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Monograph

The impact of surgical weight loss procedures on the risk of metachronous colorectal neoplasia: the differential effect of surgery type, sex, and anatomic location

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Abstract

Patients with prior colorectal polyps are at high risk for metachronous colorectal neoplasia, especially in the presence of obesity. We assessed the impact of 2 common bariatric surgeries, vertical sleeve gastrectomy and roux-n-Y gastric bypass, on the risk of colorectal neoplasia recurrence. This nationally representative analysis included 1183 postbariatric adults and 3193 propensity score–matched controls, who all had prior colonoscopy with polyps and polypectomy. Colorectal polyps reoccurred in 63.8% of bariatric surgery patients and 71.7% of controls at a mean follow-up of 53.1 months from prior colonoscopy. There was a reduced odds of colorectal polyp recurrence after bariatric surgery compared with controls (odds ratio [OR] = 0.70, 95% confidence interval [CI] = 0.58 to 0.83). This effect was most pronounced in men (OR = 0.58, 95% CI = 0.42 to 0.79), and post roux-n-Y gastric bypass (OR = 0.57, 95% CI = 0.41 to 0.79). However, the risk of rectal polyps or colorectal cancer remained consistent between groups. This study is the first to our knowledge to show a reduction in risk of polyp recurrence following bariatric surgery.

Colorectal cancer (CRC) is the most diagnosed gastrointestinal cancer, affecting approximately 150 000 adults in the United States each year. Colorectal polyps are widely recognized as intermediate surrogates of CRC risk. Furthermore, there is strong evidence that resection of colorectal polyps can reduce the risk of CRC (1). However, despite resection, patients with prior polyps remain at a high lifetime risk of developing future polyps compared with adults without polyps (2–4). As a result, patients with prior polyps are subject to more frequent surveillance colonoscopies (5). Patients with prior polyps are also at increased risk of developing interval CRC, defined as CRC diagnosed within 5 years from a prior colonoscopy (6–8).

The risk of developing recurrent polyps or CRC is higher in patients with obesity (9,10). Thus, reducing the risk of metachronous colorectal neoplasia is pivotal in adults with obesity who are also at higher risk of mortality after CRC diagnosis (11,12). In that regard, bariatric surgery offers an effective weight loss in individuals with medically complicated obesity (13). Obesity increases the risk of polyps, with a higher effect in the colon vs rectum and in men compared with women (10). However, a knowledge gap exists as to whether weight loss surgery can reduce the risk of polyp recurrence and if that effect varies by sex and anatomic location. Finally, the impact of bariatric surgery on the risk of interval CRC is largely unexplored. In a prior study, we identified an increased risk of serrated polyps after gastric bypass surgery (14). Serrated polyps are hard to detect, more likely to be incompletely removed, and may account for interval CRC (15-18).

The hypothesis evaluated in this study was that bariatric surgery is associated with a lower risk of recurrent colorectal polyps. To test this hypothesis, a nationwide database of insurance claims was evaluated using robust coding to assess the risk of recurrent polyps on colonoscopy in patients with bariatric surgery compared with propensity-matched controls. The analysis framework was intent to treat because data were not available regarding the amount of weight lost following surgery.

Methods

The MarketScan database

This was a retrospective, case-control cohort study using the IBM MarketScan Research Databases, which provides one of the longest-running and largest collections of proprietary deidentified claims data for privately and publicly insured people in the United States (19). MarketScan consists of private insurance claims from approximately 350 employers and 100 insurers in the United States and Medicaid and supplemental Medicare claims. Data from MarketScan are deidentified and thus do not meet the federal definition of "human subject" per 45 Code of the Federal

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Regulation (CFR 46.101). The Ohio State University Institutional Review Board does not necessitate approval for public deidentified databases. Therefore, our study did not require review or approval by the Ohio State University Institutional Review Board.

The study sample

The 2012-2020 MarketScan database was queried using International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10) codes, Current Procedural Terminology, and Healthcare Common Procedure Coding System codes. Details of the codes are published elsewhere (20). Severe obesity was defined using billing codes as a BMI $\geq$ 40 kg/m^2 or BMI $\geq$ 35 with medically complicated obesity as previously done (21,22). The positive predictive value of these obesity codes is 98% or greater (23-25). Bariatric surgery cases were adults who underwent elective roux-en-Y gastric bypass (RYGB) or vertical sleeve gastrectomy (VSG) with documented severe obesity. The controls were adults with severe obesity and no bariatric surgery during the whole study period. Follow-up was defined from the index visit date when obesity was documented in controls or date of bariatric operation in surgical patients until the date of repeat colonoscopy. Inclusion criteria were patients who 1) were aged 18 years or older, 2) had a polyp and polypectomy on a baseline colonoscopy before the index date, and 3) underwent a repeat colonoscopy during the follow-up period. Patients were excluded if they had additional risk factors for CRC (eg, family history of CRC, history of polyps prior to their baseline colonoscopy, or inherited gastrointestinal cancers), bariatric procedures other than VSG or RYGB, or gastric surgery done for reasons other than weight loss. Unlike specificity, the sensitivity of ICD coding for obesity is low (24-26). This can lead to detection bias due to higher tendency to document obesity codes in adults with comorbidities (27). To account for this possible bias, patients were excluded if they presented with CRC or colorectal polyps within 6 months from the index visit date, as done before (22,28). Details of the inclusion and exclusion criteria are in Supplementary Figure 1 (available online).

Outcomes and colonoscopy definitions

The primary outcome endpoint was the risk of colorectal polyp recurrence on repeat colonoscopy in bariatric surgery patients vs matched controls. With the availability of rectal polyp billing codes, it was possible to restrict the outcome to recurrence of rectal polyps. However, due to the lack of ICD-9-CM codes for colon polyps, it was not possible to specifically narrow the outcome to colon polyps or anatomic locations other than rectal polyps. Colonoscopy with a recurrent polyp was defined as repeat colonoscopy after index date with polypectomy and an associated diagnosis of polyp within 3 months after colonoscopy as previously reported (29). A colonoscopy without a recurrent polyp was defined as a complete colonoscopy after index visit without polypectomy and no polyps. In a secondary analysis, we assessed the risk of interval CRC on colonoscopy after surgery. CRC was defined using ICD codes as previously validated (having at least 2 diagnosis codes of CRC, one of which is a principal diagnosis) (20). Our colorectal polyp recurrence and CRC incidence outcomes were assessed in all patients and stratified by sex, type of surgery, and follow-up of less than 4 or 4 years and more. The 4-year cutoff was chosen because the sojourn time of CRC ranges between 4.5 and 5.8 years (8).

Definition of covariates

The Charlson Comorbidity Index (CCI) accounted for comorbidities and was used for multivariable adjustment as done in prior studies (22,28). CCI was calculated using documented comorbidities within 1 year prior to the index visit and classified as no comorbidities (0), mild (scores of 1–2), moderate (scores of 3-4), or severe comorbidities (scores $\geq$5) (30). Alcohol or tobacco use was defined by the presence of the respective codes at or prior to index visit. The follow-up period from index colonoscopy can affect the rate of polyps; hence, time from index colonoscopy to follow-up colonoscopy and from surgery to follow-up colonoscopy was determined. Adjustment was also made for indication (screening vs diagnostic) for colonoscopy, which can confound the risk or detection of polyps on colonoscopy (31). Finally, type 2 diabetes and hyperlipidemia are components of metabolic syndrome that are independently associated with an increased risk of CRC (32,33). Therefore, adjustment was made based on use of diabetes and cholesterol medications at index visit. Medications were obtained from the national drug registry as previously performed using MarketScan (34). Being on diabetes or cholesterol medications was defined as having at least 2 prescriptions belonging to these medications prior to index date, at least 6 months apart, with 1 prescription date falling within 1 year prior to index date (35).

Statistical analysis

Up to 4 controls (adults with severe obesity and no surgery) were matched to cases (adults with severe obesity who had bariatric surgery) without replacement, using propensity scores calculated from the following variables: age at time of colonoscopy, sex, years from preindex polyps to index, years from index to postindex colonoscopy, and CCI individual components (diabetes without complications, diabetes with complications, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease-rheumatic disease, mild liver disease, paraplegia and hemiplegia, renal disease, cancer after excluding CRC and metastatic cancer, and moderate to severe liver disease). Exact matches were required for sex and age (within 2 years), and then propensity scores were matched using greedy nearest neighbor methods to account for the remaining variables. Weights for controls were dependent on how many controls were matched to a case, such that the weights totaled to a 1:1 ratio. For instance, when 4 controls were matched to a case, each control was given a weight of 0.25. The standardized differences between our matched characteristics were small (<0.2, as shown in Table 1), which indicates a balanced propensity matching (36).

Patient characteristics were compared between cases and controls. Adjusted odds ratios were used to assess the risk of recurrent polyps on colonoscopy, adjusting for age at colonoscopy, sex, CCI, tobacco use, alcohol use, years from index to colonoscopy, preindex colonoscopy, screening or non-screening colonoscopy, and use of diabetes or cholesterol medications at index. Univariate odds ratios were used to estimate the differences in CRC between cases and controls. Multivariable logistic regression analysis was not performed for CRC due to low event counts. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results

General characteristics

A total of 1183 postbariatric surgery patients were included (67.3% females and 30.3% RYGB) with colonoscopy at a mean age of 57.4 $\pm$ 6.6 years. Most patients (95.7%) had a polyp less than 4 years before surgery and a subsequent colonoscopy at a mean

Table 1. Characteristics of the bariatric cohort and their matched controls[a]

Variable	BRS	Matched controls (BMI ≥40 kg/m^2)	Standardized difference
Patients included	1183	3193	n/a
Female	796 (67.3%)	2083 (65.2%)	−0.048
Age at follow-up colonoscopy, mean (SD), y	57.4 (6.6)	57.8 (6.5)	−0.075
Charlson Comorbidity Index score			−0.030
0	11 (0.9%)	38 (1.2%)	
1-2	349 (29.5%)	914 (28.6%)	
3-4	545 (46.1%)	1437 (45.0%)	
5+	278 (23.5%)	804 (25.2%)	
Months from pre-index polyps to follow-up colonoscopy (SD)	52.4 (18.5)	53.3 (19.0)	−0.140
Months from index visit date to follow-up colonoscopy (SD)	35.0 (18.3)	33.6 (17.6)	0.114
Alcohol use	15 (1.3%)	47 (1.5%)	0.010
Tobacco use	202 (17.1%)	494 (15.5%)	−0.041
Screening colonoscopy indication	510 (43.1%)	1396 (43.7%)	0.010
Surgery type		n/a	n/a
RYGB	358 (30.3%)		
VSG	825 (69.7%)		
Use diabetes medications at index	435 (36.8%)	1076 (33.7%)	−0.064
Use cholesterol medications at index	515 (43.5%)	1264 (39.6%)	−0.078

[a] BRS = adults with severe obesity who underwent bariatric surgery; Controls = adults with severe obesity and no bariatric surgery; RYGB = adults with severe obesity who underwent Roux-n-Y gastric bypass; VSG = Adults with severe obesity who underwent vertical sleeve gastrectomy.
There were 1183 cases matched with up to 4 controls using the following variables: age at colonoscopy, sex, individual Charlson score components, time from preindex colonoscopy with polyp to index visit, time from index visit to follow-up colonoscopy (0-2 years, 3-4 years, 5+ years). The number of controls each case was matched to are as follows: matching ratios: 4:1 n = 106 cases (9.0%); 3:1 n = 675 cases (57.1%); 2:1 n = 342 cases (28.9%); 1:1 n = 60 cases (5.1%).

of 35 ± 18.3 months after surgery and 52.4 ± 18.5 months from the prior colonoscopy with polypectomy. Propensity score matched these characteristics and individual comorbidities of the CCI with 3193 controls with obesity and no bariatric surgery (Table 1). After matching, both groups had similar rates of alcohol, tobacco, and screening colonoscopy indication.

Risk of colorectal polyp recurrence after bariatric surgery

The rate of colorectal polyps on follow-up colonoscopy was 63.8% in bariatric patients and 71.7% in controls (details in Supplemental Table 1, available online). Compared with matched controls, there were reduced odds of colorectal polyps on colonoscopy after bariatric surgery (OR = 0.70, 95% CI = 0.58 to 0.83; as shown in Figure 1). The reduction was more pronounced in males and after RYGB (OR = 0.58, 95% CI = 0.42 to 0.79; and OR = 0.57, 95% CI = 0.41 to 0.79, respectively). The odds ratio of recurrence was similar for less than 4 and 4 years and over after bariatric surgery, although it only reached statistical significance on a follow-up colonoscopy less than 4 years after surgery.

Risk of rectal polyps and interval CRC in adults with prior polyps

In this subanalysis, 9.1% and 10.1% were reported as rectal polyps in cases and controls, respectively (Supplemental Table 1, available online). After adjustment for multiple confounders, there was no reduction in the risk of rectal polyp recurrence after either RYGB or VSG or when stratified by sex or follow-up period (Figure 2). The rates of interval CRC were then assessed and were 0.4% in both cases and controls within a mean of 53.1 months (SD = 18.9) from a prior colonoscopy without CRC (Supplemental Table 2, available online).

Discussion

The data presented herein support a reduction in colorectal polyp recurrence after bariatric surgery compared with controls with obesity and no surgery. This is consistent with prior studies that identified a decrease in prevalence of colorectal polyps after bariatric surgery (28,37). However, those studies did not assess the timing of polyp formation and whether they formed before surgery. In contrast, all patients in this analysis had colonoscopy with polyp resection before bariatric surgery. Therefore, the data suggest a reduction in de novo polyp formation. Our novel findings are also the first, to our knowledge, to show a reduction in risk of colorectal polyp recurrence with weight loss (9). Thorough and rigorous exclusion criteria were applied. We also accounted for risk factors for polyp recurrence, including male sex, age, alcohol and tobacco use, and the follow-up interval since the index colonoscopy (38,39). Finally, adjustments were made for markers of metabolic syndrome (diabetes and dyslipidemia), which can influence the risk of colorectal neoplasia independently from obesity.

As shown in Figure 1, a 30% reduction in risk of recurrent colorectal polyps was observed after bariatric surgery. Every 5 kg/m^2 increase in BMI is associated with a 19% increase in the risk of colorectal polyps (10). Although it was not possible to assess the degree of weight loss after surgery in the 2012-2020 MarketScan database, patients' BMI is typically decreased by 15 kg/m^2 after bariatric surgery (40). Notably, the observed reduction in recurrent polyp risk is less than what would be expected with this effective weight loss, which could be due to a higher risk of formation of polyps in adults with prior polyps. Interestingly, a significant reduction in colorectal polyps was identified in males or after RYGB compared with matched controls—almost twice as much as observed in females or VSG. This could be due to a more pronounced effect of obesity on CRC in men than women, especially for colon cancer (12). RYGB is also associated with a more documented weight loss and metabolic improvement compared with VSG, which can also explain a better polyp reduction effect with RYGB (13). Notably, the effect size for reduction in colorectal polyp reoccurrence was similar for less than 4 or 4 years and more, although only significant for less than 4 years. We suspect the lack of statistical significance at 4 years and more is due to a smaller sample size. Contrary to colon polyps, the recurrence of rectal polyps remained unchanged despite bariatric surgery.

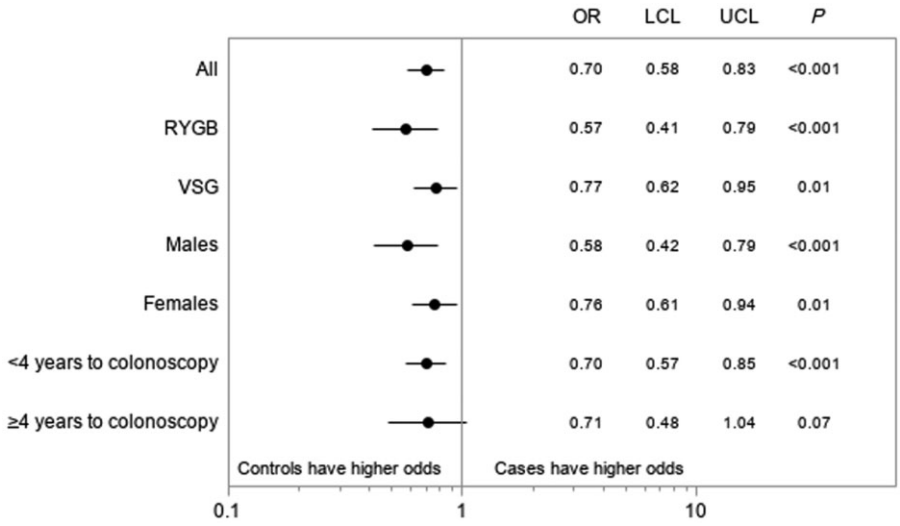

Figure 1. Colorectal polyp recurrence after bariatric surgery vs matched controls with severe obesity and no bariatric surgery. Models adjusted for cohort, sex, age at colonoscopy, alcohol use, tobacco use, Charlson index, years from index to colonoscopy, years from preindex polyps to index date, screening colonoscopy, diabetes medications at index, cholesterol medications at index. BRS = adults with severe obesity who underwent bariatric surgery; Controls = adults with severe obesity and no bariatric surgery; LCL = lower confidence level; OR = odds ratio; RYGB = adults with severe obesity who underwent Roux-n-Y gastric bypass; UCL = upper confidence level; VSG = adults with severe obesity who underwent vertical sleeve gastrectomy.

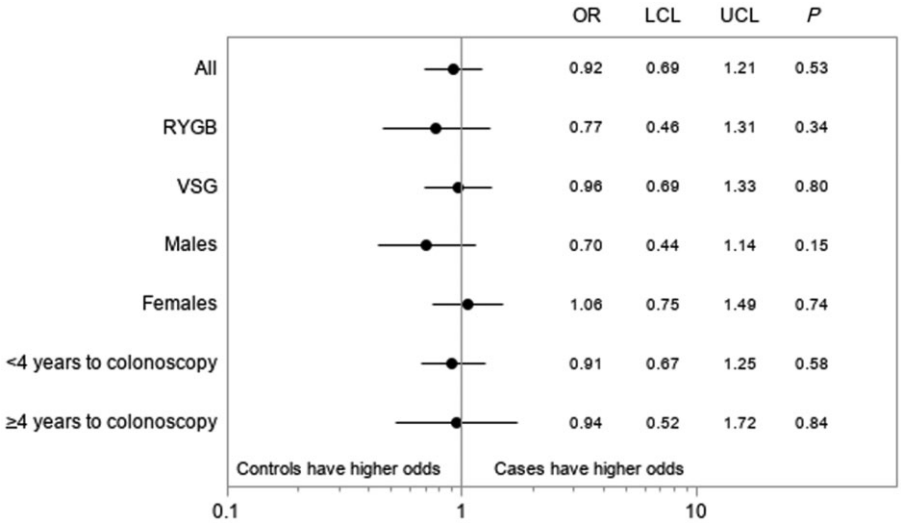

Figure 2. Rectal polyp recurrence after bariatric surgery vs matched controls with severe obesity and no bariatric surgery. Models adjusted for cohort, sex, age at colonoscopy, alcohol use, tobacco use, Charlson index, years from index to colonoscopy, years from preindex polyps to index date, screening colonoscopy, diabetes medications at index, cholesterol medications at index. BRS = adults with severe obesity who underwent bariatric surgery; Controls = adults with severe obesity and no bariatric surgery; LCL = lower confidence level; OR = odds ratio; RYGB = adults with severe obesity who underwent Roux-n-Y gastric bypass; UCL = upper confidence level; VSG = adults with severe obesity who underwent vertical sleeve gastrectomy.

These data are consistent with prior data identifying a lesser effect of obesity on risk of rectal neoplasia (10,12). Previous mechanistic studies also identify a variable effect of bariatric surgery on rectal markers of inflammation and carcinogenesis (41-45). With the increase in rectal cancer incidence in adults younger than 50 years, additional work is urgently needed to identify underlying factors that may lead to improved rectal cancer risk after bariatric surgery (46,47).

The literature on risk of CRC after bariatric surgery is heterogeneous to date, with some studies showing a puzzling increase after 10 years from surgery (48-51). In contrast, short-term cohorts identify a reduction in females with a lesser effect in males within 10 years after surgery (22,28,52). In a recent study, we confirmed a reduction in CRC risk after RYGB in females, whereas there was no reduction in males or in females after VSG (20). As a result, the risk of rectosigmoid cancer was more than twofold in males compared with females after bariatric surgery. In the current study, risk of interval CRC after bariatric surgery was also assessed, and no difference was observed compared with matched controls. This could be due to the small sample size that does not allow a detailed assessment of a rare event such as CRC.

Despite the comprehensive analysis reported herein, there are noteworthy limitations. The administrative nature of the MarketScan database has an inherent risk for coding errors and bias, which we attempted to account for using our methods. For instance, adults undergoing bariatric surgery may be inherently different from those who did not undergo bariatric surgery.

Furthermore, obesity coding may not accurately estimate BMI or the severity of obesity-related comorbidities. Efforts were made to account for that bias in the exclusion criteria adopted and by using a propensity score to match the cases and controls, which allows for quasi-randomization and unbiased analysis of outcomes based on the presence of bariatric surgery alone. In a sensitivity analysis, we assessed whether our controls without bariatric surgery were comparable with adults undergoing bariatric surgery at baseline. To do so, we compared the polyp rates on baseline colonoscopy done prior to bariatric surgery (n = 2420) and preindex date in our matched controls with severe obesity (n = 2420) after using similar methods to those described in our manuscript. In this analysis, we identified a similar rate of polyp formation at baseline in our cases and controls (46.7% vs 47.9%, respectively; $P = .42$). These data suggest a minimal degree of residual confounding using our methods. Despite including an established coding method for colonoscopy with polyps and polypectomy, we could not assess polyp size, number, or pathology in our database. Although alcohol and tobacco were included in the database, their rates may be underestimated due to the limitation of administrative databases. Still, bariatric patients are usually encouraged to quit alcohol and tobacco prior to surgery, which should hypothetically lead to a lower risk of CRC. Furthermore, it was not possible to access actual weight regain or other risk factors, such as race or ethnicity, duration of obesity, and physical activity. Similarly, the menopausal status of our female patients was not available for inclusion in the analysis.

These data are the first, to our knowledge, to investigate the recurrence of colorectal neoplasia after bariatric surgery to better inform clinicians and scientists investigating the impact of energy balance on the risk polyp recurrence after resection. These data can also help design future interventional studies using bariatric surgery as a tool to study CRC prevention with weight loss. Finally, by reducing the risk of recurrent polyps, bariatric surgery can serve as a way to lower the lifetime risk of metachronous neoplasia in adults with obesity and prior polyps and, ultimately, their need for more frequent colonoscopies (5).

Data availability

Our detailed methods and codes are described in our paper. Patient level, de-identified, data was obtained from IBM MarketScan as part of a data agreement with the Ohio State University. Our investigators will make the analytical files available to any researchers for non-commercial purposes after the researcher obtains approval for third party access from IBM MarketScan. Any researcher requesting access to the raw patient-level deidentified data that were used to generate the analytical files can access the data directly through IBM MarketScan under a license agreement with IBM MarketScan.

Author contributions

HH was involved in conceptualization, funding acquisition, methodology, writing the original draft, review and editing of the final draft; MA in methodology, review and editing of the final draft; SH in methodology, supervision, review and editing of the final draft; VL in methodology, review and editing of the final draft, EM in formal analysis, methodology, visualization, writing the original draft, and review and editing of the final draft, CC in data curation, methodology, writing the original draft, review and editing of the final draft, and HT in methodology, supervision, review and editing of the final draft.

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Conflicts of interest

The authors have no relevant conflicts of interest, including relevant financial interests, activities, relationships, or affiliations.

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References

1. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med*. 2012;366(8):687-696. doi:10.1056/NEJMoa1100370.
2. Bertario L, Russo A, Sala P, et al. Predictors of metachronous colorectal neoplasms in sporadic adenoma patients. *Int J Cancer*. 2003;105(1):82-87. doi:10.1002/ijc.11036.
3. Kim JB, Han DS, Lee HL, et al. [The recurrence rate of colon polyp after polypectomy and the interval of surveillance colonoscopy: Predictors of early development of advanced polyp]. *Korean J Gastroenterol*. 2004;44(2):77-83.
4. Avidan B, Sonnenberg A, Schnell TG, Leya J, Metz A, Sontag SJ. New occurrence and recurrence of neoplasms within 5 years of a screening colonoscopy. *Am J Gastroenterol*. 2002;97(6):1524-1529. doi:10.1111/j.1572-0241.2002.05801.x.
5. Gupta S, Lieberman D, Anderson JC, et al. Recommendations for follow-up after colonoscopy and polypectomy: a consensus update by the US multi-society task force on colorectal cancer. *Gastroenterology*. 2020;158(4):1131-1153.e5. doi:10.1053/j.gastro.2019.10.026.
6. Cooper GS, Xu F, Barnholtz Sloan JS, Schluchter MD, Koroukian SM. Prevalence and predictors of interval colorectal cancers in Medicare beneficiaries. *Cancer*. 2012;118(12):3044-3052. doi:10.1002/cncr.26602.
7. Huang Y, Gong W, Su B, Zhi F, Liu S, Jiang B. Risk and cause of interval colorectal cancer after colonoscopic polypectomy. *Digestion*. 2012;86(2):148-154. doi:10.1159/000338680.
8. Brenner H, Altenhofen L, Katalinic A, Lansdorp-Vogelaar I, Hoffmeister M. Sojourn time of preclinical colorectal cancer by sex and age: estimates from the German national screening colonoscopy database. *Am J Epidemiol*. 2011;174(10):1140-1146. doi:10.1093/aje/kwr188.
9. Laiyemo AO, Doubeni C, Badurdeen DS, et al. Obesity, weight change, and risk of adenoma recurrence: a prospective trial. *Endoscopy*. 2012;44(9):813-818. doi:10.1055/s-0032-1309837.
10. Ben Q, An W, Jiang Y, et al. Body mass index increases risk for colorectal adenomas based on meta-analysis. *Gastroenterology*. 2012;142(4):762-772. doi:10.1053/j.gastro.2011.12.050.
11. Hussan H, Gray DM 2nd, Hinton A, Krishna SG, Conwell DL, Stanich PP. Morbid obesity is associated with increased mortality, surgical complications, and incremental health care utilization in the peri-operative period of colorectal cancer surgery. *World J Surg*. 2016;40(4):987-994. doi:10.1007/s00268-015-3358-0.

12. Bardou M, Barkun AN, Martel M. Obesity and colorectal cancer. *Gut*. 2013;62(6):933-947. doi:10.1136/gutjnl-2013-304701.
13. Maciejewski ML, Arterburn DE, Van Scoyoc L, et al. Bariatric surgery and long-term durability of weight loss. *JAMA Surg*. 2016;151(11):1046-1055. doi:10.1001/jamasurg.2016.2317.
14. Hussan H, Drosdak A, Le Roux M, et al. The long-term impact of roux-en-Y gastric bypass on colorectal polyp formation and relation to weight loss outcomes. *Obes Surg*. 2020;30(2):407-415. doi:10.1007/s11695-019-04176-w.
15. Cisyk AL, Singh H, McManus KJ. Establishing a biological profile for interval colorectal cancers. *Dig Dis Sci*. 2014;59(10):2390-2402. doi:10.1007/s10620-014-3210-7.
16. Shin SP. Sessile serrated adenoma; the hard-to-catch culprit of interval cancer. *Clin Endosc*. 2017;50(3):215-216. doi:10.5946/ce.2017.052.
17. Pohl H, Srivastava A, Bensen SP, et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. *Gastroenterology*. 2013;144(1):74-80.e1. doi:10.1053/j.gastro.2012.09.043.
18. Le Clercq CM, Bouwens MW, Rondagh EJ, et al. Postcolonoscopy colorectal cancers are preventable: a population-based study. *Gut*. 2014;63(6):957-963. doi:10.1136/gutjnl-2013-304880.
19. IBM. *IBM MarketScan Research Databases*. https://www.ibm.com/watson-health/about/truven-health-analytics. Accessed April 21, 2021.
20. Hussan H, Akinyeye S, Mihaylova M, et al. Colorectal cancer risk is impacted by sex and type of surgery after bariatric surgery. *Obes Surg*. 2022;32(9):2880-2890. doi:10.1007/s11695-022-06155-0.
21. Arterburn D, Wellman R, Emiliano A, et al.; for the PCORnet Bariatric Study Collaborative. Comparative effectiveness and safety of bariatric procedures for weight loss: a PCORnet cohort study. *Ann Intern Med*. 2018;169(11):741-750. doi:10.7326/M17-2786.
22. Schauer DP, Feigelson HS, Koebnick C, et al. Bariatric surgery and the risk of cancer in a large multisite cohort. *Ann Surg*. 2019;269(1):95-101. doi:10.1097/sla.0000000000002525.
23. Ammann EM, Kalsekar I, Yoo A, et al. Assessment of obesity prevalence and validity of obesity diagnoses coded in claims data for selected surgical populations: a retrospective, observational study. *Medicine (Baltimore)*. 2019;98(29):e16438. doi:10.1097/md.0000000000016438.
24. Mocarski M, Tian Y, Smolarz BG, McAna J, Crawford A. Use of International Classification of Diseases, Ninth Revision codes for obesity: trends in the United States from an electronic health record-derived database. *Popul Health Manag*. 2018;21(3):222-230. doi:10.1089/pop.2017.0092.
25. Ammann EM, Kalsekar I, Yoo A, Johnston SS. Validation of body mass index (BMI)-related ICD-9-CM and ICD-10-CM administrative diagnosis codes recorded in US claims data. *Pharmacoepidemiol Drug Saf*. 2018;27(10):1092-1100. doi:10.1002/pds.4617.
26. Basques BA, Miller CP, Golinvaux NS, Bohl DD, Grauer JN. Morbidity and readmission after open reduction and internal fixation of ankle fractures are associated with preoperative patient characteristics. *Clin Orthop Relat Res*. 2015;473(3):1133-1139. doi:10.1007/s11999-014-4005-z.
27. McLynn RP, Geddes BJ, Cui JJ, et al. Inaccuracies in ICD coding for obesity would be expected to bias administrative database spine studies toward overestimating the impact of obesity on perioperative adverse outcomes. *Spine (Phila Pa 1976)*. 2018;43(7):526-532. doi:10.1097/BRS.0000000000002356.
28. Bailly L, Fabre R, Pradier C, Iannelli A. Colorectal cancer risk following bariatric surgery in a nationwide study of French individuals with obesity. *JAMA Surg*. 2020;155(5):395-402. doi:10.1001/jamasurg.2020.0089.
29. Gandhi SK, Reynolds MW, Boyer JG, Goldstein JL. Recurrence and malignancy rates in a benign colorectal neoplasm patient cohort: results of a 5-year analysis in a managed care environment. *Am J Gastroenterol*. 2001;96(9):2761-2767. doi:10.1111/j.1572-0241.2001.04137.x.
30. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383. doi:10.1016/0021-9681(87)90171-8
31. Ahmed S, Naumann DN, Karandikar S. Differences in screening vs non-screening colonoscopy: scope for improvement? *Colorectal Dis*. 2016;18(9):903-909. doi:10.1111/codi.13291.
32. Ma Y, Yang W, Song M, et al. Type 2 diabetes and risk of colorectal cancer in two large U.S. prospective cohorts. *Br J Cancer*. 2018;119(11):1436-1442. doi:10.1038/s41416-018-0314-4.
33. Yao X, Tian Z. Dyslipidemia and colorectal cancer risk: a meta-analysis of prospective studies. *Cancer Causes Control*. 2015;26(2):257-268. doi:10.1007/s10552-014-0507-y.
34. Liu G, Sterling NW, Kong L, et al. Statins may facilitate Parkinson's disease: insight gained from a large, national claims database. *Mov Disord*. 2017;32(6):913-917. doi:10.1002/mds.27006.
35. Cho I-J, Shin J-H, Jung M-H, et al. Antihypertensive drugs and the risk of cancer: a nationwide cohort study. *JCM*. 2021;10(4):771. doi:10.3390/jcm10040771.
36. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28(25):3083-3107. doi:10.1002/sim.3697.
37. Kedrin D, Gandhi SC, Wolf M, et al. Bariatric surgery prior to index screening colonoscopy is associated with a decreased rate of colorectal adenomas in obese individuals. *Clin Transl Gastroenterol*. 2017;8(2):e73. doi:10.1038/ctg.2017.1.
38. Hao Y, Wang Y, Qi M, He X, Zhu Y, Hong J. Risk factors for recurrent colorectal polyps. *Gut Liver*. 2020;14(4):399-411. doi:10.5009/gnl19097.
39. Chi Z, Lin Y, Huang J, et al. Risk factors for recurrence of colorectal conventional adenoma and serrated polyp. *Gastroenterol Rep (Oxf)*. 2022;10:goab038. doi:10.1093/gastro/goab038.
40. Svane MS, Madsbad S. Bariatric surgery - effects on obesity and related co-morbidities. *Curr Diabetes Rev*. 2014;10(3):208-214. doi:10.2174/1573399810666140616144141.
41. Kant P, Sainsbury A, Reed KR, et al. Rectal epithelial cell mitosis and expression of macrophage migration inhibitory factor are increased 3 years after Roux-en-Y gastric bypass (RYGB) for morbid obesity: implications for long-term neoplastic risk following RYGB. *Gut*. 2011;60(7):893-901. doi:10.1136/gut.2010.230755.
42. Sainsbury A, Goodlad RA, Perry SL, Pollard SG, Robins GG, Hull MA. Increased colorectal epithelial cell proliferation and crypt fission associated with obesity and roux-en-Y gastric bypass. *Cancer Epidemiol Biomarkers Prev*. 2008;17(6):1401-1410. doi:10.1158/1055-9965.epi-07-2874.
43. Mills SJ, Mathers JC, Chapman PD, Burn J, Gunn A. Colonic crypt cell proliferation state assessed by whole crypt microdissection in sporadic neoplasia and familial adenomatous polyposis. *Gut*. 2001;48(1):41-46.
44. Gordon-Weeks AN, Lim SY, Yuzhalin AE, Jones K, Muschel R. Macrophage migration inhibitory factor: a key cytokine and therapeutic target in colon cancer. *Cytokine Growth Factor Rev*. 2015;26(4):451-461. doi:10.1016/j.cytogfr.2015.03.002.

45. Garibay D, Zaborska KE, Shanahan M, et al. TGR5 protects against colitis in mice, but vertical sleeve gastrectomy increases colitis severity. *Obes Surg*. 2019;29(5):1593-1601. doi:10.1007/s11695-019-03707-9.
46. Bailey CE, Hu CY, You YN, et al. Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975-2010. *JAMA Surg*. 2015;150(1):17-22. doi:10.1001/jamasurg.2014.1756.
47. Ward ZJ, Bleich SN, Cradock AL, et al. Projected U.S. state-level prevalence of adult obesity and severe obesity. *N Engl J Med*. 2019;381(25):2440-2450. doi:10.1056/NEJMsa1909301.
48. Ostlund MP, Lu Y, Lagergren J. Risk of obesity-related cancer after obesity surgery in a population-based cohort study. *Ann Surg*. 2010;252(6):972-976. doi:10.1097/SLA.0b013e3181e33778.
49. Tao W, Artama M, von Euler-Chelpin M, et al. Colon and rectal cancer risk after bariatric surgery in a multicountry Nordic cohort study. *Int J Cancer*. 2020;147(3):728-735. doi:10.1002/ijc.32770.
50. Mackenzie H, Markar SR, Askari A, et al. Obesity surgery and risk of cancer. *Br J Surg*. 2018;105(12):1650-1657. doi:10.1002/bjs.10914.
51. Derogar M, Hull MA, Kant P, Östlund M, Lu Y, Lagergren J. Increased risk of colorectal cancer after obesity surgery. *Ann Surg*. 2013;258(6):983-988. doi:10.1097/SLA.0b013e318288463a.
52. Rustgi VK, Li Y, Gupta K, et al. Bariatric surgery reduces cancer risk in adults with nonalcoholic fatty liver disease and severe obesity. *Gastroenterology*. 2021;161(1):171-184.e10. doi:10.1053/j.gastro.2021.03.021.