

# UC San Diego

## UC San Diego Previously Published Works

### Title

Sex-Based Differences in IBD Surgical Outcomes.

### Permalink

<https://escholarship.org/uc/item/6vz9k7ch>

### Journal

Diseases of the Colon & Rectum, 67(2)

### Authors

Sundel, Margaret

Newland, John

Blackburn, Kyle

et al.

### Publication Date

2024-02-01

### DOI

10.1097/DCR.0000000000002984

Peer reviewed



Published in final edited form as:

*Dis Colon Rectum*. 2024 February 01; 67(2): 246–253. doi:10.1097/DCR.0000000000002984.

## Sex-Based Differences in Inflammatory Bowel Disease Surgical Outcomes

Margaret H. Sundel, M.D., M.S.<sup>1</sup>, John J. Newland, M.D., M.S.<sup>1</sup>, Kyle W. Blackburn, B.S.<sup>1</sup>, Roumen M. Vesselinov, Ph.D.<sup>2</sup>, Samuel Eisenstein, M.D.<sup>3</sup>, Andrea C. Bafford, M.D.<sup>1</sup> NSQIP IBD Collaborative

<sup>1</sup>Department of Surgery, University of Maryland, Baltimore, Maryland

<sup>2</sup>Department of Epidemiology and Public Health, University of Maryland, Baltimore, Maryland

<sup>3</sup>Department of Surgery, University of California San Diego, San Diego, California

### Abstract

**BACKGROUND:** Although there are discrepancies in the development and progression of inflammatory bowel disease based on biologic sex, little is known about differences in postoperative outcomes between men and women undergoing surgery for this condition.

**OBJECTIVE:** Our objective was to compare rates of anastomotic leaks, wound complications, and serious adverse events between men and women undergoing surgery for inflammatory bowel disease.

**DESIGN:** This was a retrospective cohort study.

**SETTINGS:** Data were obtained from the American College of Surgeons National Surgical Quality Improvement Program Inflammatory Bowel Disease Collaborative database, which includes 15 high-volume inflammatory bowel disease surgery centers.

**PATIENTS:** All adult patients undergoing surgery for inflammatory bowel disease were included. Subjects with missing data for exposure or outcome variables were excluded.

**MAIN OUTCOME MEASURES:** Rates of anastomotic leaks, wound complications, and serious adverse events were compared between women and men.

**RESULTS:** A total of 3143 patients were included. There was a significant association between sex and body mass index, inflammatory bowel disease type, and preoperative medication use. Women had decreased odds of serious adverse events compared to men (OR=0.73, 95% CI: 0.55–0.96), but there was no significant association between sex and anastomotic leaks or wound complications. Inflammatory bowel disease type was found to be an effect measure modifier of the relationship between sex and serious adverse events. Among ulcerative colitis patients, women

---

**Correspondence:** Margaret H. Sundel, M.D., M.S., Department of Surgery, University of Maryland, 22 S. Greene Street, S8B13, Baltimore, MD 21201., Maggie.sundel@som.umaryland.edu.

**Financial Disclosures:** None reported.

A portion of the results were previously presented at the American Society of Colon and Rectal Surgeons Annual Scientific Meeting, Tampa, FL, April 30 to May 4, 2022.

had a 54% decrease in the odds of serious adverse events compared to men, while there was no significant difference between women and men with Crohn's disease.

**LIMITATIONS:** This study was limited by capturing only 30 days of postoperative outcomes.

**CONCLUSIONS:** Women undergoing surgery for ulcerative colitis had decreased odds of serious adverse events compared to men. Understanding sex-based differences in outcomes allows clinicians to make patient-centered decisions regarding surgical planning and perioperative management for inflammatory bowel disease patients. See Video Abstract at <http://links.lww.com/DCR/Bxxx>.

## Abstract

Aunque existen discrepancias en el desarrollo y la progresión de la enfermedad inflamatoria intestinal según el sexo biológico, se sabe poco sobre las diferencias en los resultados posoperatorios entre hombres y mujeres sometidos a cirugía por esta afección.

Nuestro objetivo fue comparar las tasas de fugas anastomóticas, complicaciones de las heridas y eventos adversos graves entre hombres y mujeres sometidos a cirugía por enfermedad inflamatoria intestinal.

Este fue un estudio de cohorte retrospectivo.

Los datos se obtuvieron de la base de datos colaborativa del Programa Nacional de Mejora de la Calidad Quirúrgica del Colegio Americano de Cirujanos para la Enfermedad Inflamatoria Intestinal, que incluye 15 centros de cirugía de enfermedad inflamatoria intestinal de alto volumen.

Se incluyeron todos los pacientes adultos sometidos a cirugía por enfermedad inflamatoria intestinal. Se excluyeron los sujetos a los que les faltaban datos sobre exposición o variables de resultado.

Se compararon las tasas de fugas anastomóticas, complicaciones de las heridas y eventos adversos graves entre mujeres y hombres.

Se incluyeron un total de 3.143 pacientes. Hubo una asociación significativa entre el sexo y el índice de masa corporal, el tipo de enfermedad inflamatoria intestinal y el uso de medicación preoperatoria. Las mujeres tuvieron menores probabilidades de sufrir eventos adversos graves en comparación con los hombres (OR = 0,73; IC del 95 %: 0,55 a 0,96), pero no hubo una asociación significativa entre el sexo y las fugas anastomóticas o las complicaciones de las heridas. Se encontró que el tipo de enfermedad inflamatoria intestinal era un modificador de la medida del efecto de la relación entre el sexo y los eventos adversos graves. Entre los pacientes con colitis ulcerosa, las mujeres tuvieron una disminución del 54 % en las probabilidades de sufrir eventos adversos graves en comparación con los hombres, mientras que no hubo diferencias significativas entre mujeres y hombres con enfermedad de Crohn.

Este estudio estuvo limitado al capturar solo 30 días de resultados posoperatorios.

Las mujeres sometidas a cirugía por colitis ulcerosa tuvieron menores probabilidades de sufrir eventos adversos graves en comparación con los hombres. Comprender las diferencias en los resultados basadas en el sexo permite a los médicos tomar decisiones centradas en el paciente con respecto a la planificación quirúrgica y el manejo perioperatorio de los pacientes con enfermedad

inflammatoria intestinal. Consulte Video Resumen en <http://links.lww.com/DCR/Bxxx>. (*Pre-proofed version*)

## Keywords

Inflammatory bowel disease; Postoperative outcomes; Sex differences

## INTRODUCTION

Inflammatory bowel disease (IBD) is a group of conditions, including ulcerative colitis (UC), Crohn's disease (CD), and indeterminate colitis, with complications that are potentially life-threatening and often require surgical management. Unlike in other autoimmune disorders, the prevalence of IBD does not have a clear female preponderance.<sup>1</sup> Studies have found Crohn's disease to be slightly more common in women than men in Western countries,<sup>2</sup> though this trend is reversed in Asian countries.<sup>3</sup> The incidence of UC has not been found to consistently differ based on sex except over the age of 45, when UC seems to be more common in men than women.<sup>2</sup> There is also evidence that men with IBD have worse outcomes compared to women, including higher rates of disease-related complications<sup>4</sup> such as osteopenia,<sup>5,6</sup> some types of pancreatitis,<sup>7</sup> and colon cancer<sup>8</sup>; hospital readmission after initial diagnosis<sup>9</sup>; escalation of medical therapy<sup>10</sup>; and need for surgical intervention.<sup>11–14</sup>

Surgical complications are relatively more common in patients with IBD than in patients undergoing bowel surgery for other reasons and most commonly include wound infection and anastomotic complications<sup>15</sup>; rates of wound infections have been reported to vary from 1–19%<sup>16–18</sup> and rates of anastomotic leak range from 0.5–13%.<sup>16–19</sup> While it is fairly well-established that men are more likely to require surgery for IBD, much less is known about the outcomes of surgery for men as compared to women. Rottoli et al. examined all cases of ileal pouch anal anastomosis (IPAA) over the course of 25 years at a single institution and found higher rates of anastomotic leak within the first 30 days and higher rates of diverting ileostomy creation at the time of initial operation among men.<sup>20</sup> Further work is needed, however, to clarify the disparities in outcomes between men and women with IBD undergoing a broader range of surgical procedures.

The aim of our study was to compare postoperative outcomes, including anastomotic leak, wound complications, and serious adverse events, between men and women after surgery for IBD. Based on evidence supporting less severe outcomes overall in women with IBD, as well as the prior findings regarding leak rate after IPAA, we hypothesized that women would have decreased postoperative complications when compared to men. Understanding outcomes based on sex can help clinicians to provide better patient centered care pre- and postoperatively and may encourage further study of the mechanisms underlying these differences to allow the development of interventions targeted at improving disparities.

## METHODS

### Study Population

Our study is a retrospective cohort study performed using a subset of the American College of Surgeon's National Surgical Quality Improvement Program (NSQIP) database called the NSQIP-IBD collaborative. The NSQIP-IBD dataset includes all patients over the age of 18 identified with a diagnosis of IBD based on ICD-10 code (UC includes codes beginning with K51, CD includes codes beginning with K50, indeterminate colitis includes code K52.3) at 15 high-volume IBD surgery centers across the United States. Additional variables on these patients were collected by participating centers, including use of biologic agents and immune modulators, IPAA, ileostomy formation, and colonic dysplasia. The current study includes data from March 2017-March 2021.

All patients with ICD-10 codes matching the diagnoses of UC, CD, or indeterminate colitis were included in this study. Patients were excluded if they were missing data for sex or any of the outcome variables. Using the algorithm described previously to classify subtotal colectomy and IPAA in the NSQIP-IBD database,<sup>21</sup> patients who had undergone subtotal colectomy or any patients with a diverting ileostomy were excluded from the analysis of anastomotic leak occurrence.

### Sex

The exposure variable in this study was sex, defined as a binary variable of male or female. This variable is captured in NSQIP via medical chart abstraction and refers specifically to the biological sex designated in a patient's medical record. NSQIP also includes a third level of this variable, non-binary; however, no patients in this dataset identified as non-binary and thus this category was not included in the current analysis.

### Postoperative Outcomes

The primary outcome variables in this study were anastomotic leak, wound complications, and serious adverse events, all of which are binary variables. Postoperative outcomes within NSQIP are based on clinically abstracted variables for events occurring within the first 30 days after surgery. Anastomotic leak is a variable that exists within the NSQIP-IBD dataset. Wound complications and serious adverse events are both composite variables created for the purpose of this study. Wound complication was defined as the presence of any one of the following postoperative outcomes: wound disruption or superficial, deep, or organ space surgical site infections. Serious adverse event (SAE) was defined as the presence of any one of the following postoperative outcomes: pneumonia, unplanned re-intubation, pulmonary embolism, ventilator requirement greater than 48 hours, progressive renal insufficiency, acute renal failure, cerebrovascular accident, myocardial infarction, cardiac arrest, deep venous thrombosis requiring therapy, sepsis, septic shock, or unplanned return to the operating room.

### Covariates

Our covariates of interest included age (continuous); race (White, Black/African American, or Other, composed of Asian/American Indian/Alaska Native/Native Hawaiian/Other Pacific

Islander); ethnicity (Hispanic or Not Hispanic); institution (categorical); body mass index (BMI); smoking status (binary); type of IBD (Crohn's disease, ulcerative colitis, or indeterminate colitis); surgical approach (open, converted to open, or minimally invasive, composed of endoscopic, laparoscopic, and robotic); classification of surgery as elective versus emergency (binary); American Society of Anesthesiologists (ASA) classification (I-V); steroid use (binary); immunologic/biologic use (binary); and ileostomy formation (no ileostomy present or created, new ileostomy created, or existing ileostomy revised or maintained). For our analysis, BMI was converted into a categorical variable using standard categories from the National Institute of Health<sup>22</sup>: underweight (BMI<18.5), normal and overweight (BMI 18.5–30) and obese (BMI>30). ASA classification was converted into a binary variable, with class I and II categorized as healthy/mild disease and class III-V categorized as severe disease.

### Statistical Analysis

Descriptive statistics were used to identify sample characteristics, including means for continuous variables and proportions for binary and categorical variables.

We computed odds ratios (OR) and 95% confidence intervals (95% CI) for the association between sex and each of our outcome variables using separate logistic regression models. The referent group consisted of men for all models.

We performed a multivariable logistic regression adjusted for age, race, ethnicity, BMI, smoking status, IBD type, elective surgery, ASA classification, preoperative medication use, and ileostomy formation. We chose these variables for adjustment based on associations of these factors with sex and postoperative outcomes in the literature.

We were interested in whether type of IBD may have been an effect measure modifier of our exposure and outcome variables. We determined p-values for interaction based on the p-value for an interaction term between sex and IBD type in our multivariable logistic regression model for each outcome. To assess for potential effect modification, we stratified our sample based on type of IBD. We then performed logistic regression of the relationship between sex and postoperative outcomes within each stratum to compare the stratum-specific odds ratios. Due to the small sample size in the indeterminate colitis group, we did not include this IBD type in our multivariable analyses.

Data analysis was generated using SAS Studio software (version 3.81, SAS Institute Inc. Cary, NC, USA).

## RESULTS

Out of 4264 patients included in the NSQIP-IBD dataset from 2017–2021, we identified 3143 patients with complete data for all exposure and outcome variables (Fig. 1). Among the IBD patients in our study, 49.3% were female. There was a significant association between sex and BMI, with more men in the intermediate BMI range from 18.5–30 (76.2% vs. 68.2%), and more women in both the underweight and obese groups. There was also a significant association with sex and type of IBD; 64.2% of women had Crohn's

disease, while more patients with ulcerative colitis were men (56.3% men versus 43.7% women). Additionally, more men were using steroid medications prior to surgery, underwent conversion to an open surgery, and had a new ileostomy created (62.9% vs. 58.1%, 9.7% vs. 6.5%, and 48.1% vs. 43.1%, respectively) (Table 1).

### Multivariable-Adjusted Model

Our multivariable adjusted logistic regression of SAE against sex demonstrated a 27% decrease in the odds of SAE for women compared to men (OR=0.73, 95% CI: 0.55–0.96) (Table 2). There was no significant association between sex and anastomotic leaks or wound complications in our adjusted logistic regression models (OR=1.29, 95% CI: 0.48–3.44; and OR 1.04, 95% CI: 0.79–1.37, respectively) (Table 2).

We assessed for potential effect modification of the association between sex and postoperative outcomes by IBD type and observed evidence of effect modification for the sex-SAE association ( $p = 0.03$ ), but not for anastomotic leaks or wound complications ( $p$  value of interaction terms  $>0.05$ ). Our multivariable adjusted logistic regression of SAE against sex stratified by type of IBD demonstrated a 54% decrease in the odds of SAE for women compared to men among patients with ulcerative colitis (OR=0.46, 95% CI: 0.28–0.74) (Table 3). For patients with Crohn's disease, the association between sex and SAE did not reach statistical significance (OR=1.03, 95% CI: 0.70–1.51).

## DISCUSSION

We compared postoperative outcomes, including anastomotic leaks, wound complications, and serious adverse events, between men and women undergoing surgery for IBD. Women had decreased odds of SAE after surgery compared to men, although there were no significant associations between biologic sex and the occurrence of anastomotic leaks or wound complications. We investigated whether IBD type was an effect measure modifier of the relationship between sex and postoperative outcomes, and we found evidence of effect measure modification by IBD type for the association between sex and postoperative serious adverse events. Specifically, for patients with ulcerative colitis, we found a significantly decreased odds of SAE among women compared to men. In contrast, for Crohn's disease patients, the association was attenuated and did not approach statistical significance.

In a previous single center study, men had a higher rate of anastomotic leaks than women after undergoing IPAA.<sup>20</sup> Our study findings differed from this previous study, as we did not observe a significant sex difference in anastomotic leak; however, our cohort includes the results from 15 high-volume centers, rather than a single institution. It is possible that factors related to individual surgeons or institutional policies could have had a larger impact on the results seen in the single center study, leading to the observed difference in that study.

Although prior studies have not directly examined the relationship between sex and wound complications or serious adverse events in IBD patients, these associations have been studied in other surgical populations. There have been mixed findings depending on disease state; men had increased rates of surgical site infections after shoulder arthroplasty, although no difference in complication rates.<sup>23</sup> Amongst cardiac surgery patients, female sex

predicted in-hospital mortality after coronary artery bypass grafting.<sup>24</sup> A study of patients undergoing intraabdominal surgeries found a lower risk of 30-day mortality, readmission, and major complications among women on unadjusted analysis, although this difference was not significant after adjusting for other patient characteristics.<sup>25</sup> Taken together, these results suggest that there is a nuanced relationship between sex and postoperative outcomes, which underscores the importance of examining these relationships in specific patient populations.

Several mechanisms could explain our finding of increased odds of serious adverse events after surgery in men compared to women. Men with IBD have worse outcomes related to many aspects of their condition, including more frequent medical readmissions<sup>9</sup> and need for escalation of medical therapy.<sup>10</sup> It is possible that the higher rate of serious complications after surgery in men could be related to their poorer preoperative health status, despite controlling for relevant confounders in our analysis. Additionally, men tend to have a deeper and narrower pelvis than women, making operations in this region more technically challenging.<sup>20</sup> This anatomical difference between men and women may have influenced the type of operation, duration of surgery, or choice to use diverting ileostomy, factors which can all impact postoperative morbidity.<sup>26–28</sup> Given the known higher rate of surgical intervention in men with IBD,<sup>11–14</sup> it is also possible that male patients were more likely to have previously undergone surgery, again putting them at a higher risk for a more technically difficult and complication-prone surgery.

There has been no literature to date considering IBD type as an effect measure modifier of the association between sex and postoperative outcomes. Given the difference in prevalence and disease course of Crohn's disease and ulcerative colitis between women and men, there is a clear role for stratifying an analysis of surgical outcomes by IBD type. We found no significant change in the odds of serious adverse events for men versus women with Crohn's disease. The reason for this lack of significant findings may be related to more severe disease in women with Crohn's disease, partially obscuring the advantage in postoperative outcomes that female sex might otherwise confer. For example, women with Crohn's disease have been found to have more extraintestinal manifestations and earlier recurrence of disease after bowel resection than men.<sup>29</sup> Surgical treatment differs significantly between Crohn's disease and ulcerative colitis; it is possible that differences in outcomes between the two strata may owe more to the type of surgery performed than the underlying condition.

Our results may also be related to gender-based disparities and not solely to biological sex-based differences. Findings regarding social factors related to gender among IBD patients have been inconsistent; for example, both female and male sex have been found in different studies to be associated with decreased adherence to medical treatment for inflammatory bowel disease.<sup>30</sup> However, among general adult patients in the United States, men have been shown to utilize healthcare services less frequently<sup>31</sup> and to have shorter hospital stays than women.<sup>32</sup> Thus, lack of engagement with the medical system may play a role in the worse outcomes seen among men in this study.

One of the strengths of this study is in its relative novelty. There has been a significant amount of research looking at the relationship between sex and other medical outcomes in IBD patients, but few that examine surgery specifically. This study also had a large sample



size of over 3000 patients and included data from multiple centers across the country; this helped enhance the generalizability of our findings. Additionally, this cohort was specifically designed to study the IBD population. Unlike the broader NSQIP database, the NSQIP IBD collaborative includes variables that are relevant specifically to IBD patients, including details of the use of immunosuppressant and biologic medications, which were important variables to adjust for to account for the preoperative status of the patient.

There were several limitations to our study. Because of the nature of using retrospective cohort data obtained from NSQIP, our data quality may be impacted. Our outcome variables were all dependent on variables that are clinically abstracted by study personnel at each institution, and thus are susceptible to errors in coding or data abstraction. We also did not have data available on some confounders that may have been of interest in this study, such as duration of surgery or patients' past surgical history. NSQIP only captures up to 30 days of postoperative outcomes; because IBD is a chronic disease process, complications continue to arise much further out from surgery. Limiting our assessment to only 30 days of complications may have biased our results towards the null. It is possible that our study was underpowered and thus we were unable to detect a true difference between groups for the outcomes of anastomotic leak and wound complication, again limiting our findings to a null result. Finally, our analysis included many different surgery types that may be performed for several surgical indications related to IBD. Because different surgeries can have very different risks, this lack of granularity may obscure important associations between sex and outcomes that may be observed for only certain surgical procedures.

We have shown that women with ulcerative colitis undergoing surgery for IBD had decreased odds of serious adverse events after surgery. These results are impactful for physicians considering how to provide patient-centered care for individuals with IBD, and in particular patients with ulcerative colitis. Both modifiable and immutable patient characteristics must be considered when making the decision to take a patient to the operating room. Although biologic sex is not a modifiable risk factor, it is important for a surgeon to recognize that the risk of postoperative morbidity for a man with ulcerative colitis undergoing surgery may be greater than for a woman. This decision making comes in to play particularly for elective surgeries related to quality of life, when the risk versus benefit of surgery must be carefully considered. It may also be worth considering enhanced preoperative screening and prehabilitation; optimization of other aspects of disease and overall health, such as tapering of immunosuppressive medications, improvement in nutritional status, and control of infection and inflammation; risk factor modification, including smoking cessation; and close postoperative monitoring for men in particular undergoing surgery for IBD.

## CONCLUSIONS

Further studies can build upon these results. First, it is important to examine the longer-term and functional outcomes of surgery in IBD patients. While surviving surgery without a significant postoperative complication is important, it is equally crucial, particularly when discussing patients with IBD, to understand how surgery has impacted outcomes like quality of life and frequency of bowel movements. It is also essential to further explore the

underlying mechanism of the difference in postoperative morbidity between women and men. Whether it is due to social disparities, immunologic factors, or anatomic variations, understanding why a discrepancy in outcomes occurs will aid in the development of interventions to resolve this difference.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## ACKNOWLEDGMENTS

### NSQIP IBD Collaborative

Samuel Eisenstein, Sonia Ramamoorthy, Nicholas Hilbert, Austin Du (Department of Colon & Rectal Surgery, Cleveland Clinic, 9500 Euclid Avenue A30, Cleveland OH 44195); Tracy Hull, Stefan Holubar, Xue Jia, Nancy Anzlovar, Sue Bohne (Department of Surgery, Baylor University Medical Center, 3409 Worth Street, Worth Tower, Suite 600, Dallas, TX 75246); Alessandro Fichera, Debbie Aguilar, Martha Mueller (Colorectal Surgery Program, Massachusetts General Hospital, 15 Parkman Street, Boston, MA 02114–3117); Rocco Riccardi, Liliana Bordeianou, Hiroko Kunitake, Donna Antonelli, Kathy Swierzewski, Lynn Devaney (Stanford Health Care, 500 Pasteur Dr, Palo Alto, CA 94304); Cindy Kin, David Spain, Roxanne Hyke, Elmer De Leon, Aimee Torbela (Division of General Surgery, Albany Medical Center, 50 New Scotland Avenue MC-193, 5th Floor, Albany, NY 12208); Edward Lee, Brian Valerian, Megan Keenan, Andrea Goyette (Division of Colon and Rectal Surgery, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Shapiro Building, 3rd Floor, Boston, MA 02215–5400); Evangelos Messaris, Richard Whyte, Mary Ward, Mary Beth Cotter (Division of Colon and Rectal Surgery, Lahey Hospital and Medical Center, 41 Mall Road Burlington, MA 01805); Julia Saraidaridis, W. David Lewis, Mary Sansone, Lynne Crawford (Department of Surgery, Penn State Health, 200 Campus Dr, Suite 3100 Hershey, PA 17033); Michael Deutsch, Jeffrey Scow, Pam Huggins (Department of Surgery, Emory University School of Medicine, Room B206, 1364 Clifton Road, NE, Atlanta, GA 30322); Virginia Shaffer, Joe Sharma, Shamsah Sitafalwalla (Department of Surgery, Washington University School of Medicine in St. Louis, 660 S Euclid Ave, St. Louis, MO 63110); Radhika Smith, Matthew Mutch, Bruce Hall, Mitzi Hirbe, JoAnn Batten (Department of Surgery, Box 1259, Mount Sinai Medical Center, One Gustave L. Levy Place, NY, NY 10029); Randolph Steinhagen, Sergey Khaitov, Patricia Sylla, Celia Divino, Reba Miller (Department of Surgery, University of Chicago, 5841 S. Maryland Ave, MC 5095, Chicago, IL 60637); Kinga Skowron Olortegui, Neil Hyman, Vivek Prachand, Sue Sullivan, Lorice Pullins, Carmen Barc (Department of Surgery, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, IA 52242); Jennifer Hrabe, Muneera Kapadia\*, Mary Belding-Schmitt (Iowa City, IA 52242); James Yoo, Joel Goldberg, Felix Akinbami, Jill Steinberg (Department of Surgery, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115)

\*Now Currently at University of North Carolina School of Medicine, Chapel Hill, NC 27599–7081

### Funding/Support:

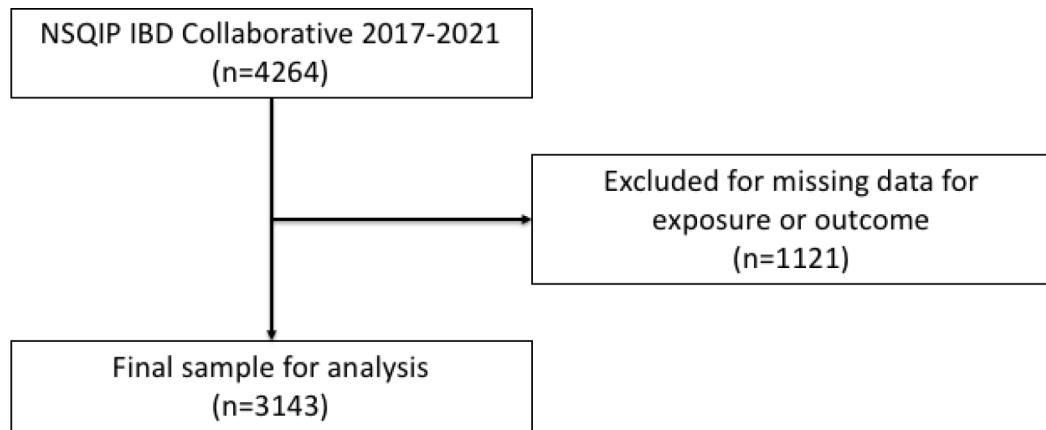
MS was supported by the National Institutes of Health grant T32DK067872.

## REFERENCES

1. Greuter T, Manser C, Pittet V, et al. Gender differences in inflammatory bowel disease. *Digestion*. 2020;101 Suppl 1:98–104. [PubMed: 31995797]
2. Shah SC, Khalili H, Gower-Rousseau C, et al. Sex-based differences in incidence of inflammatory bowel diseases-pooled analysis of population-based studies from Western countries. *Gastroenterology*. 2018;155:1079–1089.e3. [PubMed: 29958857]
3. Prideaux L, Kamm MA, de Cruz PP, et al. Inflammatory bowel disease in Asia: a systematic review. *J Gastroenterol Hepatol*. 2012;27:1266–1280. [PubMed: 22497584]
4. Mazor Y, Maza I, Kaufman E, et al. Prediction of disease complication occurrence in Crohn's disease using phenotype and genotype parameters at diagnosis. *J Crohn's Colitis*. 2011;5:592–597. [PubMed: 22115380]

5. Walldorf J, Krummenerl A, Engler K, et al. Health care for osteoporosis in inflammatory bowel disease: unmet needs in care of male patients? *J Crohn's Colitis*. 2013;7:901–907. [PubMed: 23333038]
6. Severs M, Spekhorst LM, Mangen MJJ, et al. Sex-related differences in patients with inflammatory bowel disease: results of 2 prospective cohort studies. *Inflamm Bowel Dis*. 2018;24:1298–1306. [PubMed: 29688413]
7. Ramos LR, Sachar DB, DiMaio CJ, Colombel JF, Torres J. Inflammatory bowel disease and pancreatitis: a review. *J Crohn's Colitis*. 2016;10:95–104. [PubMed: 26351384]
8. Söderlund S, Granath F, Broström O, et al. Inflammatory bowel disease confers a lower risk of colorectal cancer to females than to males. *Gastroenterology*. 2010;138:1697–1703.e2. [PubMed: 20167217]
9. Mudireddy P, Scott F, Feathers A, Lichtenstein GR. Inflammatory bowel disease: predictors and causes of early and late hospital readmissions. *Inflamm Bowel Dis*. 2017;23:1832–1839. [PubMed: 28858068]
10. Billioud V, Sandborn WJ, Peyrin-Biroulet L. Loss of response and need for adalimumab dose intensification in Crohn's disease: A systematic review. *Am J Gastroenterol*. 2011;106:674–684. [PubMed: 21407178]
11. Hofer B, Böttger T, Hernandez-Richter T, Seifert JK, Junginger T. The impact of clinical types of disease manifestation on the risk of early postoperative recurrence in Crohn's disease. *Hepatogastroenterology*. 2001;48:152–155. <https://europepmc.org/article/med/11268954>. Accessed February 9, 2022. [PubMed: 11268954]
12. Peyrin-Biroulet L, Harmsen WS, Tremaine WJ, Zinsmeister AR, Sandborn WJ. Loftus E v. Surgery in a population-based cohort of Crohn's disease from Olmsted County, Minnesota (1970–2004). *Am J Gastroenterol*. 2012;107:1693–1701. [PubMed: 22945286]
13. Samuel S, Ingle SB, Dhillon S, et al. Cumulative incidence and risk factors for hospitalization and surgery in a population-based cohort of ulcerative colitis. *Inflamm Bowel Dis*. 2013;19:1858–1866. [PubMed: 23660997]
14. Targownik LE, Singh H, Nugent Z, Bernstein CN. The epidemiology of colectomy in ulcerative colitis: results from a population-based cohort. *Am J Gastroenterol*. 2012;107:1228–1235. [PubMed: 22613902]
15. Li Y, Zhu W. Common Complications of Surgery for Crohn's Disease and Ulcerative Colitis. In: Bo Shen, ed. *Interventional Inflammatory Bowel Disease: Endoscopic Management and Treatment of Complications*. Academic Press; 2018:273–286.
16. Randall J, Singh B, Warren BF, Travis SPL, Mortensen NJ, George BD. Delayed surgery for acute severe colitis is associated with increased risk of postoperative complications. *Br J Surg*. 2010;97:404–409. [PubMed: 20101648]
17. Kasperek MS, Bruckmeier A, Beigel F, et al. Infliximab does not affect postoperative complication rates in Crohn's patients undergoing abdominal surgery. *Inflamm Bowel Dis*. 2012;18:1207–1213. [PubMed: 21928373]
18. Waterland P, Athanasiou T, Patel H. Post-operative abdominal complications in Crohn's disease in the biological era: systematic review and meta-analysis. *World J Gastrointest Surg*. 2016;8:274. [PubMed: 27022455]
19. Peyrin-Biroulet L, Germain A, Patel AS, Lindsay JO. Systematic review: outcomes and post-operative complications following colectomy for ulcerative colitis. *Aliment Pharmacol Ther*. 2016;44:807–816. [PubMed: 27534519]
20. Rottoli M, Remzi FH, Shen B, Kiran RP. Gender of the patient may influence perioperative and long-term complications after restorative proctocolectomy. *Colorectal Dis*. 2012;14:336–341. [PubMed: 21689322]
21. Luo WY, Holubar SD, Bordeianou L, et al. Better characterization of operation for ulcerative colitis through the National surgical quality improvement program: A 2-year audit of NSQIP-IBD. *Am J Surg*. 2021;221:174–182. [PubMed: 32928540]
22. Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. *StatPearls*. Published online June 29, 2021. Accessed July 23, 2022.

23. Knapp BM, Botros M, Sing DC, Curry EJ, Eichinger JK, Li X. Sex differences in complications and readmission rates following shoulder arthroplasty in the United States. *JSES Int.* 2020;4:95–99. [PubMed: 32195469]
24. Swaminathan RV, Feldman DN, Pashun RA, et al. Gender differences in in-hospital outcomes after coronary artery bypass grafting. *Am J Cardiol.* 2016;118:362–368. [PubMed: 27269585]
25. He JW, Sun LY, Wijesundera D, Vogt K, Jones PM. Patient sex and postoperative outcomes after inpatient intraabdominal surgery: a population-based retrospective cohort study. *Anesthesiology.* 2022;136:577–587. [PubMed: 35188547]
26. Ziv Y, Fazio VW, Church JM, et al. Stapled ileal pouch anal anastomoses are safer than handsewn anastomoses in patients with ulcerative colitis. *Am J Surg.* 1996;171:320–323. [PubMed: 8615465]
27. Jakobson T, Karjagin J, Vipp L, et al. Postoperative complications and mortality after major gastrointestinal surgery. *Medicina (B Aires).* 2014;50:111–117.
28. Ikeuchi H, Nakano H, Uchino M, et al. Safety of one-stage restorative proctocolectomy for ulcerative colitis. *Dis Colon Rectum.* 2005;48:1550–1555. [PubMed: 15937613]
29. Wagtmans MJ, Verspaget HW, Lamers CBHW, van Hogezaand RA. Gender-related differences in the clinical course of Crohn’s disease. *Am J Gastroenterol.* 2001;96:1541–1546. [PubMed: 11374696]
30. Rustgi SD, Kayal M, Shah SC. Sex-based differences in inflammatory bowel diseases: a review. <https://doi.org/10.1177/1756284820915043>. 2020;13.
31. Bertakis KD, Azari R, Helms LJ, et al. Gender differences in the utilization of health care services. *J Fam Pract.* 2000;49:147–152. [PubMed: 10718692]
32. Pinkhasov RM, Wong J, Kashanian J, et al. Are men shortchanged on health? Perspective on health care utilization and health risk behavior in men and women in the United States. *Int J Clin Pract.* 2010;64:475–487. [PubMed: 20456194]



**Figure 1.**

Flowchart of NSQIP IBD Collaborative 2017–2021 study population with exclusion criteria used to determine final sample

Exposure variable is biologic sex

Outcome variables are anastomotic leak, wound complications, and serious adverse events

**Table 1**

Demographic and baseline characteristics for patients with IBD undergoing surgery from the NSQIP IBD Collaborative 2017–2021, overall and by sex

Characteristic	Total (n=3143)	Women (n=1550)	Men (n=1593)	<i>p</i> *
<b>Age</b> (years), mean (SD)	43.3 (16.7)	43.7 (16.6)	42.9 (16.8)	0.23
<b>Race</b> , n (col%)				<b>0.01</b>
White	2680 (93.0)	1347 (93.3)	1333 (92.6)	
Black or African American	146 (5.1)	79 (5.5)	67 (4.7)	
Other	57 (2.0)	18 (1.3)	39 (2.7)	
<b>Ethnicity</b> , n (col%)				0.57
Not Hispanic	2893 (94.5)	1443 (94.7)	1450 (94.3)	
Hispanic	168 (5.5)	80 (5.3)	88 (5.7)	
<b>BMI</b> , mean (SD)	25.4 (5.9)	25.4 (6.3)	25.3 (5.4)	0.87
<b>BMI category</b> , n (col%)				<b>&lt;0.0001</b>
BMI<18.5	270 (8.6)	155 (10.0)	115 (7.3)	
BMI 18.5–30	2260 (72.2)	1053 (68.2)	1207 (76.2)	
BMI>30	599 (19.1)	336 (21.8)	263 (16.6)	
<b>Current Smoker</b> , n (col%)				0.81
Nonsmoker	2754 (87.6)	1356 (87.5)	1398 (87.8)	
Smoker	389 (12.4)	194 (12.5)	195 (12.2)	
<b>IBD Type</b> , n (col%)				<b>&lt;0.0001</b>
Crohn's Disease	1842 (59.5)	980 (64.2)	862 (55.0)	
Ulcerative Colitis	1241 (40.1)	542 (35.5)	699 (44.6)	
Indeterminate Colitis	12 (0.4)	5 (0.3)	7 (0.5)	
<b>Surgical Approach</b> , n (col%)				<b>0.004</b>
Open	780 (24.8)	393 (25.4)	387 (24.3)	
Converted to open	256 (8.1)	101 (6.5)	155 (9.7)	
Minimally invasive	2106 (67.0)	1056 (68.1)	1050 (66.0)	
<b>Elective Surgery</b> , n (col%)				0.11
Non-elective	769 (25.7)	359 (24.4)	410 (27.0)	
Elective	2220 (74.3)	1110 (75.6)	1110 (73.0)	
<b>ASA Classification</b> , n (col%)				0.20
I	17 (0.5)	7 (0.5)	10 (0.6)	
II	1620 (51.5)	805 (51.9)	815 (51.2)	
III	1438 (45.8)	713 (46.0)	725 (45.5)	
IV	66 (2.1)	25 (1.6)	41 (2.6)	
V	2 (0.1)	0	2 (0.1)	

Characteristic	Total (n=3143)	Women (n=1550)	Men (n=1593)	<i>p</i> <sup>*</sup>
<b>Steroid use, n (col%)</b>				<b>0.005</b>
No steroid use	1233 (39.5)	646 (41.9)	587 (37.1)	
Steroid use	1892 (60.5)	895 (58.1)	997 (62.9)	
<b>Immunologic or biologic use, n (col%)</b>				0.19
No medication use	924 (35.9)	468 (37.1)	456 (34.7)	
Use of one or more immunologic/biologic medications	1653 (64.1)	793 (62.9)	860 (65.4)	
<b>Ileostomy formation, n (col%)</b>				<b>0.02</b>
No ileostomy present/created	1315 (44.5)	686 (46.9)	629 (42.1)	
New ileostomy created	1349 (45.6)	630 (43.1)	719 (48.1)	
Ileostomy revised/maintained	293 (9.9)	146 (10.0)	147 (9.8)	

Abbreviations: BMI—body mass index, IBD—inflammatory bowel disease, ASA—American Society of Anesthesiologists, SAE—serious adverse event

Column percentages are shown for categorical variables

\* T test performed for continuous variables and Chi-squared test for categorical variables, except when >20% of expected cell counts were less than 5, where Fisher's Exact Test was utilized; bolding denotes statistical significance (p<0.05).

**Table 2**

Adjusted associations between sex and postoperative outcomes of surgery for IBD patients from the NSQIP IBD Collaborative 2017–2021

Sex	Anastomotic Leak <sup>†</sup> N (row %)	No Anastomotic Leak N (row %)	Adjusted OR* OR (95% CI)	<i>p</i> <sup>*</sup>
Men	8 (2.1)	374 (97.9)	1.00 (ref)	
Women	13 (2.9)	428 (97.1)	1.29 (0.48, 3.44)	0.61
Sex	Wound Complication <sup>††</sup> N (row %)	No Wound Complication N (row %)	Adjusted OR* OR (95% CI)	<i>p</i> <sup>*</sup>
Men	122 (11.2)	969 (88.8)	1.00 (ref)	
Women	133 (12.3)	949 (87.7)	1.04 (0.79, 1.37)	0.79
Sex	SAE <sup>††</sup> N (row %)	No SAE N (row %)	Adjusted OR* OR (95% CI)	<i>p</i> <sup>*</sup>
Men	140 (12.8)	951 (87.2)	1.00 (ref)	
Women	104 (9.6)	978 (90.4)	0.73 (0.55, 0.96)	<b>0.027</b>

\* ORs, 95% CIs and *p*-values from logistic regression of postoperative outcomes of surgery for IBD on sex, with male sex as reference group; bolding denotes statistical significance ( $p < 0.05$ ).

<sup>†</sup> Adjusted for age, race, ethnicity, institution, BMI, smoking status, IBD type, surgical approach, elective surgery, ASA classification, steroid use, and immunologic/biologic use.

<sup>††</sup> Adjusted for age, race, ethnicity, institution, BMI, smoking status, IBD type, surgical approach, elective surgery, ASA classification, steroid use, immunologic/biologic use, and ileostomy formation.



**Table 3**

Adjusted association between sex and serious adverse events after surgery stratified by IBD type for patients from the NSQIP IBD Collaborative 2017–2021

IBD Type	SAE <sup>†</sup> N (row %)	No SAE N (row %)	Adjusted OR* OR (95% CI)	<i>p</i> *
<b>Crohn's Disease</b>				
Men	64 (10.2)	562 (89.8)	1.00 (ref)	
Women	73 (10.1)	6749 (89.9)	1.03 (0.70, 1.51)	0.89
<b>Ulcerative Colitis</b>				
Men	75 (16.3)	384 (83.7)	1.00 (ref)	
Women	31 (8.7)	327 (91.3)	0.46 (0.28, 0.74)	<b>0.001</b>

\* ORs, 95% CIs and *p*-values from logistic regression of postoperative outcomes of surgery for IBD on sex, with male sex as reference group; bolding denotes statistical significance (*p*<0.05).

<sup>†</sup> Adjusted for age, race, ethnicity, institution, BMI, smoking status, IBD type, surgical approach, elective surgery, ASA classification, steroid use, immunologic/biologic use, and ileostomy formation.