5 years)	Long-term (5–7 years)	
Females (N=1413)[c]						
Total non-fatal CVD events	499	9891	50.4 (41.6–61.2)	42.5 (33.8–53.3)	61.1 (48.5–77.0)	0.004
Nonfatal myocardial infarction	37	7065	5.3 (3.6–7.8)	4.1 (2.6–6.6)	7.0 (4.3–11.4)	0.07
Stroke	22	5182	4.2 (2.5–6.9)	2.7 (1.3– 5.5)	7.4 (3.9– 13.8)	0.02
Ischemic heart disease	206	6278	33.6 (27.7–40.7)	30.5 (24.3–38.3)	37.4 (29.7–47.1)	0.11
Congestive heart failure	25	5182	4.8 (2.8–8.1)	4.0 (2.1–7.5)	6.5 (3.3–12.7)	0.21
Angina	181	6738	27.1 (22.1–33.4)	22.6 (17.5–29.1)	33.4 (26.2–42.5)	0.005
Revascularization	28	6749	3.9 (2.2–6.7)	2.0 (1.0–4.3)	6.3 (3.6–11.1)	0.001
Percutaneous coronary intervention	22	6749	3.3 (1.9–5.8)	1.3 (0.5–3.2)	6.0 (3.3–10.9)	0.002
Coronary artery bypass grafting	6	6748	0.9 (0.3–2.1)	1.0 (0.4–2.7)	0.6 (0.2–2.6)	0.50
CVD Mortality	8	8452	0.9 (0.5–1.9)	0.8 (0.3–2.1)	1.2 (0.5–3.3)	0.52
Males (N=357)[d]						
Total non-fatal CVD events	179	2499	71.6 (53.7–95.5)	76.3 (53.9–108.1)	65.4 (45.7–93.6)	0.47
Nonfatal myocardial infarction	15	1727	8.6 (4.9–15.1)	9.6 (4.9–18.8)	7.3 (3.0–17.6)	0.62
Stroke	10	1297	6.7 (3.2–14.4)	5.5 (2.2–13.3)	9.4 (3.7–23.6)	0.29
Ischemic heart disease	63	1552	39.6 (29.0–54.1)	46.7 (32.0–68.3)	31.0 (19.5–49.4)	0.16
Congestive heart failure	21	1293	15.3 (8.7–26.9)	12.3 (6.0–25.2)	22.2 (11.6–42.3)	0.14
Angina	42	1684	24.1 (16.0–36.2)	25.5 (15.3–42.5)	22.2 (12.7–39.0)	0.70
Revascularization	28	1682	14.6 (9.0–23.6)	11.5 (5.8–22.7)	19.2 (10.4–35.4)	0.24
Percutaneous coronary intervention	22	1682	12.6 (7.6–20.9)	8.7 (4.6–16.5)	18.3 (9.8–34.1)	0.057
Coronary artery bypass grafting	6	1680	3.3 (1.1–10.0)	5.0 (1.4–17.6)	1.2 (0.1–11.3)	0.28
CVD Mortality	9	2087	4.3 (2.3–8.2)	1.6 (0.4–6.2)	8.8 (4.2–18.3)	0.03

Abbreviations: CVD, cardiovascular disease; No., number.

[a] Includes participants with pre-surgery history of CVD (n=145).

[b] Comparing short and long term rates

[c] Number of events for females with a pre-surgery history of CVD (N=82): myocardial infarction:13; stroke: 9; ischemic heart disease: 51; congestive heart failure: 16; angina: 41; revascularization: 16; CVD mortality: 2

[d] Number of events for males with a pre-surgery history of CVD (N=63): myocardial infarction: 9; stroke: 4; ischemic heart disease: 42; congestive heart failure: 15; angina:27; revascularization: 21; CVD mortality: 3

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