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Comparative Effectiveness of Vertical Sleeve Gastrectomy vs. Roux en Y Gastric Bypass for Diabetes Treatment: A Claims-Based Cohort Study

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Introduction

Vertical Sleeve Gastrectomy (VSG) has become the most common bariatric procedure performed in the United States and worldwide.[1,2] Little over a decade ago, VSG made up just 5% of bariatric procedures, compared to 50% for Roux-en-Y Gastric Bypass (RYGB). By 2016, over half of new bariatric procedures (54%) were VSGs, with RYGB declining to account for only 30%.[1] However, the popularity of VSG has preceded the availability of solid evidence about its long-term impact on weight and comorbidity resolution.

Type 2 diabetes mellitus is one of the most concerning comorbidities of severe obesity, causing an estimated 80,058 deaths per year in the United States.[3] Nearly half (43%) of Americans with BMI ≥40kg/m^2 have diabetes[4]; therefore, along with other obesity comorbidities, it is a commonly-cited reason for pursuing bariatric surgery.[5] Compared to medical management, bariatric surgery results in superior long-term diabetes outcomes.[6–9] Bariatric surgical patients have up to 40% lower incidence of subsequent macrovascular events than medically-managed patients,[6,10] with 30–60% achieving durable remission of diabetes up to a decade after surgery.[7,11–13]

Despite demonstration of superior outcomes following surgery vs. medical therapy, there remains uncertainty about what type of bariatric procedure is most effective for treating diabetes. Most prior studies have compared a single procedure type (frequently RYGB) or multiple procedures grouped together, against non-operative management,[7,8,12] have lacked

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VSG patients,[14] or in some cases lacked comparison groups.[15,16] Two groundbreaking randomized trials of VSG vs. RYGB were recently published, finding no difference in diabetes remission rates between procedures, however the number of VSG patients with diabetes in these trials was small (both <60).[17,18] To date, there remain few multicenter effectiveness studies of VSG vs. RYGB for diabetes outcomes, offering little data to guide procedure choice for surgical candidates with diabetes.

Using a nationwide commercial insurance claims database, we compared matched cohorts of VSG and RYGB patients with respect to complete diabetes medication discontinuation and reduction of diabetes medication burden, up to 24 months after surgery. Based on published within-procedure remission estimates, we hypothesized that RYGB would be more effective than VSG for inducing initial medication discontinuation and reducing overall diabetes medication burden.

Methods

Study Design & Data Source

We conducted a retrospective cohort study using Optum's de-identified Clinformatics® Data Mart Database; 2000–2017 U.S.-wide commercial insurance claims, including enrollment and demographic information, as well as inpatient, outpatient and pharmacy claims for all members. Additionally, on a subset of approximately 30% of members, we had laboratory results including hemoglobin A1c measures. The study was approved by the Harvard Pilgrim Institutional Review Board, with a waiver of informed consent.

Study Population

We identified members age 18–64 years who underwent a primary VSG or RYGB between January 2010 and December 2016. First, we flagged all bariatric surgical procedures using Current Procedural Terminology (CPT) and International Classification of Diseases, 9th- or 10th Revision (ICD-9, ICD-10) codes (Supplement, A1/A2). If members had more than one procedure type during enrollment, we defined the earliest as their index procedure, then restricted to RYGB or VSG. We excluded members with any CPT codes for revisional procedures prior to their index date, evidence of gastrointestinal malignancy in the 720 days prior to surgery, codes for perforated gastrointestinal ulcer within 30 days before surgery, or BMI<30kg/m^2 to avoid including those with surgical indications other than obesity (Figure 1). We further limited our analyses to members continuously enrolled for ≥6 months before and after their index procedures. To identify patients with diabetes, we required members to have at least one fill for a diabetes medication (oral, insulin or other injectable) in the 6 months prior to surgery. We excluded women with polycystic ovarian syndrome taking metformin and no other antidiabetic medications, and patients with likely type 1 diabetes (those on insulin only with >50% of diabetes codes listed as Type 1). VSG and RYGB patients with diabetes were then followed from 6 months before surgery, up to 24 months after.

Outcome Measures

The primary outcome was diabetes medication discontinuation, defined when a patient had zero diabetes medications on hand for a period of ≥180 days. Because most patients did not have A1c measures available in our database, we could not look at diabetes remission, defined by the American Diabetes Association as 1 year of normoglycemia off all medications.[19] However, we feel that persistent discontinuation of all medications is a clinically-relevant surrogate for improvement of diabetes, given the nature of our data.

To understand how medication burden changed over time, we also examined change in median daily dose (MDD) of total diabetes medications from pre-to-post surgery. MDD is a measure that allows for comparison of dosing and total medication burden for a given indication, across drug classes. We calculated the MDD of a drug by dividing a member's dose of that medication by the median dose for the overall population in the dataset. For example, if a patient was on 1,500mg metformin, and the median metformin dose in our claims dataset was 750mg, that patient's MDD for metformin would be 2.0. We summed the total diabetes-related MDD across medications, and averaged it by month, creating a repeated measure with which to examine the changing dosage of diabetes drugs over time. Months were characterized as 30-day time periods relative to the index date, before and after surgery. We characterized MDD in three different ways: total diabetes medication burden, MDD for oral medications only and MDD for insulin only.

Covariates

Demographic measures included age group (<40y, 40–49, 50–59, 60–64), sex, and region of the U.S. (West, South, Midwest, Northeast). We used the E-Tech classification system (Ethnic Technologies)[20] to identify members as White, Black, Hispanic, or Asian. For educational level, we used a variable provided by the data vendor, which classified members as having: less than high school, high school degree, some college, or college degree.[21] Year of procedure was grouped according to 2010–12 vs. 2013–16.

We captured baseline weight category using the last body mass index (BMI) diagnosis coded before the index procedure (Supplement A3). These data were well-populated in our cohort; 86% had a specific BMI code on the day of surgery, 89% within 180 days prior. We categorized baseline BMI as: "30–39.9"; "40–49.9"; "50–59.9"; "≥60" kg/m^2, or "non-specific obesity", in the case where a generic obesity code (e.g. ICD9 278.01 ICD10 E66.01), but no specific code, was available, and "missing" if no BMI code or generic code was listed (<1%).

We used ACG software[22,23] to calculate an overall measure of morbidity based on medical claims in the baseline 6 months, and we classified patients as having lower morbidity (score <3) or higher morbidity (score ≥3). We also used ACG software to flag several relevant clusters of conditions: hypertension, cardiovascular disease (e.g. congestive heart failure, ischemic heart disease, peripheral or cerebrovascular disease), and mental illness (e.g. depression, anxiety, bipolar disorder).

Diabetes-specific covariates included baseline insulin use (yes/no), presence of baseline acute preventable diabetes complications (e.g. ketoacidosis, candidiasis; yes/no),[24] and

presence of chronic microvascular complications (e.g. retinopathy, nephropathy and neuropathy; yes/no) (Supplement A4/A5).

Matching Strategy

Comparison of VSG and RYGB would be subject to confounding by indication if patients with differing likelihood of diabetes remission were systematically triaged to a given procedure. To mitigate this risk, we matched VSG and RYGB patients on baseline variables chosen to approximate the DIAREM score, a validated clinical prediction tool for diabetes remission following bariatric surgery.[25,26] These variables included: age group (<40y, 40–49y, 50–59y, 60+y), insulin use, and tertile of diabetes MDD (total medication burden). DIAREM score calculation requires a preoperative A1c measure, however, because most patients in our dataset lacked laboratory data, we instead approximated baseline glycemic control by matching on presence of our acute and chronic diabetes complications flags.

We conducted coarsened exact matching[27] (CEM) which is similar to exact matching, but uses categories instead of exact values (for example, matching on 10-year age groups rather than exact age). The software for CEM creates weights for each stratum that adjust for differences between study groups in the proportion of persons in the stratum. In addition to matching on DIAREM score predictors, we also matched on duration of post-surgical enrollment and tertile of a propensity score for undergoing a VSG vs. RYGB procedure. The propensity score was based on remaining covariates such as sex, race/ethnicity, BMI category and comorbidity burden. Our pre-match pool included 1,398 VSG and 1,167 RYGB patients, and the final sample included 1,111 VSG and 922 RYGB patients (2,033 total).

Analytic Approach

We used a standardized differences approach to compare baseline characteristics of VSG and RYGB patients before and after matching.[28]

Medication discontinuation was examined in a time-to-event fashion, with the first day a member was on zero diabetes medications set as his/her date of discontinuation, provided (s)he did not resume medication in the following 180 days. We constructed CEM-weighted Kaplan-Meier curves with 95% confidence intervals to visualize medication discontinuation during post-operative follow-up for our matched VSG and RYGB groups, and to estimate the percent of patients in each group who had completely discontinued all medications immediately after surgery, and over follow-up. Members were censored either upon achieving the discontinuation outcome, or on the date 180 days prior to their disenrollment, to ensure that all had enough follow-up time available to achieve the outcome of interest. To compare cumulative chances of medication discontinuation between VSG and RYGB, we used Cox proportional hazards models, adjusting for all matched covariates to account for potential imbalance introduced by censoring or dropout. Additionally, we examined whether the procedures differed in effectiveness among the subgroup of baseline insulin users by adding an interaction term (procedure type × insulin use) to our models.

To visualize changes in the levels and trends of our repeated measures outcomes (MDD: total, oral and insulin), we generated time series plots of the adjusted mean daily values in

each month. We performed difference-in-differences (DID) analysis on the three MDD measures, comparing VSG to RYGB in 6-month segments during postoperative years 1 and 2, against the baseline 6 months. For these outcomes, we used generalized estimating equations with a Poisson distribution and log link function to account for patient-level clustering in repeated measures. We adjusted for the same covariates used in Cox models. Estimates are presented as the absolute and relative per-period pre-to-post change in outcome for the procedure of interest (VSG) compared to the control procedure (RYGB).

Sensitivity Analyses

To examine whether 180 days free of medications was sufficiently long to identify patients who persisted in remaining off medication, we re-analyzed the medication discontinuation outcome, instead requiring 360 days off all medications to qualify. For this analysis, we selected a subset of patients with at least 360 days of follow-up, re-matched VSG to RYGB within this subgroup, and then repeated our Cox models.

Also, to more closely approximate the factors used in the DIAREM score, we selected the ~30% of patients with preoperative A1c values, and repeated our medication discontinuation analyses substituting mean baseline A1c category (<7%; 7–8.9%; ≥9.0%) as a matching variable instead of complication flags.

To understand the effect of surgery on diabetes medication use among patients who did not achieve discontinuation, a clinically-important subgroup, we created separate time-series plots of total MDD among VSG and RYGB patients who remained on medication after surgery. Because these groups were selected based on conditioning on a future event (non-remission), potentially imbalancing the comparison on a number of characteristics, we limited analyses of between-procedure differences in MDD to a sensitivity DID analysis, with results presented in the Supplement.

Finally, to examine whether selecting for a population with more severe diabetes would change our findings, we repeated our Cox analyses on a subset of patients with either baseline insulin use or baseline evidence of acute or microvascular diabetes complications.

Results

Study Population

Our final matched cohort included 1,111 VSG and 922 RYGB patients; 67% were female, 51% were non-Hispanic White, and mean (sd) age was 48.6(8.7) years. The groups were well-matched on measured baseline characteristics predictive of diabetes remission (Table 1). Body weight status was typical of a bariatric surgical population, with 21% coded as having BMI 30–39.9 kg/m^2, 46% with BMI 40–49.9 kg/m^2, and 22% with BMI ≥50 kg/m^2. In the 6 months prior to surgery, 23% used insulin, 9% had an acute diabetes complication, and 11% had a chronic microvascular complication. By one year after surgery, 13% were lost to follow-up, rising to 30% by the end of the second postoperative year.

Medication Discontinuation

Immediately following surgery, over half of patients in both groups discontinued all diabetes medications (58% (95% CI 55%, 61%) for VSG, 68% (65%, 71%) for RYGB), with gradual increases in medication discontinuation rates continuing over the subsequent 2 years (Table 2; Figure 2). In adjusted Cox models, patients undergoing VSG were less likely to achieve complete medication discontinuation than those undergoing RYGB (HR 0.80 (0.72, 0.88)) over 24 months of follow-up. Immediate postoperative medication discontinuation was much less likely among insulin users in both procedure categories (33% (25%, 37%) for VSG vs. 39% (33%, 46%) for RYGB), and we did not find evidence that RYGB benefited insulin users more than VSG (p=0.62 for surgery × insulin interaction).

Sensitivity analyses requiring patients to have 360 days off medication resulted in lower medication discontinuation rates for both procedures, but similar between-procedure differences in Cox models, still favoring RYGB (HR 0.78 (0.70, 0.88)) (Table 2; Supplement A6). Our sensitivity analysis among the subset of patients with baseline hemoglobin A1c data demonstrated a similar, but non-significant hazard ratio (HR 0.81 (0.65, 1.01)) (Table 2; Supplement A7). The sensitivity analysis among patients with more severe baseline diabetes yielded a similar HR, still favoring RYGB (HR 0.82 (0.67, 1.01); Table 2), but with lower overall medication discontinuation rates for both procedures (Supplement A11).

Changes in Medication Use Intensity

VSG and RYGB patients experienced sharp declines in total diabetes medication MDD after surgery (Figure 3). Within each post-operative time period, VSG patients remained on relatively higher total doses of diabetes medications than their matched RYBG counterparts. Relative differences ranged from the VSG MDD being 79% higher than RYGB in the first 6 months after surgery, up to 142% higher in the third period (12–18 months) after surgery (Table 3). The overall low absolute MDD in both groups after surgery should be considered when interpreting these large relative differences. Because of the substantial medication discontinuation rates, a minority of enrolled patients contributed non-zero MDD measures in the later two post-operative periods.

We separately examined changes in insulin and oral medication MDD, which were similar. For insulin, relative between-procedure differences in dosing changes were slightly smaller than for oral medications (Table 3, Supplement A8/A9).

A visual inspection of time series MDD plots among patients who remained on diabetes medications after surgery (Figure 4) showed that these individuals tended to have been on much higher baseline doses of medications than our overall cohort (preoperative MDD ~2.3 vs. 1.4 in plots for main analytic cohort). Despite not discontinuing all medications, this subgroup still experienced an immediate, >50% drop in MDD following surgery (post-operative year 1 MDD ~1.0 for VSG and ~0.8 for RYGB). Our sensitivity DID analysis examining these patients showed smaller between-procedure differences in MDD, however still favored RYGB over VSG for greater reductions in total medication burden (Supplement, A10).

Discussion

In this nationwide comparison of the two most common bariatric procedures, RYGB patients were more likely than matched VSG patients to achieve complete diabetes medication discontinuation. Similarly, although the total medication burden dropped considerably for both groups after surgery, RYGB patients had a larger decrease in cumulative dosing of diabetes medications.

We observed a rate of complete medication discontinuation that was consistent with published early postoperative diabetes remission estimates - ranging from 30 to 86% for VSG (we estimated 58% with initial drug discontinuation)[16,29,30] and 50% to 82% for RYGB (we estimated 68%).[7,12,14,29,31,32] This finding is reassuring that our claims-based outcome of diabetes medication discontinuation, while not an ideal proxy due to lack of laboratory data, was consistent with prior studies of diabetes remission. However, in contrast to recently-published trials that found no difference in diabetes remission between procedures,[17,18] we observed that RYGB was more effective for medication discontinuation than VSG. Our large sample size may have contributed to the ability to detect a difference of relatively small absolute magnitude (absolute difference of 8 percentage points between 1-year discontinuation rates).

The findings in this study should be more generalizable than prior research because we used a larger and more diverse patient population than most clinical trials or single center cohorts. Our sample was therefore exposed to a wide variety of surgical practices and skillsets, between centers and over time, possibly providing a more realistic estimate of the comparative effectiveness of these procedures in clinical practice.

Results of our DID analyses of medication use intensity largely paralleled our discontinuation analyses, showing a striking and near immediate impact of both procedures, and favoring RYGB over VSG. The fact that over half of patients in each group achieved complete medication discontinuation in the year after surgery – thus moving to an MDD of zero - probably had a large influence on these results. We therefore felt it was important to separately examine patients who remained on medication, and found that they also had clinically-significant and near immediate reductions in total diabetes medication burden. This may be an important finding for practicing clinicians and patients, for whom reduced medication burden is a very positive result of surgery even in the absence of full diabetes remission.

Our study has several important limitations. We did not assess durability of medication discontinuation, but we suspect, based on recently-published longer-term studies,[6–11] that a subset of VSG and RYGB patients who we classified as achieving initial discontinuation may resume diabetes treatment within 5 years. This suspicion is supported by our sensitivity analysis requiring 12 months off all medications, which produced slightly lower medication discontinuation rates (67% vs. 72% of VSG discontinued at 1 year, and 75% vs. 84% for RYGB). Because of the relatively short follow-up duration in our study, we are uncertain whether the observed large early reductions in medication burden will persist beyond 2 years. As more follow-up data become available, we will conduct analyses that better

address the durability of the initial effects reported here, and examine potential variability in resumption of medications by procedure type.

Because we were working with an administrative claims dataset, 30% of our initial cohort was lost to follow-up by 24 months. However, we do not feel that attrition is a major threat to the validity of our findings. For our main outcome of interest, complete medication discontinuation, the majority of outcomes occurred in the first six months of follow-up, when we had complete retention of all members.

Owing to the observational nature of our study, it was important to match VSG and RYGB patients on key predictors of diabetes outcomes that might be imbalanced in nonrandomized comparisons. Although our matching approach produced cohorts of VSG and RYGB patients that were very similar in terms of all measured characteristics, it may have reduced the generalizability of our findings to some groups of patients. Patients in our pre-match cohort who had evidence of more severe disease, more commonly RYGB patients, were more likely to be excluded in the CEM process due to lack of appropriate matches between comparison groups. For example, 19% of the pre-match cohort had preoperative evidence of chronic microvascular complications, dropping to 11% of the post-match cohort. Similarly, 3% of pre-match RYGB patients were insulin users, compared to 23% post-match. Our sensitivity analysis among patients with more severe baseline diabetes (86% on insulin, 40% with microvascular complications) indeed showed a lower medication discontinuation rate than in our main analysis, for both procedures. Finally, although we employed a robust matching strategy, this observational study of real clinical data may be subject to residual confounding by indication on unmeasured characteristics that could impact both procedure choice and diabetes outcomes.

Conclusions

Our findings generally favor the continued use of RYGB over VSG among bariatric candidates for whom diabetes medication discontinuation is of paramount importance. However, the magnitude of the differences between RYGB and VSG was clinically small and the long-term durability of changes is unknown. Thus, it will be important for patients to consider other outcomes, such as long-term safety and side effect profile, when choosing a procedure. It will also be important for future studies to examine whether a larger difference emerges between RYGB and VSG for durability of diabetes outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Angrisani L, Santonicola A, Iovino P, et al. IFSO Worldwide Survey 2016: Primary, Endoluminal, and Revisional Procedures. Obes Surg. 2018;28(12):3783–3794. [PubMed: 30121858]
2. Angrisani L, Santonicola A, Iovino P, Formisano G, Buchwald H, Scopinaro N. Bariatric Surgery Worldwide 2013. Obes Surg. 2015.
3. (CDC) CfDCaP. FastStats: Diabetes (National Center for Health Statistics). Fast Stats 2017; https://www.cdc.gov/nchs/fastats/diabetes.htm. Accessed January 22, 2019.
4. Nguyen NT, Nguyen XM, Lane J, Wang P. Relationship between obesity and diabetes in a US adult population: findings from the National Health and Nutrition Examination Survey, 1999–2006. Obes Surg. 2011;21(3):351–355. [PubMed: 21128002]
5. Munoz DJ, Lal M, Chen EY, et al. Why patients seek bariatric surgery: a qualitative and quantitative analysis of patient motivation. Obes Surg. 2007;17(11):1487–1491. [PubMed: 18219776]
6. Fisher DP, Johnson E, Haneuse S, et al. Association Between Bariatric Surgery and Macrovascular Disease Outcomes in Patients With Type 2 Diabetes and Severe Obesity. JAMA. 2018;320(15):1570–1582. [PubMed: 30326126]
7. Adams TD, Davidson LE, Litwin SE, et al. Weight and Metabolic Outcomes 12 Years after Gastric Bypass. The New England journal of medicine. 2017;377(12):1143–1155. [PubMed: 28930514]
8. Schauer PR, Bhatt DL, Kashyap SR. Bariatric Surgery or Intensive Medical Therapy for Diabetes after 5 Years. The New England journal of medicine. 2017;376(20):1997. [PubMed: 28514616]
9. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet. 2015;386(9997):964–973. [PubMed: 26369473]
10. Sheng B, Truong K, Spitler H, Zhang L, Tong X, Chen L. The Long-Term Effects of Bariatric Surgery on Type 2 Diabetes Remission, Microvascular and Macrovascular Complications, and Mortality: a Systematic Review and Meta-Analysis. Obes Surg. 2017;27(10):2724–2732. [PubMed: 28801703]
11. Arterburn DE, Bogart A, Sherwood NE, et al. A Multisite Study of Long-term Remission and Relapse of Type 2 Diabetes Mellitus Following Gastric Bypass. Obes Surg. 2012.
12. Jakobsen GS, Smastuen MC, Sandbu R, et al. Association of Bariatric Surgery vs Medical Obesity Treatment With Long-term Medical Complications and Obesity-Related Comorbidities. JAMA. 2018;319(3):291–301. [PubMed: 29340680]
13. Dicker D, Yahalom R, Comaneshter DS, Vinker S. Long-Term Outcomes of Three Types of Bariatric Surgery on Obesity and Type 2 Diabetes Control and Remission. Obes Surg. 2015.
14. Courcoulas AP, King WC, Belle SH, et al. Seven-Year Weight Trajectories and Health Outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) Study. JAMA surgery. 2018;153(5):427–434. [PubMed: 29214306]
15. Golomb I, Ben David M, Glass A, Kolitz T, Keidar A. Long-term Metabolic Effects of Laparoscopic Sleeve Gastrectomy. JAMA surgery. 2015.
16. Capoccia D, Coccia F, Guarisco G, et al. Long-term Metabolic Effects of Laparoscopic Sleeve Gastrectomy. Obes Surg. 2018;28(8):2289–2296. [PubMed: 29497961]
17. Salminen P, Helmio M, Ovaska J, et al. Effect of Laparoscopic Sleeve Gastrectomy vs Laparoscopic Roux-en-Y Gastric Bypass on Weight Loss at 5 Years Among Patients With Morbid Obesity: The SLEEVEPASS Randomized Clinical Trial. JAMA. 2018;319(3):241–254. [PubMed: 29340676]
18. Peterli R, Wolnerhanssen BK, Peters T, et al. Effect of Laparoscopic Sleeve Gastrectomy vs Laparoscopic Roux-en-Y Gastric Bypass on Weight Loss in Patients With Morbid Obesity: The SM-BOSS Randomized Clinical Trial. JAMA. 2018;319(3):255–265. [PubMed: 29340679]
19. Buse JB, Caprio S, Cefalu WT, et al. How do we define cure of diabetes? Diabetes Care. 2009;32(11):2133–2135. [PubMed: 19875608]
20. Technologies Ethnic. Frequently Asked Questions. www.ethnictechnologies.com/faq. Accessed 24 October, 2018.
21. Products. WD. AmeriLINK Consumer Database. 2018; http://www.kbmg.com/products/amerilink/.

22. ACG. The Johns Hopkins ACG System. https://www.hopkinsacg.org/advantage/. Accessed 2 June, 2018.

23. Reid RJ, Roos NP, MacWilliam L, Frohlich N, Black C. Assessing population health care need using a claims-based ACG morbidity measure: a validation analysis in the Province of Manitoba. Health Serv Res. 2002;37(5):1345–1364. [PubMed: 12479500]

24. Wharam JF LC, Zhang F, Callahan MC, Xu X, Wallace J, Soumerai S, Ross-Degnan D, Newhouse J. High-deductible Insurance and Delay in Care for the Macrovascular Complications of Diabetes. Annals of internal medicine. 2018;In press.

25. Craig Wood G, Horwitz D, Still CD, et al. Performance of the DiaRem Score for Predicting Diabetes Remission in Two Health Systems Following Bariatric Surgery Procedures in Hispanic and non-Hispanic White Patients. Obes Surg. 2018;28(1):61–68. [PubMed: 28717860]

26. Still CD, Wood GC, Benotti P, et al. Preoperative prediction of type 2 diabetes remission after Roux-en-Y gastric bypass surgery: a retrospective cohort study. Lancet Diabetes Endocrinol. 2014;2(1):38–45. [PubMed: 24579062]

27. Iacus SM, King G, Porro G. Causal Inference Without Balance Checking: Coarsened Exact Matching. Political Analysis. 2012;20(1):1–24.

28. Yang DDJ. A unified approach to measuring the effect size between two groups using SAS. 2012. https://www.lerner.ccf.org/qhs/software/lib/stddiff.pdf.. Accessed May 12 2017.

29. Hariri K, Guevara D, Jayaram A, Kini SU, Herron DM, Fernandez-Ranvier G. Preoperative insulin therapy as a marker for type 2 diabetes remission in obese patients after bariatric surgery. Surg Obes Relat Dis. 2018;14(3):332–337. [PubMed: 29339030]

30. Cho JM, Kim HJ, Lo Menzo E, Park S, Szomstein S, Rosenthal RJ. Effect of sleeve gastrectomy on type 2 diabetes as an alternative treatment modality to Roux-en-Y gastric bypass: systemic review and meta-analysis. Surg Obes Relat Dis. 2015;11(6):1273–1280. [PubMed: 26071847]

31. Ahuja A, Tantia O, Chaudhuri T, et al. Predicting remission of diabetes post metabolic surgery: a comparison of ABCD, diarem, and DRS scores. Obes Surg. 2018;28(7):2025–2031. [PubMed: 29435812]

32. de Oliveira VLP, Martins GP, Mottin CC, Rizzolli J, Friedman R. Predictors of Long-Term Remission and Relapse of Type 2 Diabetes Mellitus Following Gastric Bypass in Severely Obese Patients. Obes Surg. 2018;28(1):195–203. [PubMed: 28770424]

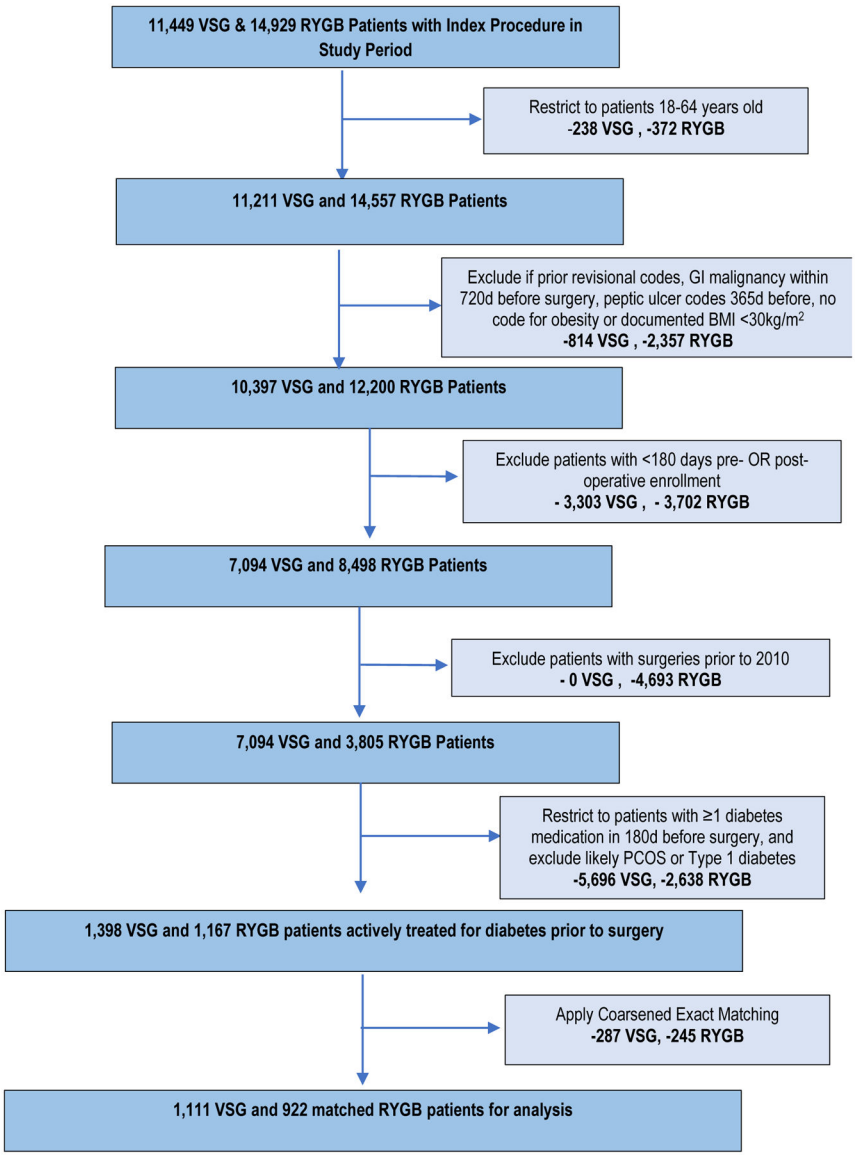
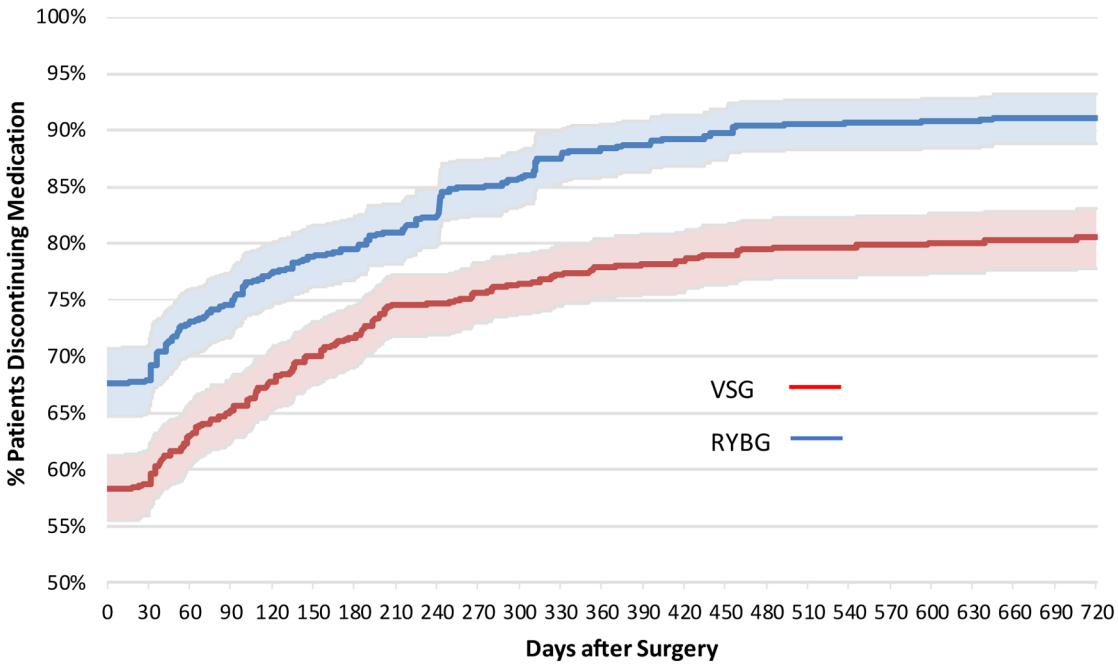


Figure 1: Flow Diagram for Cohort Selection

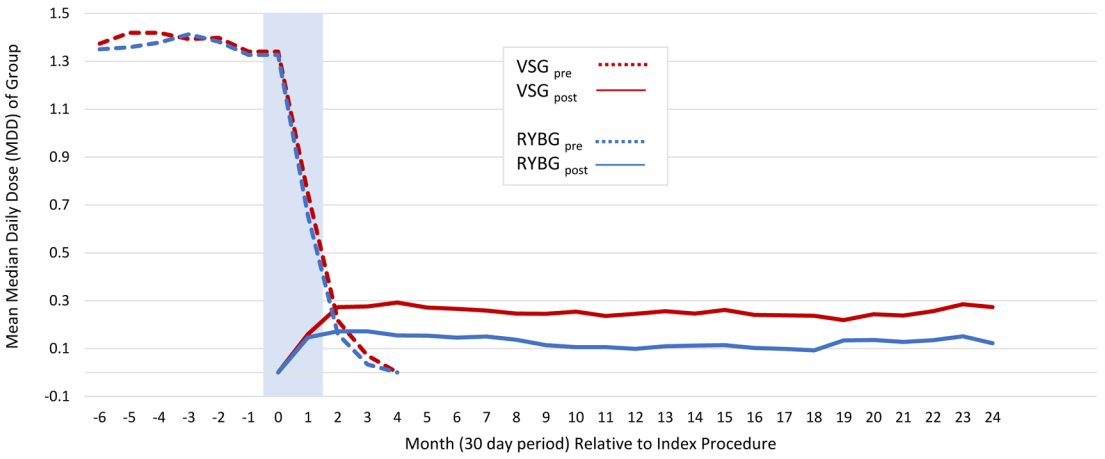
Figure 1 shows the application of inclusion/exclusion criteria and resulting impact on sample size of VSG and RYGB patients.



	Day 0	Day 180	Day 360	Day 540	Day 720
$VSG_{denominator}$	1111	1111	957	856	719
$RYGB_{denominator}$	922	922	831	750	637
VSG $N_{followup}$ (% denom)	1111 (100%)	1111 (100%)	848 (89%)	675 (79%)	519 (72%)
RYGB $N_{followup}$ (% denom)	922 (100%)	922 (100%)	704 (85%)	560 (75%)	431 (68%)
VSG $N_{eligible}$	463	244	151	108	78
RYGB $N_{eligible}$	298	143	67	42	31

Figure 2: Time to Diabetes Medication Discontinuation Among Matched Cohorts of VSG and RYGB Patients

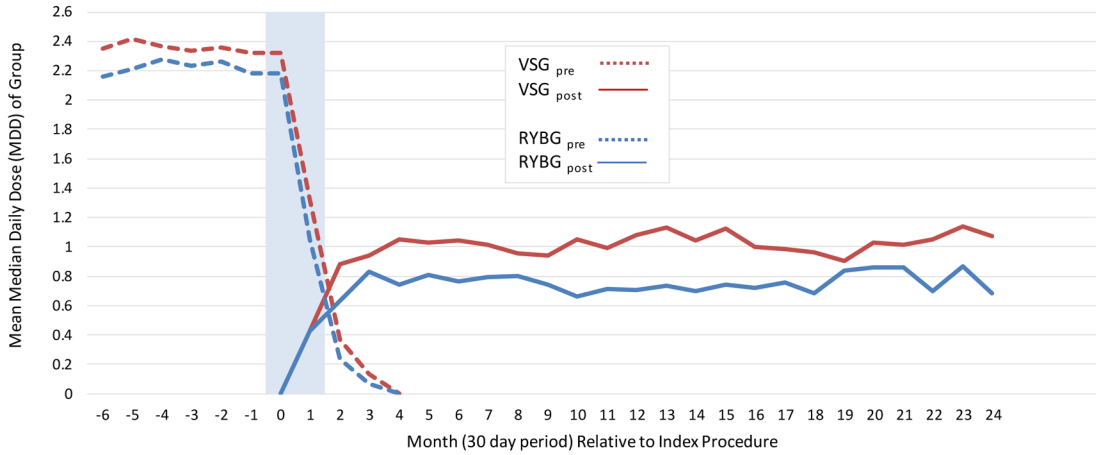
Curves represent percent of patients who have achieved medication discontinuation, among matched cohorts of RYGB (blue) and VSG (red). Days since surgery are represented on the x-axis, and percent achieving medication discontinuation on the y-axis. Below the graph, we present data on completeness of follow-up. In the top 2 table rows, for each time point, we indicate the functional denominator – the number of patients whose surgical date far enough preceded the end of our dataset (7/30/2016) to potentially contribute (VSG/ $RYGB_{denominator}$). The $N_{follow-up}$ rows, by group indicate the n/percent of patients with complete enrollment data (i.e. not lost to follow-up) at each time point, relative to the functional denominator. $N_{eligible}$ by group indicates the number who are enrolled but have not yet achieved the medication discontinuation outcome at each time point. After day 30 post-surgery, there is an uptick in remission rates for both surgeries, owing to a subset of patients who were given at least one 30-day script for diabetes medication on the date of surgery but who never received another dispensing.



	Baseline & Index Month (zero) (Referent Period 0)	End Month 6 (Post-Op Period 1)	End Month 12 (Post-Op Period 2)	End month 18 (Post-Op Period 3)	End Month 24 (Post-Op Period 4)
VSG $N_{followup}$	1111 (100%)	1111 (100%)	848 (89%)	675 (79%)	519 (72%)
RYGB $N_{followup}$	992 (100%)	922 (100%)	704 (85%)	560 (75%)	431 (68%)

Figure 3: Adjusted Time Series Plot of Median Daily Dose (MDD) for All Diabetes Medications Combined, Before and After Surgery, Comparing Matched Cohorts of VSG and RYGB Patients

Curves represent the average adjusted MDD for all combined diabetes medications (including oral, insulin and other injectables) by group, per month (30 day period – shown on x-axis) from 6 months before, through 2 years after surgery. Preoperative curves (dashed lines, starting far left) illustrate MDD for medications that patients had on-hand before surgery, supplies that are gradually exhausted by up to 3 months after surgery. Postoperative curves (solid lines, emerging at index month) illustrate MDD for medications newly supplied and on hand beginning on the date of surgery forward, thus increasing from month 1 to 3. The semi-transparent blue rectangle represents the immediate perioperative period (index date through day 30) which we treat as the primary washout period to allow for time for most medication on hand as of the index date (preoperative supply) to be used up, and owing to some patients receiving a one-time fill for medications on or around the day of surgery. See Table 3 for statistical comparisons of between procedure changes in MDD from pre- to post-surgery. Completeness of follow-up is detailed below the graph, with $N_{followup}$ by group indicating the number (%) of patients with complete enrollment data (i.e. not lost to follow-up) at each time point, relative to a denominator of patients who should have had sufficient follow-up time to contribute at each time point.



	Baseline & Index Month (zero)	End Month 6	End Month 12	End month 18	End Month 24
VSG $N_{enrolled}$	265 (100%)	265 (100%)	177 (81%)	133 (70%)	101 (62%)
RYGB $N_{enrolled}$	132 (100%)	132 (100%)	70 (64%)	52 (58%)	39 (49%)

Figure 4: Adjusted Time Series Plots of Median Daily Dose for Diabetes Medications Before and After Surgery, Comparing Unmatched Cohorts of VSG and RYGB Patients who did not have Diabetes Medication Discontinuation

Curves represent the mean MDD for all combined diabetes medications (including oral, insulin and other injectables) by group, per month (30 day period – shown on x-axis) from 6 months before, through 2 years after surgery, for the 397 patients who did not achieve diabetes remission. Preoperative curves (starting far left) illustrate MDD for medications that patients have on-hand before surgery, supplies that are gradually exhausted by up to 3 months after surgery. Postoperative curves illustrate MDD for medications newly supplied and on hand beginning on the date of surgery forward, thus increasing from month 1 to 3.

Table 1:

Baseline Characteristics of VSG vs. RYGB Patients - Pre and Post Matching[a]

	Pre-Match			Post-Match		
Variable	**RYGB % (n=1,167)**	**VSG % (n=1,398)**	**Standardized Difference[b]**	**RYGB % (n=922)**	**VSG % (n=1,111)**	**Standardized Difference[b]**
Age Group						
18–39 y	14%	19%		16%	16%	
40–49y	32%	32%	0.14	34%	34%	0.00
50–59y	40%	36%		40%	40%	
60–64y	14%	13%		10%	10%	
Female Sex	65%	65%	0.00	69%	64%	−0.11
Non-Hispanic White Race/Ethnicity[c]	55%	52%	−0.04	50%	52%	−0.05
Education[c]						
< HS	1%	1%		1%	1%	
HS Graduate	27%	27%	0.02	28%	27%	0.04
Some College	59%	59%		60%	59%	
College Graduate	12%	12%		10%	13%	
Missing	1%	1%		1%	1%	
Region						
West	26%	20%		22%	20%	
South	42%	52%	0.15	47%	51%	0.10
Midwest	22%	19%		20%	20%	
Northeast	10%	10%		11%	9%	
Time Period						
2010–12	47%	23%	0.52	27%	26%	0.02
2013–16	53%	77%		73%	74%	
BMI (kg/m^2) Category						
30–39.9	18%	22%		20%	22%	
40–49.9	43%	46%	0.18	47%	45%	0.05
50–59.9	20%	18%		19%	19%	
≥60	3%	3%		2%	3%	
Non-specific obesity	15%	10%		11%	10%	
Missing	1%	1%		1%	1%	
ACG Score ≥3[c]	25%	26%	0.01	21%	23%	0.06
Hypertension[c]	69%	66%	−0.06	66%	65%	−0.02
Cardiovascular Disease[c]	12%	12%	−0.02	8%	11%	0.10
Mental Illness[c]	16%	15%	−0.03	14%	15%	0.02
Acute DM Complications[c]	18%	17%	−0.04	9%	9%	0.00

	Pre-Match			Post-Match		
Variable	**RYGB % (n=1,167)**	**VSG % (n=1,398)**	**Standardized Difference[b]**	**RYGB % (n=922)**	**VSG % (n=1,111)**	**Standardized Difference[b]**
Chronic Microvascular Complications[c]	21%	16%	−0.13	11%	11%	0.00
Baseline Insulin Users[c]	38%	26%	−0.26	23%	23%	0.00
Baseline Metformin Only Users[c]	28%	37%	0.19	40%	40%	0.00

[a]We conducted coarsened exact matching on key predictors of diabetes remission: age group, baseline insulin use, baseline total diabetes medication burden (tertile of total MDD in the 6 months prior to surgery), and presence or absence of acute diabetes complications and chronic microvascular complications in the 6 months prior to surgery. Additionally, we exact matched on duration of enrollment after surgery to minimize bias introduced by differential loss to follow-up, and tertile of a propensity score for undergoing VSG vs. RYGB, based on sex, race, education, region, year group, BMI category, ACG score, and comorbidities.

[b]Standardized differences are the difference in means between the intervention and control groups divided by the SD of the difference in means. Lower values indicate greater similarity between VSG and RYGB, and values <0.2 indicate minimal differences between groups.

[c]for complete descriptions of how we constructed baseline variables, please refer to the methods section.

Table 2:

Results from Cox Proportional Hazards Models[a] Comparing Diabetes Medication Discontinuation Among Matched Cohorts of VSG and RYGB Patients, Up to 24 Months After Surgery

VSG vs. RYGB for the outcome of complete diabetes medication discontinuation	Baseline Sample Size of VSG and RYGB matched cohorts	Adjusted Cox Model Hazard Ratio (95% Confidence Interval)	Discontinuation Rate (95% CI) for VSG and RYGB Immediately Following Surgery[e]	Discontinuation Rate (95% CI) for VSG and RYGB by end of Year 1 of Post-Operative Follow-up[e]
Main Analysis: Medication Discontinuation defined as ≥180d off all medications	VSG n=1,111 RYGB n= 922	**0.80 (0.72, 0.88)**[f]	VSG 58.3% (55.4% to 61.2%) RYGB 67.7% (64.6% to 70.7%)	VSG 77.9% (75.2% to 80.5%) RYGB 88.4% (85.9% to 90.6%)
Sensitivity Analysis: Medication Discontinuation defined as ≥360d off all medications[b]	VSG n= 848 RYGB n=724	**0.78 (0.70, 0.88)**[f]	VSG 54.2% (50.9% to 57.6%) RYGB 65.1% (61.6% to 68.6%)	VSG 71.7% (68.5% to 74.9%) RYGB 83.5% (80.4% to 86.5%)
Sensitivity Analysis: Using Hemoglobin A1c as a matching variable[c]	VSG n= 272 RYGB n= 203	0.81 (0.65, 1.01)	VSG 57.7% (51.9% to 63.6%) RYGB 62.4% (56.4% to 69.7%)	VSG 80% (74.5% to 85%) RYGB 89.1% (83.7% to 93.3%)
Sensitivity Analysis: Among Patients with more Severe Preoperative Diabetes[d]	VSG n=293 RYGB n=335	0.82 (0.67, 1.01)[g]	VSG 35.2% (30%, 40.9%) RYGB 41.9% (36.8%, 47.4%)	VSG 55.4% (49.4%, 61.5%) RYGB 67.6% (62.1%, 73.1%)

[a] In addition to baseline CEM, models adjusted for all matching variables.

[b] For this analysis, patients were excluded if they did not have at least 360 days of follow-up as they would not be able to be assessed for the outcome of interest, we then repeated the CEM match on the remaining subset before building Cox models;

[c] For this analysis, we selected only patients who had available HbA1c measures within the 180 days prior to surgery, again repeating the CEM match on the remaining subset before building Cox models;

[d] - limited to patients with baseline insulin use or evidence of acute or microvascular complications of diabetes;

[e] -From adjusted Kaplan-Meier plots at day 0 and day 180 relative to index procedure;

[f] statistical significance at p<0.0001.;

[g] statistical significance at p=0.01.

Table 3:

Results from Multivariable Difference-in-Differences Analyses[a] Comparing VSG vs. RYGB for Measures of Diabetes Medication Use Intensity

	Post-Operative 1–6m, VSG vs. RYGB		Post-Operative 6–12m, VSG vs. RYGB		Post-Operative 12–18m, VSG vs. RYGB		Post-Operative 18–24m, VSG vs. RYGB	
	Absolute Difference[b] (95% CI)	Relative Difference[c] (%) (95% CI)	Absolute Difference (95% CI)	Relative Difference (%) (95% CI)	Absolute Difference (95% CI)	Relative Difference (%) (95% CI)	Absolute Difference (95% CI)	Relative Difference (%) (95% CI)
Total MDD[d]	0.14[g] (0.09, 0.20)	79%[g] (42%, 117%)	0.14[g] (0.10, 0.19)	108%[g] (57%, 158%)	0.16[g] (0.12, 0.21)	142%[g] (80%, 205%)	0.13[g] (0.08, 0.19)	86%[g] (32%, 140%)
Insulin-only MDD[e]	0.14(0.01, 0.26)[h]	55% (−9%, 119%)	0.15[g] (0.05, 0.25)	95%[h] (11%, 179%)	0.17[g] (0.06, 0.28)	106%[h] (15%, 197%)	0.14[h] (0.03, 0.24)	75% (2%, 149%)
Oral DM-only MDD[f]	0.11[g] (0.07, 0.15)	88%[g] (42%, 134%)	0.10[g] (0.06, 0.14)	103%[g] (43%, 164%)	0.12[g] (0.08, 0.16)	151%[g] (72%, 229%)	0.09[g] (0.03, 0.14)	76% (7%, 145%)

[a] Generalized estimating equations adjusting for all matched variables were used to generate between-group estimates for change in each outcome, at each time period, relative to a preoperative baseline period spanning months −6 to 0. The initial post-operative comparison period omits month 0 (days 0 to 30). This first month after surgery acts as a washout period to allow for time for medication on hand as of the index date (preoperative supply) to be used up, and owing to some patients receiving a one-time fill for medications on or around the day of surgery;

[b] Absolute differences in each period refer to the estimated actual change in MDD among VSG patients minus that in RYGB patients in that segment versus baseline (months −6 to 0), accounting for all other periods. For example, in post-operative months 1–6, the total MDD for VSG was 0.14 higher than for RYGB;

[c] Relative differences in each period refer to the estimated relative difference between VSG and RYGB patients versus baseline, accounting for all other periods. For example, in post-operative months 1–6, the MDD for VSG was 71% higher than for RYGB;

[d] Total MDD includes all types of medication for diabetes (insulin, injectable, oral) as a proxy for total medication burden;

[e] Insulin-only MDD includes only insulin prescriptions, so reflects differential change in burden of insulin use between procedures;

[f] Oral-only MDD includes only prescriptions for oral medications, so reflects differential change in burden of oral meds between procedures;

[g] $p<0.01$;

[h] $p<0.05$