Prospective Cohort Study to Investigate the Safety of Preoperative Tumor Necrosis Factor Inhibitor Exposure in Patients with Inflammatory Bowel Disease Undergoing Intra-abdominal Surgery

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Title: Prospective Cohort Study to Investigate the Safety of Preoperative Tumor Necrosis Factor Inhibitor Exposure in Patients with Inflammatory Bowel Disease Undergoing Intra-abdominal Surgery

Short Title: PUCCINI

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Abbreviations:

Adalimumab (ADA)

Crohn's disease (CD)

Inflammatory bowel disease (IBD)

Infliximab (IFX)

Lower limit of quantitation (LLoQ)

Surgical site infection (SSI)

Tumor Necrosis Factor inhibitor (TNFi)

Ulcerative colitis (UC)

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Higgins	X	Х	Х		X		
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Bohl		X	Х		X		

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Abstract

Background & Aims: It remains controversial whether pre-operative treatment of inflammatory bowel disease (IBD) with Tumor Necrosis Factor inhibitors (TNFi) increases the risk of postoperative infectious complications. The primary aim of this study was to determine if preoperative exposure to TNFi is an independent risk factor for post-operative infectious complications within 30 days of surgery.

Methods: We conducted a multi-center prospective observational study of IBD patients undergoing intraabdominal surgery across 17 sites from the Crohn's & Colitis Foundation Clinical Research Alliance. Infectious complications were categorized as surgical site infections (SSI) or non-SSI. Current TNFi exposure was defined as use within 12 weeks of surgery and serum was collected for drug level analyses. Multivariable models for occurrence of the primary outcome, any infection, or SSI were adjusted by pre-defined covariates (age, gender, preoperative steroid use, and disease type), baseline variables significantly associated (p<0.05) with any infection or SSI separately, and TNFi exposure status. Exploratory models used TNFi exposure based on serum drug concentration.

Results: A total of 947 patients were enrolled from September 2014 through June 2017. Current TNFi exposure was reported by 382 patients. Any infection (18.1% vs. 20.2%, p=0.469) and SSI (12.0% vs. 12.6%, p=0.889) rates were similar in patients currently exposed to TNFi and those unexposed. In multi-variable analysis, current TNFi exposure was not associated with any infection (odds ratio, 1.050; 95% CI, 0.716-1.535) or SSI (odds ratio, 1.249; 95% CI, 0.793-1.960). Detectable TNFi drug concentration was not associated with any infection or SSI.

Conclusions: Preoperative TNFi exposure was not associated with postoperative infectious complications in a large prospective multi-center cohort.

Key words: Crohn's disease, ulcerative colitis, surgery, infection, tumor necrosis factor inhibitor

Introduction:

Current therapies for inflammatory bowel disease (IBD) focus on immunosuppression and studies have shown combination therapy using both tumor necrosis factor inhibitors (TNFi) and thiopurines to be among the most effective approaches for both moderate to severe ulcerative colitis (UC) and Crohn's disease (CD) ^{1,2}. Despite the use of more effective therapies, the risk of requiring surgery remains high in the biologic era ³⁻⁵. Data from referral center cohorts have shown that up to 50% of patients are exposed to TNFi prior to their first surgery ⁶. There is concern that preoperative treatment with immunosuppressive medications including TNFi increases the risk of potential postoperative infectious complications. While the literature is consistent in showing that corticosteroid use prior to surgery increases the risk of postoperative infectious complications ⁷⁻⁹, the evidence regarding TNFi remains inconsistent.

Over the last two decades, numerous retrospective studies have been published with some showing increased risk of postoperative complications or infection associated with preoperative TNFi exposure¹⁰⁻¹⁹ and others showing no increased risk.²⁰⁻⁴³ In addition to retrospective design, limitations of these studies have included being mostly single institution experiences, difficulty controlling for disease severity, confounding effect of concomitant immunosuppressive therapy, including steroids, variable complications studied and differing definitions of TNFi exposure. A 2020 Cochrane review of the available literature found an association of preoperative TNFi use with postoperative total infection (OR 1.60, 95% CI 1.20-2.13), but the certainty of evidence was very low and the authors stated that no firm conclusions could be drawn about their safety in the perioperative period.⁴⁴

Two prospective French cohorts have assessed for an association of preoperative TNFi use with postoperative infectious complications after ileocolic resection for CD with conflicting results.^{45,46} The larger GETAID Chirurgie cohort found an association of TNFi use < 3 months prior to ileocolic resection for CD with 30-day postoperative morbidity and mortality as well as intra-abdominal septic morbidity, but did not assess serum drug exposure. TNFi serum drug exposure association with postoperative complication has only been assessed in two retrospective studies^{43,47} and one prospective study (N=76 exposed).⁴⁶

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We sought to determine if preoperative TNFi exposure is an independent risk factor for infectious complications in IBD patients undergoing intra-abdominal surgery. The secondary aim was to explore the association of serum TNFi drug exposure with postoperative infectious complications.

Materials and Methods:

Study Design:

The <u>P</u>rospective Cohort of <u>U</u>lcerative <u>C</u>olitis and <u>C</u>rohn's Disease Patients Undergoing Surgery to Identify Risk Factors for Post-Operative <u>IN</u>fection <u>I</u>(PUCCINI) was a multi-center prospective observational study that enrolled subjects undergoing intra-abdominal surgery for IBD with the primary aim to determine if preoperative exposure to TNFi is an independent risk factor for postoperative infectious complications within 30 days of surgery (ClinicalTrials.gov, Number NCT02054533).

Study Setting and Participants:

Patients with confirmed IBD were enrolled between September 2014 through June 2017 from seventeen participating sites among the Crohn's & Colitis Foundation Clinical Research Alliance (CRA). The participating sites were academic centers diverse in size, geography, and patient population. The inclusion criteria were as follows: 1) age 18 or older at entry; 2) diagnosis of Crohn's disease, ulcerative colitis, or indeterminate colitis by standard criteria; 3) planned to have intra-abdominal surgery or has had intra-abdominal surgery in the preceding 4 days; and 4) ability to provide written informed consent. Exclusion criteria included: 1) current enrollment in a clinical trial of an investigational therapy for IBD; 2) surgery performed to repair a complication from a recent surgery within 90 days; and 3) inability or unwillingness to provide informed consent. Institutional Review Boards at each site approved the study and written informed consent was obtained.

Data Collection:

Patients were screened between 1 month prior to surgery and up to 4 days postoperatively to ensure capture of patients who may have had urgent or emergent surgeries. Demographic information, disease

history, preoperative medication use, comorbidities via the Self-Administered Comorbidity Questionnaire⁴⁸ and other relevant medical information was obtained through both structured patient interview and medical record abstraction at baseline. Additional medical record abstraction was performed for operative details, postoperative risk factors, infectious and non-infectious outcomes both at patient discharge and 30 days post-operatively. Patients were also contacted by structured telephone interview at 30 days postoperatively to assess for outcomes including infections that may not have been captured in the medical record. Supportive documentation was obtained by the sub-sites as needed to confirm infectious outcomes.

Serum Collection and Testing:

Serum was obtained from patients at their baseline visit and stored locally at the sites at -80°C until the conclusion of the study. Serum drug concentrations and anti-drug antibody concentrations were measured for infliximab (IFX) and adalimumab (ADA) with a drug-tolerant homogenous mobility shift assay (Prometheus Laboratories Inc., San Diego, CA). Serum drug concentration testing was performed in patients with current IFX or ADA use (≤12 weeks from surgery) and in some patients with past use of IFX or ADA within 6 months of surgery. Testing was not available for certolizumab or golimumab concentrations.

Outcomes:

Surgical Site Infections (SSI) were defined by CDC criteria and classified as superficial incisional, deep incisional, or organ/space infections.⁴⁹ All other postoperative infections were defined as non-SSI and classified as sepsis, bacteremia, pneumonia, urinary tract infection, fever > 101.5 F without an identifiable source, or other. The primary outcome was occurrence of any infection (SSI or non-SSI) within 30 days of surgery. Secondary outcomes included SSI, hospital readmission within 30 days of surgery, re-operation within 30 days of surgery, 30-day post-operative mortality, duration of postoperative hospitalization, thrombotic complication within 30 days of surgery, and hypomotility complication (ileus > 5 days or small bowel obstruction).Outcomes were assessed by review of the medical record at discharge and 30 days postoperatively as well as by telephone interview with the patient 30 days postoperatively.

TNFi Exposure Definitions:

The pre-specified primary definition of TNFi exposure was patient reported use of TNFi within 12 weeks prior to surgery. Patients with TNFi exposure greater than 12 weeks from surgery or never having used a TNFi were considered unexposed in the primary analysis. Secondary analyses were performed to examine the effects of perioperative serum TNFi drug levels on the outcomes of interest. Serum TNFi exposure was explored both using the commercial assay lower limit of quantitation (LLoQ) for IFX and ADA assays as detectable and separately using a level greater than 0 µg/mL as detectable. Patients were classified as having an undetectable serum TNFi drug level using the commercial assay LLoQ if their IFX level was less than 1 µg/mL, ADA level was less than 1.6 µg/mL, or they had not used any TNFi within 180 days of surgery. In a second definition, serum TNFi exposure definition, was defined as having an undetectable serum TNFi greater than 180 days from surgery were considered to have undetectable levels for the analyses even if serum levels were not available for analysis. Based on a reported median half-life of 7.7-9.5 days for IFX⁵⁰ and mean 2 weeks for ADA⁵¹, the 180 day cutoff was chosen to avoid any potential misclassification of an exposure as undetectable. Sensitivity analyses were performed using a 120-day cutoff.

Statistical Analysis:

The primary analysis was to determine the independent contribution of TNFi exposure during the preoperative period (patient reported TNF use within 12 weeks of surgery) to the development of any infection (dichotomized as yes/no) within 30 days following surgery. The secondary analysis was to determine the independent contribution of TNFi exposure to development of SSI. A logistic regression of the binary response variable, rate of any infection (yes/no), on the binary independent variable, patient reported TNFi exposure (yes/no), with a sample size of 821 observations (of which 60% are in the TNFi unexposed group and 40% are in the TNFi exposed group) achieves 80% power at a 0.05 significance level to detect a change in the probability of infection at 30 days from the baseline value of 10% to 17%. While the literature was conflicted on the true infectious risk associated with TNFi exposure, these

estimates were based on two of the more commonly quoted studies at the time the study was conceived.^{16,38} For the multivariable models, at least 10 patients with infection were estimated to be needed for each covariate in the multivariable model to maintain validity.⁵²⁻⁵⁴

Continuous variables were reported as the mean (range) or the median (interquartile range (IQR)), and categorical variables were reported as the number (percentage). Continuous variables were compared using the Wilcoxon test. Categorical variables were compared using chi-square or Fisher's exact test as appropriate.

Univariable logistic regression was performed to identify predictors of the primary outcome, any infection, as well as SSI. Multivariable models for occurrence of any infection or SSI were adjusted by pre-defined "core" covariates (age, gender, pre-operative corticosteroid use, and disease type), any baseline variable found to be significantly associated (p<0.05) with any infection or SSI separately, as well as patient reported TNFi exposure status. Separate exploratory models were created using TNFi exposure based on serum drug concentration as outlined in the TNFi exposure definitions. Final models were selected through machine learning (random forest) method. In the serum analyses, dose effect was assessed by comparing serum drug concentration quartiles.

All analyses were performed using R (package version 4.0.3).

Results:

Patient Characteristics:

The cohort's demographic and clinical characteristics at the time of intra-abdominal surgery are described in Table 1. A total of 947 patients, including 453 (47.8%) females were enrolled from September 2014 through June 2017. As expected, the patients were young and had few comorbid conditions, most commonly anemia or other blood disease or depression. Over two-thirds of the cohort had a diagnosis of CD. The median disease duration was 10 years (IQR=14). Prior bowel resection was reported by 326 patients (34.4%) with an additional 166 patients (17.5%) reporting prior abdominal surgery without a

bowel resection. Active smoking at the time of surgery was reported by 94 patients (9.9%). The median body mass index (BMI) was 24.28 (IQR=6.27). Poor preoperative nutritional status defined as weight loss > 10% of body weight was present in 128 patients (13.5%) and 54 patients (5.7%) were on total parenteral nutrition pre-operatively.

Medication Exposures:

Medication exposures of the cohort are summarized in Table 2. Notably, 387 patients (40.9%) had used systemic corticosteroids within 2 weeks of surgery. Thiopurine use was reported by 235 patients (24.8%) and methotrexate use by 74 patients (7.8%) in the month prior to surgery. Antibiotics were used within 2 weeks of surgery by 401 patients (42.3%). Vedolizumab and ustekinumab gained approval for treatment of IBD during the study and was used within 12 weeks of surgery by 136 patients (14.4%) and 21 patients (2.2%) respectively.

TNFi Exposures:

A total of 382 patients (40.3%) reported use of at least one TNFi within 12 weeks of surgery. Most of the patients exposed to TNFi prior to surgery used adalimumab (n=183) or infliximab (n=165) with far fewer using certolizumab (n=44) or golimumab (n=10). Among patients not using TNFi within 12 weeks of surgery, 224 patients (23.7%) were TNFi naïve and 341 patients (36.0%) reported past use of TNFi. Patients exposed to TNFi within 12 weeks of surgery differed significantly from unexposed patients with regards to age (39 vs. 43 years, p<0.001), disease duration (11 vs. 14 years, p<0.001), prior bowel resection (28% vs. 39%, p=0.001), prior hospital admission within 30 days (22% vs. 15%, p=0.009), self-administered comorbidity score (1.10 vs. 1.39, p=0.001), and preoperative albumin (3.62 vs. 3.79, p=0.001).

Serum TNFi drug concentrations were checked in 322 patients, of whom 280 patients had reported TNFi use within 12 weeks of surgery. Using the commercial assay LLoQ threshold for detectability, 213 patients (22.5%) had a detectable TNFi level perioperatively. Using any drug concentration > 0 µg/mL as the threshold for detectability, 244 patients (25.8%) had a detectable TNFi level perioperatively. Among

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patients reporting TNFi use within 12 weeks of surgery in whom serum drug levels were available (n=280), 208 (74.3%) had detectable levels perioperatively using the commercial assay LLoQ threshold for detectability and 234 (83.6%) had detectable levels perioperatively using any drug concentration > 0 μ g/mL as the threshold for detectability. Serum drug levels were unavailable for 102 patients who had reported TNFi use within 12 weeks of surgery. In patients with past use of TNFi greater than 12 weeks before surgery for whom perioperative drug levels were available, 5 patients had detectable levels using the commercial assay LLoQ threshold for detectability and 10 patients had detectable levels using the commercial assay LLoQ threshold for detectability and 10 patients had detectable levels antibodies to IFX or ADA were identified in 28 patients.

Surgical Factors:

Characteristics of the surgery are described in Table 3. Surgery was performed on an urgent/emergent basis within 24 hours of admission in 14 patients (1.5%). The surgical approach was laparoscopic in 605 patients (63.9%). Bowel resection was performed in 905 patients (95.6%) with a bowel anastomosis created in 584 patients (61.7%). A total colectomy was performed in 330 patients (34.8%) with an ileoanal pouch created in 78 patients (8.2%). A stoma was either created or revised in 454 patients (47.9%). Surgical blood loss was > 250 mL in 115 patients (12.1%) with 53 patients (5.6%) requiring at least one unit of blood transfused.

Post-operative Infectious Outcomes

There was no difference in the primary outcome of any post-operative infection between patients reporting TNFi use within 12 weeks of surgery and those not using TNFi preoperatively (18.1% vs 20.2%, p=0.469). Similarly, there was no difference in SSI between patients reporting TNFi use within 12 weeks of surgery and those not using TNFi preoperatively (12.0% vs. 12.6%, p=0.889). No significant differences were present in the distribution of SSI by preoperative TNFi use (Figure 1A and Supplementary Table 1).

When defining TNFi drug exposure by having a serum drug concentration above the commercial assay LLoQ threshold, there was no difference between TNFi exposed vs. unexposed patients in the rate of any infection (18.8% vs. 19.7%, p=0.873) or SSI (12.7% vs. 11.8%, p=0.814). Similarly, when defining TNFi drug exposure by having a serum drug concentration > 0 µg/mL, there was no difference between TNFi exposed vs. unexposed patients in the rate of any infection (18.0% vs. 20.1%, p=0.861) or SSI (11.9% vs. 12.1%, p=0.998). Distributions of SSI by TNFi exposure using serum drug concentrations were similar (Figure 1B, Figure 1C and Supplementary Table 1). Any infection and SSI outcomes by TNFi exposure type are summarized in Supplementary Table 1. Sensitivity analyses including patients with last use of TNFi >120 days from surgery defined as undetectable when drug concentration results were unavailable yielded similar results (Supplementary Table 2).

Univariable and Multivariable Analyses for Any Infection

Results of univariable logistic regression for any infection are available in the supplementary material (Supplementary Table 3). Important covariates not associated with any infection postoperatively in univariable analysis include the study site, preoperative weight loss >10% body weight, preoperative albumin, preoperative hemoglobin, immunomodulator or methotrexate use in the last month, antibiotic use within 2 weeks of surgery, preoperative abscess, creation of an IPAA, type of bowel resection, creation of an anastomosis or formation of a stoma. Results of multivariable logistic regression for any infection including the primary definition of TNFi exposure (patient reported use within 12 weeks of surgery) are reported in Table 4. TNFi use was not independently associated with any infection. Covariates independently associated with any infection included age, preoperative corticosteroid use, history of prior bowel resection, current smoking, history of anemia or other blood disorders⁴⁸, diabetes⁴⁸, depression⁴⁸, rheumatoid arthritis⁴⁸, genitourinary fistula, ureteral stent placement, and preoperative nonabdominal infection. Preoperative budesonide use was inversely associated with any infection. Sensitivity analyses comparing current and past TNFi use to those who were TNFi naïve did not find any association of current or past TNFi use with any infection on univariable (Supplementary Table 3) or multivariable analysis. Detectable serum TNFi concentration using either the commercial assay LLoQ threshold for detectability or any level > 0 µg/mL was not independently associated with any infection post-operatively

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(Supplementary Tables 4 and 5). A separate multivariable analysis comparing quartiles of serum TNFi drug concentration exposure (undetectable, 0.1-4.4 μ g/mL, 4.5-11.7 μ g/mL, and > 11.7 μ g/mL) did not demonstrate any independent association of drug level with any infection (Supplementary Table 6). Detectable antibodies to IFX or ADA were not associated with any infection on univariable analysis (Supplementary Table 3).

Univariable and Multivariable Analyses for SSI

Results of univariable logistic regression for SSI are available in the supplementary material (Supplementary Table 7). Important covariates not associated with SSI postoperatively in univariable analysis include study site, preoperative weight loss > 10% body weight, preoperative albumin, preoperative hemoglobin, immunomodulatory or methotrexate use in the last month, antibiotic use within 2 weeks of surgery, preoperative abscess, creation of an IPAA, type of bowel resection, creation of an anastomosis or formation of a stoma. Covariates independently associated with SSI include preoperative corticosteroid use, history of prior bowel resection, diabetes⁴⁸, hypertension⁴⁸, and current smoking (Table 5). Sensitivity analyses comparing current and past TNFi use to those who were TNFi naïve did not find any association of current or past TNFi use with SSI on univariable (Supplementary Table 7) or multivariable analysis. Detectable serum TNFi concentration using either the commercial assay LLoQ threshold for detectability or any level > 0 µg/mL was not independently associated with any infection postoperatively (Supplementary Tables 8 and 9). A separate multivariable analysis comparing quartiles of serum TNFi drug concentration exposure (undetectable, 0.1-4.4 µg/mL, 4.5-11.7 µg/mL, >11.7 µg/mL) did not demonstrate any independent association of drug level with SSI (Supplementary Table 10). Detectable antibodies to IFX or ADA were not associated with SSI on univariable analysis (Supplementary Table 7).

Secondary Non-Infectious Post-Operative Outcomes

Non-infectious postoperative outcomes are reported in Table 6. More patients reporting TNFi use within 12 weeks of surgery developed a postoperative venous thromboembolism (3.7% vs. 1.4%, p=0.024). When controlling for corticosteroid use, the association of TNFi use within 12 weeks of surgery with

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postoperative venous thromboembolism remained significant (OR 2.641, 95%CI 1.096-6.367). There was no other difference in secondary outcomes of 30-day readmission, 30-day reoperation, postoperative ileus, or length of stay by patient reported TNFi exposure status. There were no differences in incidence of any non-infectious post-operative outcomes by TNFi serum drug concentration detectability using either the commercial assay LLoQ threshold or > 0 μ g/mL as the cutoff for exposure. There were no deaths within 30 days of surgery. Detectable antibodies to IFX or ADA were not associated with any of the secondary outcomes.

Discussion:

In this prospective cohort of IBD patients undergoing intra-abdominal surgery, the use of TNFi within 12 weeks prior to surgery was not associated with occurrence of any infection or SSI 30 days postoperatively. Secondary analyses also did not find any association of detectable serum TNFi drug concentrations with any infection or SSI postoperatively. Risk factors found to be independently associated with both any infection or SSI included preoperative corticosteroid use, current smoking, prior bowel resection, and diabetes.

PUCCINI is the largest prospective study to assess risk factors for postoperative infection following intraabdominal surgery in IBD patients. Two prospective French cohorts previously reported on risk factors for postoperative complications including infection following surgery for ileocolonic CD with conflicting results. The GETAID Chirurgie Group found TNFi use <3 months prior to surgery to be independently associated with overall postoperative morbidity (OR 1.99; 95%CI 1.17-3.39) and intra-abdominal septic morbidity (OR 2.22; 95%CI 1.22-4.04). However, TNFi exposure in this cohort was defined by patient reported use and the effect of serum drug concentrations at the time of surgery was not explored. Similarly, the authors did not find a significant difference in the rate of postoperative complication or infection by timing of the last dose of TNFi. Only 24% of the GETAID Chirurgie cohort was on TNFi preoperatively as compared to over 40% of the PUCCINI cohort, suggesting differences in practice patterns or characteristics of the study population. Over 60% of the GETAID Chirurgie cohort had surgery for stricturing disease as compared to

only 30% of the PUCCINI cohort. While PUCCINI was a mixed IBD cohort, controlling for diagnosis along with many other factors related to disease activity, severity, and phenotype did not alter the TNFi findings.

In contrast to the GETAID Chirurgie Group findings, the REMIND group did not find TNFi use within 3 months of surgery or serum TNFi drug concentrations to be associated with overall postoperative complications or intraabdominal septic complications following ileocolic resection for Crohn's disease. However, this cohort consisted of only 209 patients, of whom 76 were TNFi exposed. Though not specifically designed to control for risk factors for postoperative complications, our results are also supported by the findings of large nationwide Danish registry studies which did not find an association of TNFi use within either 14 days or 12 weeks of CD surgery or 12 weeks of UC surgery with postoperative complications including infections such as anastomotic leak, intra-abdominal abscess or bacteremia.^{55,56}

Confirming the findings of our primary analysis through secondary analyses defining TNFi exposure by perioperative serum drug concentrations differentiates PUCCINI from the other studies evaluating TNFi risk. Most previously published studies have used varying definitions of TNFi exposure, with the most common being last use within 12 weeks of surgery. However, patients with active IBD are known to have increased clearance of TNFI, potentially leading to misclassification of exposure when defining by last use alone.⁵⁷ Among patients having used infliximab within 12 weeks of surgery, 18% had undetectable levels perioperatively and among patients having used adalimumab, 9% had undetectable levels perioperatively. A smaller percentage of patients with last dose of TNFi >12 weeks from surgery in whom drug level analyses were available had detectable levels. Commercial drug assays may report small, but detectable amounts of drug as undetectable and therefore we evaluated serum drug concentrations defining detectable by a level of >0 µg/mL and separately as greater than the commercial lab LLoQ for the assay. TNFi was not associated with any infection or SSI by either definition of detectability. Lau et al. previously reported detectable serum TNFi levels were not associated with postoperative infections in CD or UC in a cohort including 143 patients exposed to TNFi preoperatively.⁵⁸ However, when using a cut point of \geq 3 µg/mL vs. < 3 µg/mL the authors found significantly more infectious complications in the CD patients with higher levels of TNFi. Due to the smaller size of the CD cohort, the authors were limited in their ability to control for

multiple risk factors in the analysis and a Cochrane Armitage trend analysis did not demonstrate significant results. Our sensitivity analysis defining serum drug concentration exposure by quartiles did not show any range of TNFi exposure to be associated with infectious complications compared to patients with undetectable TNFi.

It has been reported that subjects taking corticosteroids preoperatively may have double the risk of infectious complications compared to those not taking corticosteroids ⁵⁹. Both PUCCINI and the REMIND cohort found preoperative systemic corticosteroid use to be associated with postoperative infectious complications, confirming the findings of prior studies.⁴⁶ In patients undergoing elective surgery, attempts to minimize corticosteroid exposure should be made. Randomized studies have previously shown no benefit to using stress dose corticosteroids for IBD surgery in the absence of confirmed adrenal insufficiency.⁶⁰ Uncontrolled retrospective studies have suggested benefits to preoperative nutritional optimization and corticosteroid weaning, but this needs to be studied prospectively.⁶¹

Although the data are limited, most studies have shown that treatment with azathioprine, 6-mercaptopurine, or methotrexate prior to surgery is not a risk factor for post-operative complications ^{7,8,24,62}. Neither thiopurine use nor methotrexate use were associated with postoperative infections in our cohort. Based on the totality of the evidence, surgery does not need to be delayed on account of taking these medications and decisions on whether to hold thiopurines or methotrexate should be made based on other factors besides infectious risk.

Current smoking preoperatively was a significant risk factor for both any infection and surgical site infection in our cohort. Smoking represents one of the most important modifiable risk factors for postoperative complications and its association with postoperative infection, particularly wound infection, has been established in other non-IBD surgical cohorts.⁶³⁻⁶⁷ Wound inflammation and fibroblast proliferation have been shown to be attenuated in smokers, potentially decreasing wound healing.⁶⁸ Recently, investigators from the Mayo Clinic have shown stopping smoking even if only on the day of surgery to be associated with decreased frequency of SSI in a large mixed cohort of patients including those undergoing GI surgery.⁶⁹

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Low intensity smoking cessation interventions have been shown to stop perioperative smoking in 20% of patients.⁷⁰ Despite the known risks of smoking both to postoperative outcomes and CD disease activity, perioperative smoking cessation interventions have not been specifically studied in IBD. While integration of smoking cessation strategies into the normal workflow of perioperative care may be challenging, implementation science may guide us in incorporating evidenced based approaches into routine care.⁷¹

Preoperative TNFi use was not associated with any of the secondary outcomes with the notable exception of postoperative venous thromboembolism. Prior studies have demonstrated an association of corticosteroid use, but not TNFi use with venous thromboembolism.⁷²⁻⁷⁵ However, the association of preoperative TNFi use within 12 weeks of surgery with postoperative venous thromboembolism persisted after adjusting for preoperative corticosteroid use. When defining TNFi exposure as having detectable serum drug concentrations, the association was no longer significant suggesting other factors may be at play. The absolute number of thromboembolic events in the cohort was small, making it difficult to explore how much of this association is due to the TNFi exposure versus other risk factors such as severe disease, malnutrition, or postoperative deconditioning.

Strengths of our study include its prospective enrollment of a large number of IBD patients from a geographically diverse group of centers in the United States among the Crohn's & Colitis Foundation CRA as well as the incorporation of serum drug concentrations into the analyses. The size of the cohort enabled controlling for a larger number of concomitant risk factors than was possible in other studies of TNFi association with postoperative infections. Limitations of our study include non-consecutive patient enrollment, participation of largely academic centers that may affect the generalizability of our findings, potential for missed infections diagnosed at outside centers not accounted for in our chart review or telephone follow-up, as well as the fact that our observations may already reflect prejudice in surgical decision making such as approach and timing of surgery.

In the largest multicenter prospective surgical cohort studying the association of preoperative TNFi use with 30-day postoperative infectious complications, neither patient reported use of TNFi nor detectable serum

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TNFi levels were independent risk factors for any postoperative infection or SSI. Therefore, preoperative use of TNFi should not affect surgical decisions in most IBD patients. Instead, focus should be placed on modifiable risk factors such as smoking and preoperative systemic corticosteroid use.

Figure Legends:

Figure 1. Frequency of surgical site infection types by (A) patient reported TNFi exposure; (B) serum TNFi exposure with undetectable defined as below commercial assay lower limit of quantitation threshold, never on a TNFi, or no TNFi within 180 days of surgery; and (C) serum TNFi exposure with undetectable defined as level = 0 µg/mL, never on a TNFi, or no TNFi within 180 days of surgery.

TNFi – tumor necrosis factor

Journal Prevention

Table Legends:

Table 1. Demographic and Disease Characteristics of Cohort

- Table 2. Preoperative Medication Exposures
- Table 3. Surgery Characteristics of the Cohort
- Table 4. Multivariable Analysis of Risk Factors for Any Infection Postoperatively using Patient Reported

TNFi Exposure

Table 5. Multivariable Analysis of Risk Factors for Surgical Site Infection Postoperatively using Patient

Reported TNFi Exposure

Table 6. Non-Infectious Postoperative Outcomes by TNFi Exposure Type

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Table 1. Demographic and Disease Characteristics of Cohort

		Crohn's [Disease	Llicerativ	e colitis
		TNEi uso withir	12 wooks of	TNEi uso withi	n 12 wooks of
			AIV	eur	
	Overall	No	Ves	No	Ves
	(n-947)	(n = 368)	(n=272)	(n=197)	(n-110)
Age median (01-03)	39 (29-53)	39 (30-52)	35 (27-49)	45 (33-57)	35 (27-53)
Male Gender, n (%	494 (52.2)	187 (50.8)	135 (49.6)	113 (57 4)	59 (53 6)
Disease Duration (years) median (01-03)	10 (4-18)	13 (6-20)	10 (4-18)	9 (4-18)	4 (2-11)
UC Disease Location in (%)	10 (4 10)	10 (0 20)	10 (4 10)	3 (4 10)	+ (2-11)
Proctitis	18 (1 9)			16 (8 1)	2 (1 8)
Left-Sided	55 (5.8)			33 (16.8)	22 (20 0)
Extensive	233 (24 6)			148 (75.1)	85 (77.3)
NA	1 (0.1)			0 (0.0)	1 (0.9)
CD Disease Location. n (%)				- (/	
lleum	242 (25.6)	125 (34.0)	117 (43.0)		
Colon	89 (9.4)	65 (17.7)	24 (8.8)		
Ileum and Colon	305 (32.2)	175 (47.6)	130 (47.8)		
NA	4 (0.4)	3 (0.8)	1 (0.4)		
Upper GI Tract CD, n (%)	36 (3.8)	21 (5.7)	15 (5.5)	0 (0.0)	0 (0.0)
Perianal CD, n (%)	108 (11.4)	71 (19.3)	37 (13.6)	0 (0.0)	0 (0.0)
CD Disease Behavior, n (%)					
Non-stricturing, nonpenetrating	385 (40.7)	51 (13.9)	27 (9.9)		
Stricturing	285 (30.1)	164 (44.6)	121 (44.5)		
Penetrating	109 (11.5)	65 (17.7)	44 (16.2)		
Stricturing and Penetrating	165 (17.4)	85 (23.1)	80 (29.4)		
NA	3 (0.3)	3 (0.8)	0 (0.0)		
Prior Abdominal Surgery, n (%)					
No prior abdominal surgery	453 (47.8)	130 (35.3)	123 (45.2)	113 (57.4)	87 (79.1)
Abdominal surgery without bowel resection	166 (17.5)	59 (16.0)	48 (17.6)	43 (21.8)	16 (14.5)
Prior bowel resection	326 (34.4)	177 (48.1)	101 (37.1)	41 (20.8)	7 (6.4)
NA	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker, n (%)	94 (9.9)	56 (15.2)	26 (9.6)	7 (3.6)	5 (4.5)
ASA Status, n (%)		000 (00 0)	4.45 (50.0)	404/54 0)	
1-2	529(55.9)	222 (60.3)	145 (53.3)	101(51.3)	61(55.5)
3-5 NA	417(44.0)	146 (39.7)	126 (46.3)	96 (48.7)	49(44.5)
INA Redu Mass Index, median (Q1, Q2)	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Body Mass muex, median (QT-Q3)	24.20 (21.43-27.70)	(21.00-27.38)	$(21 \Lambda A_{-} 27 \Lambda A)$	24.00 (22.32-28.00)	24.27 (21 17-27 87)
Weight Loss >10% Body Weight n (%)	128 (13 5)	55 (1/ 0)	20 (10 7)	23 (11 7)	(21.14-27.07) 21 (10.1)
Pre-On LOS median days n (%)	120 (13.3)	55 (14.5)	23 (10.7)	23(11.7)	21 (13.1)
	722 (76 2)	304 (82 6)	203 (74 6)	156 (79 2)	59 (53 6)
1-3	90 (9.5)	30 (8 2)	28 (10.3)	18 (9 1)	14 (12 7)
≥4	132 (13.9)	34 (9.2)	39 (14.3)	23 (11.7)	36 (32.7)
NA	3 (0.3)	0(0.0)	2 (0.7)	0 (0.0)	1 (0.9)
Outside Hospital Transfer, n (%)	36 (3.8)	10 (2.7)	12 (4.4)	4 (2.0)	10 (9.1)
Prior hospital admission within 30 days, n (%)	167 (17.6)	67 (18.2)	50 (18.4)	17 (8.6)	33 (30.0)
Associated Comorbidity, n (%)	- (-/	- (- /		(
Anemia or other blood disease	251 (26.5)	115 (31.2)	52 (19.1)	51 (25.9)	33 (30.0)
Depression	160 (16.9)	64 (17.4)	48 (17.6)	29 (14.7)	19 (17.3)
Hypertension	114 (12.0)	38 (10.3)	25 (9.2)	34 (17.3)	17 (15.5)
Osteoarthritis/Degenerative arthritis	86 (9.1)	37 (10.1)	24 (8.8)	18 (9.1)	7 (6.4)
History of deep vein thrombosis	54 (5.7)	15 (4.1)	11 (4.0)	19 (9.6)	9 (8.2)
Heart disease	38 (4.0)	9 (2.4)	8 (2.9)	16 (8.1)	5 (4.5)
Rheumatoid Arthritis	37 (3.9)	21 (5.7)	6 (2.2)	9 (4.6)	1 (0.9)
Diabetes	34 (3.6)	10 (2.7)	7 (2.6)	12 (6.1)	5 (4.5)
Kidney disease	31 (3.3)	14 (3.8)	2 (0.7)	11 (5.6)	4 (3.6)
History of cancer	30 (3.2)	12 (3.3)	6 (2.2)	12 (6.1)	0 (0.0)
Lung disease	24 (2.5)	8 (2.2)	6 (2.2)	5 (2.5)	5 (4.5)
	21 (2.2)	9 (2.4)	2 (0.7)	6 (3.0)	4 (3.6)
History of pulmonary embolus	20 (2.1)	4 (1.1)	5 (1.8)	8 (4.1)	3 (2.7)
Self-Administered Comorbidity Score, n (%)	207 (24 5)	100 (00 0)	111 (11 0)		20 (25 5)
	327 (34.5)	120 (32.6)	114 (41.9)	54 (27.4)	39 (35.5)
1-2	400 (49.1)	1/5 (47.6)	123 (45.2)		57 (51.8) 14 (12.7)
	1 (0 1)	1 (0 2)	0 (0 0)	0 (0 0)	0 (0 0)
	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)

Pre-Op Disease Features/Intervention, n (%)					
TPN	54 (5.7)	20 (5.4)	22 (8.1)	5 (2.5)	7 (6.4)
Fever	33 (3.5)	6 (1.6)	14 (5.1)	2 (1.0)	11 (10.0)
Clostridium difficile infection	27 (2.9)	9 (2.4)	4 (1.5)	3 (1.5)	11 (10.0)
Non-abdominal infection	44 (4.6)	18 (4.9)	14 (5.1)	6 (3.0)	6 (5.5)
Abscess	98 (10.3)	55 (14.9)	40 (14.7)	2 (1.0)	1 (0.9)
Abscess drainage	43 (4.5)	26 (7.1)	15 (5.5)	0 (0.0)	2 (1.8)
Toxic megacolon or free perforation	28 (3.0)	14 (3.8)	7 (2.6)	4 (2.0)	3 (2.7)
Pre-Op Hemoglobin (g/dL), median (Q1-Q3)	12.30	12.50	12.40	12.20	11.40
	(10.78-13.83)	(10.90-13.90)	(10.90-13.90)	(11.20-14.00)	(9.65-12.90)
Pre-Op White Blood Cells (/mm ³), median (Q1-Q3)	7900	8100	7600	8039	8699
	(6100-10300)	(6200-10300)	(6000-10190)	(6100-10450)	(6700-11100)
Pre-Op Platelets (/mm ³), median (Q1-Q3)	308500	304000	291000	312000	381000
	(240000-	(244250-	(234500-	(231000-	(281000-
	389000)	373000)	371750)	395000)	471500)
Pre-Op Albumin (g/dL), median (Q1-Q3)	3.80	3.90	3.85	3.95	3.50
	(3.30-4.20)	(3.40-4.20)	(3.40-4.20)	(3.42-4.30)	(2.80-3.98)
Pre-Op creatinine (mg/dL), median (Q1-Q3)	0.80	0.80	0.80	0.80	0.80
	(0.70-1.00)	(0.70-1.00)	(0.70-0.90)	(0.70-1.00)	(0.70-0.95)

TNFi – tumor necrosis factor inhibitor; UC – ulcerative colitis; CD – Crohn's disease; NA – not available; GI – gastrointestinal; ASA – American Society of Anesthesiologists physical status classification; Pre-Op – preoperative; LOS – length of stay; TPN – total parenteral nutrition

-ν – preoperative; LC

Table 2. Preoperative Medication Exposures

		Crohn's	Disease	Ulcerative	e colitis
		TNFi use withi	n 12 weeks of	TNFi use within 12 weeks	
		surg	jery	of surgery	
	Overall	No	Yes	No	Yes
	(n=947)	(n=368)	(n=272)	(n=197)	(n=110)
Budesonide, n (%)	108 (11.4)	46 (12.5)	36 (13.2)	18 (9.1)	8 (7.3)
Corticosteroids, n (%)	387 (40.9)	128 (34.8)	92 (33.8)	91 (46.2)	76 (69.1)
Stress dose corticosteroids, n (%)	566 (59.8)	208 (56.5)	156 (57.4)	125 (63.5)	77 (70.0)
Thiopurines, n (%)	235 (24.8)	84 (22.8)	87 (32.0)	37 (18.8)	27 (24.5)
Methotrexate, n (%)	74 (7.8)	23 (6.2)	28 (10.3)	13 (6.6)	10 (9.1)
Natalizumab, n (%)	4 (0.4)	4 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
Cyclosporine, n (%)	10 (1.1)	3 (0.8)	1 (0.4)	4 (2.0)	2 (1.8)
Ustekinumab, n (%)	21 (2.2)	15 (4.1)	3 (1.1)	3 (1.5)	0 (0.0)
Vedolizumab, n (%)	136 (14.4)	71 (19.3)	6 (2.2)	50 (25.4)	9 (8.2)
Opioid pain medications, n (%)	321 (33.9)	129 (35.1)	100 (36.8)	56 (28.4)	36 (32.7)
Antibiotics, n (%)	401 (42.3)	171 (46.5)	130 (47.8)	59 (29.9)	41 (37.3)

TNFi - tumor necrosis factor inhibitor

Table 3. Surgery Characteristics of the Cohort

		Crohn's Disease		Ulcerative colitis	
		TNFi use within 12	2 weeks of surgery	TNFi use with	nin 12 weeks of
			0,7	sur	gery
	Overall	No	Yes	No	Yes
	(n=947)	(n=368)	(n=272)	(n=197)	(n=110)
Surgery duration (min), median (Q1-Q3)	180	173	164	210	207
	(124-250)	(120-240)	(120-221)	(140-300)	(148-270)
Surgical timing, n (%)					
Elective/Staged	760 (80.3)	308 (83.7)	217 (79.8)	169 (85.8)	66 (60.0)
Semi-Urgent	170 (18.0)	56 (15.2)	49 (18.0)	24 (12.2)	41 (37.3)
Urgent/Emergent	14 (1.5)	3 (0.8)	5 (1.8)	4 (2.0)	2 (1.8)
NA	3 (0.3)	1 (0.3)	1 (0.4)	0 (0.0)	1 (0.9)
Surgical Approach, n (%)					
Laparoscopic	605 (63.9)	197 (53.5)	164 (60.3)	153 (77.7)	91 (82.7)
Laparoscopic converted to open	110 (11.6)	61 (16.6)	33 (12.1)	10 (5.1)	6 (5.5)
Open	231 (24.4)	110 (29.9)	74 (27.2)	34 (17.3)	13 (11.8)
NA	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Bowel prep used, n (%)	510 (53.9)	200 (54.3)	143 (52.6)	107 (54.3)	60 (54.5)
Surgical wound protector used, n (%)	638 (67.4)	244 (66.3)	186 (68.4)	127 (64.5)	81 (73.6)
Bowel Resection Performed, n (%)	905 (95.6)	354 (96.2)	254 (93.4)	190 (96.4)	107 (97.3)
Anastomosis created, n (%)	584 (61.7)	275 (74.7)	218 (80.1)	70 (35.5)	21 (19.1)
Anastomosis type, n (%)					
None	363 (38.3)	93 (25.3)	54 (19.9)	127 (64.5)	89 (80.9)
Hand-Sewn	173 (18.3)	78 (21.2)	68 (25.0)	21 (10.7)	6 (5.5)
Stapled	410 (43.3)	197 (53.5)	149 (54.8)	49 (24.9)	15 (13.6)
NA	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Ileocolic resection, n (%)	446 (47.1)	242 (65.8)	195 (71.7)	8 (4.1)	1 (0.9)
Segmental small bowel only or colon resection	185 (19.5)	98 (26.6)	65 (23.9)	19 (9.6)	3 (2.7)
only, n (%)					
Colectomy, n (%)	330 (34.8)	46 (12.5)	17 (6.2)	164 (83.2)	103 (93.6)
Pouch created, n (%)	78 (8.2)	1 (0.3)	1 (0.4)	58 (29.4)	18 (16.4)
Genitourinary Fistula Repair, n (%)	25 (2.6)	12 (3.3)	12 (4.4)	1 (0.5)	0 (0.0)
Internal Fistula Repair, n (%)	77 (8.1)	42 (11.4)	34 (12.5)	0 (0.0)	1 (0.9)
Cutaneous Fistula Repair, n (%)	28 (3.0)	18 (4.9)	8 (2.9)	2 (1.0)	0 (0.0)
Surgical abscess drainage, n (%)	70 (7.4)	31 (8.4)	36 (13.2)	3 (1.5)	0 (0.0)
Stricturoplasty performed, n (%)	32 (3.4)	16 (4.3)	16 (5.9)	0 (0.0)	0 (0.0)
Stoma formed or revised, n (%)	454 (47.9)	120 (32.6)	66 (24.3)	167 (84.8)	101 (91.8)
Incidental appendectomy, n (%)	292 (30.8)	83 (22.6)	81 (29.8)	78 (39.6)	50 (45.5)
Surgical blood loss, n (%)					
≤ 50 mL	459 (48.5)	170 (46.2)	144 (52.9)	88 (44.7)	57 (51.8)
51-250	373 (39.4)	148 (40.2)	98 (36.0)	78 (39.6)	49 (44.5)
> 250 mL	115 (12.1)	50 (13.6)	30 (11.0)	31 (15.7)	4 (3.6)
Peri-operative blood transfusion (units), n (%)					
0	894 (94.4)	352 (95.7)	254 (93.4)	187 (94.9)	101 (91.8)
1-3	46 (4.9)	14 (3.8)	15 (5.5)	8 (4.1)	9 (8.2)
≥4	7 (0.7)	2 (0.5)	3 (1.1)	2 (1.0)	0 (0.0)
Intra-Operative hypotension, n (%)	357 (37.7)	144 (39.1)	108 (39.7)	69 (35.0)	36 (32.7)
Highest Intra-Operative Heart rate, median (Q1-	110 (97-120)	110 (96-120)	110 (95- 120)	108 (95-120)	112 (100-122)
Q3)					
Ureteral Stent Placed, n (%)	115 (12.1)	51 (13.9)	29 (10.7)	27 (13.7)	8 (7.3)
Post-Op Blood Sugar ≥ 200 mg/dL, n (%)	47 (5.0)	11 (3.0)	15 (5.5)	11 (5.6)	10 (9.1)
Foley Catheter > 24 hrs Post-Op, n (%)	411 (43.4)	166 (45.1)	95 (34.9)	101 (51.3)	49 (44.5)

TNFi - tumor necrosis factor inhibitor; NA - not available Post-Op - postoperative

Predictor	OR Any	95% CI	p-value
	Infection		-
TNFi use within 12 weeks of surgery	1.050	0.716-1.535	0.80
Age	1.014	1.001-1.027	0.034
Male gender	0.878	0.604-1.275	0.49
Pre-Op Corticosteroids	1.836	1.258-2.687	0.002
Pre-Op Budesonide	0.403	0.189-0.785	0.012
UC/Indeterminate colitis	0.883	0.564-1.369	0.58
Prior Bowel Resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	0.665	0.356-1.192	0.18
Yes bowel resection	2.614	1.653-4.169	<0.001
Genitourinary Fistula	3.654	1.394-9.335	0.007
Current smoking	1.976	1.147-3.352	0.013
Anemia or other Blood disorder	1.775	1.187-2.641	0.005
Ureteral Stent	1.994	1.194-3.282	0.007
Diabetes	3.310	1.448-7.425	0.004
Pre-Op TPN	1.967	0.977-3.829	0.051
Pre-Op Non-Abdominal Infection	2.397	1.158-4.824	0.016
Depression	1.697	1.070-2.661	0.023
Rheumatoid Arthritis	2.538	1.062-5.774	0.030
Surgical Approach			
Laparoscopic	REF	REF	
Laparoscopic convert to open	1.354	0.768-2.345	0.29
Open	0.626	0.382-1.013	0.060

Table 4. Multivariable Analysis of Risk Factors for Any Infection Postoperatively using PatientReported TNFi Exposure

OR – Odds Ratio; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; UC – ulcerative colitis; Pre-Op – Preoperative; TPN – total parenteral nutrition

Predictor	OR SSI	95% CI	p-value
TNFi use within 12 weeks of surgery	1.249	0.793-1.960	0.34
Age	1.010	0.994-1.027	0.22
Male gender	1.172	0.744-1.856	0.49
Pre-Op Corticosteroids	2.525	1.587-4.056	<0.001
UC/Indeterminate colitis	0.650	0.282-1.576	0.32
Prior Bowel Resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	0.971	0.465-1.933	0.94
Yes bowel resection	2.465	1.410-4.358	0.002
Diabetes	3.491	1.403-8.358	0.006
Hypertension	1.956	1.011-3.702	0.042
IBD Disease Behavior			
Neither stricturing or penetrating	REF	REF	
Penetrating only	1.768	0.741-4.412	0.21
Stricturing only	0.847	0.385-1.975	0.69
Stricturing and penetrating	0.542	0.216-1.388	0.19
Surgical Approach			
Laparoscopic	REF	REF	
Laparoscopic convert to open	1.809	0.929-3.436	0.075
Open	0.884	0.487-1.578	0.68
Current smoking	2.695	1.431-4.936	0.002
Anemia or other Blood Disorder	1.469	0.892-2.385	0.12
Ureteral Stent	1.825	0.978-3.300	0.051
Pre-Op Ustekinumab	2.585	0.800-7.571	0.093

Table 5. Multivariable Analysis of Risk Factors for Surgical Site Infection Postoperatively using Patient Reported TNFi Exposure

OR – Odds Ratio; SSI – surgical site infection; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; UC – ulcerative colitis; Pre-Op – Preoperative; IBD – inflammatory bowel disease; TPN – total parenteral nutrition

Outcomes	Patient Rep TNFi Use	ported		Serum TNF Detectable (below commercial assay lower limit of quantitation threshold, never on a TNFi, or no TNFi within 180 days of surgery)			Serum TNF (level = 0, ne TNFi, or no 180 days of	Detectable ever on a TNFi within surgery)	
	No N (9()	Yes	p-		Yes	p-		Yes	p-
	IN (%)	IN (%)	value	IN (%)	IN (%)	value	IN (%)	IN (%)	value
Readmission	110	65	0.340	98	31	0.315	93	36	0.307
	(19.5)	(17.0)		(18.0)	(14.6)		(18.1)	(14.8)	
Reoperation	32	15	0.227	32	7	0.208	30	9	0.285
	(5.7)	(3.9)		(5.9)	(3.3)		(5.8)	(3.7)	
Thrombosis	8	14	0.024	13	6	0.931	10	9	0.234
	(1.4)	(3.7)		(2.4)	(2.8)		(1.9)	(3.7)	
Hypomotility	60	39	0.840	63	22	0.731	58	27	1
	(10.6)	(10.2)		(11.6)	(10.3)		(11.3)	(11.1)	
Length of Stay,	5.82	6.06	0.451	5.98	6.08	0.808	5.94	6.13	0.631
mean (SD)	(4.03)	(5.12)		(4.25)	(5.35)		(4.18)	(5.37)	

Table 6. Non-Infectious Postoperative Outcomes by TNFi Exposure Type

TNFi - tumor necrosis factor inhibitor

 Image: start in the start

2/24/2022

А



Frequency of Surgical Site Infection Type by Patient Reported TNFi Exposure

В



2/24/2022

С



Frequency of Surgical Site Infection Type by Serum TNFi Exposure (Undetectable = Level 0 or no TNFi within 180 days)

What You Need to Know:

Background and Context:

The postoperative infectious risk of preoperative tumor necrosis factor inhibitor use has been controversial due to the lack of large prospective cohort studies allowing for control of confounding risk factors and limited studies exploring exposure defined by serum drug concentrations.

New Findings:

In the largest multicenter prospective surgical cohort on the topic, PUCCINI showed that neither patient reported use of tumor necrosis factor inhibitors within 12 weeks of surgery nor detectable serum drug concentrations were independent risk factors for any postoperative infection or surgical site infection.

Limitations:

Study limitations include non-consecutive patient enrollment as well as the fact that our observations may already reflect prejudice in surgical decision making such as approach and timing of surgery.

Impact:

Preoperative use of tumor necrosis factor inhibitors should not affect surgical decisions in most inflammatory bowel disease patients

Lay summary:

In the largest multicenter prospective surgical cohort on the topic, PUCCINI showed that preoperative tumor necrosis factor inhibitor use was not associated with any postoperative infections, including surgical site infections.

Supplementary Table Legends:

Supplementary Table 1. Postoperative Infectious Outcomes by TNFi Exposure Type

Supplementary Table 2. Sensitivity Analysis for Postoperative Infectious Outcomes by Serum TNFi Exposure

Supplementary Table 3. Univariable logistic regression for risk factors associated with any infection Supplementary Table 4. Multivariable analysis of risk factors for any infection postoperatively using serum TNFi exposure with undetectable defined as below commercial assay lower limit of quantitation threshold, never on a TNFi, or no TNFi within 180 days of surgery

Supplementary Table 5. Multivariable analysis of risk factors for any infection postoperatively using serum TNFi exposure with undetectable defined as level = $0 \mu g/mL$, never on a TNFi, or no TNFi within 180 days of surgery

Supplementary Table 6. Multivariable analysis of risk factors for any infection postoperatively using Serum TNF quartile analysis with undetectable defined as level = $0 \mu g/mL$, never on a TNFi, or no TNFi within 180 days of surgery

Supplementary Table 7. Univariable logistic regression for risk factors associated with surgical site infection

Supplementary Table 8. Multivariable analysis of risk factors for Surgical Site Infection postoperatively using serum TNFi exposure with undetectable defined as below commercial assay lower limit of quantitation threshold, never on a TNFi, or no TNFi within 180 days of surgery Supplementary Table 9. Multivariable analysis of risk factors for Surgical Site Infection postoperatively using serum TNFi exposure with undetectable defined as level = 0 μ g/mL, never on a TNFi, or no TNFi within 180 days of surgery

Supplementary Table 10. Multivariable analysis of risk factors for Surgical Site Infection postoperatively using Serum TNF quartile analysis with undetectable defined as level = $0 \mu g/mL$, never on a TNFi, or no TNFi within 180 days of surgery

Outcomes	Patient Repo Use	orted TNFi	p- value	Serum TNF Detectable (below commercial assay lower limit of quantitation threshold, never on a TNFi, or no TNFi within 180 days of surgery)		p- value	Serum TNF Detectable (level = 0 µg/mL, never on a TNFi, or no TNFi within 180 days of surgery)		p- value
	No	Yes,		No,	Yes,		No,	Yes,	
	(n=565),	(n=382)		(n=544)	(n=213)		(n=513)	(n=244)	
	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Any Infection	114 (20.2)	69 (18.1)	0.469	107 (19.7)	40 (18.8)	0.873	103 (20.1)	44 (18.0)	0.861
SSI	71 (12.6)	46 (12.0)	0.889	64 (11.8)	27 (12.7)	0.814	62 (12.1)	29 (11.9)	0.998
Organ Space SSI	30 (5.3)	16 (4.2)	0.527	26 (4.8)	7 (3.3)	0.485	26 (5.1)	7 (2.9)	0.233
Deep incisional SSI	11 (1.9)	6 (1.6)	0.859	9 (1.7)	5 (2.3)	0.733	9 (1.7)	5 (2.0)	0.999
Superficial Incisional SSI	30 (5.3)	24 (6.3)	0.624	29 (5.3)	15 (7.0)	0.457	27 (5.2)	17 (7.0)	0.431
Non-SSI	47 (8.3)	26 (6.8)	0.464	47 (8.6)	15 (7.0)	0.578	45 (8.8)	17 (7.0)	0.491
Sepsis	4 (0.7)	1 (0.3)	0.637	4 (0.7)	1 (0.5)	0.454	3 (0.6)	2 (0.8)	0.391
Bacteremia	3 (0.5)	0 (0)	0.888	2 (0.4)	0 (0)	0.943	2 (0.4)	0 (0)	0.873
Pneumonia	5 (0.9)	0 (0)	0.861	4 (0.7)	0 (0)	0.872	4 (0.8)	0 (0)	0.873
Urinary Tract Infection	18 (3.2)	11 (2.9)	0.939	19 (3.5)	8 (3.8)	0.823	18 (3.5)	9 (3.7)	0.983
Fever > 101.5 F	1 (0.2)	3 (0.8)	0.365	1 (0.2)	2 (0.9)	0.397	1 (0.2)	2 (0.8)	0.507
Other	16 (2.8)	11 (2.9)	0.993	17 (3.1)	4 (1.9)	0.495	17 (3.3)	4 (1.6)	0.286

Supplementary Table 1. Postoperative Infectious Outcomes by TNFi Exposure Type

TNFi – tumor necrosis factor inhibitor; TNF – tumor necrosis factor; SSI – surgical site infection

Supplementary Table 2. Sensitivity Analysis for Postoperative Infectious Outcomes by Serum TNFi Exposure

Outcomes	Serum TNF (below comr assay lower quantitation never on a T TNFi within surgery)	Detectable nercial limit of threshold, 'NFi, or no 120 days of	p- value	Serum TNF Detectable (level = 0 µg/mL, never on a TNFi, or no TNFi within 120 days of surgery)		p- value
	No, (n=572)	Yes,		No, (n=541)	Yes,	
	(II=572) N (%)	(II=213) N (%)		(n=541) N (%)	(1=244) N (%)	
Any Infection	112 (19.6)	40 (18.8)	0.891	108 (20.0)	44 (18.0)	0.604
SSI	65 (11.4)	27 (12.7)	0.684	63 (11.6)	29 (11.9)	0.999
Organ Space SSI	26 (4.5)	7 (3.3)	0.567	26 (4.8)	7 (2.9)	0.294
Deep incisional SSI	10 (1.7)	5 (2.3)	0.796	10 (1.8)	5 (2.0)	0.999
Superficial Incisional SSI	29 (5.1)	15 (7.0)	0.365	27 (5.0)	17 (7.0)	0.337
Non-SSI	51 (8.9)	15 (7.0)	0.494	49 (9.1)	17 (7.0)	0.411
Sepsis	4 (0.7)	1 (0.5)	0.345	3 (0.6)	2 (0.8)	0.821
Bacteremia	2 (0.4)	0 (0)	0.953	2 (0.4)	0 (0)	0.954
Pneumonia	5 (0.9)	0 (0)	0.834	5 (0.9)	0 (0)	0.866
Urinary Tract Infection	19 (3.3)	8 (3.8)	0.932	18 (3.3)	9 (3.7)	0.951
Fever > 101.5 F	1 (0 2)	2 (0.9)	0.37	1 (0 2)	2 (0.8)	0 476
Other	20 (3.5)	4 (1.9)	0.352	20 (3.7)	4 (1.6)	0.182

TNFi - tumor necrosis factor inhibitor; TNF - tumor necrosis factor; SSI - surgical site infection

Predictor	OR	95% CI	p-value
TNFi use within 12 weeks of surgery	0.87	0.62-1.21	0.4
TNFi use within 12 weeks of surgery			
Naïve	REF	REF	REF
Past	0.848	0.559-1.284	0.437
Current	0.805	0.534-1.212	0.300
Serum TNFi detectable (≥commercial assay lower	1.24	0.66-2.39	0.51
limit of quantitation threshold)			
Serum TNFi detectable (>0 µg/mL)	1.06	0.55-2.26	0.81
Serum TNFi			
1 st quartile (undetectable)	REF	REF	
2 nd quartile (0.1-4.4 µg/mL)	1.15	0.15-4.83	0.91
3 rd quartile (4.5-11.7 μg/mL)	1.01	0.43-2.83	0.68
4 th quartile (>11.7 μg/mL)	0.91	0.64-1.27	0.51
Detectable antibodies to IFX or ADA	0.671	0.23-1.98	0.47
Ulcerative colitis/indeterminate colitis	0.74	0.51-1.05	0.10
Age	1.01	1.00-1.03	0.006
Male Gender	0.89	0.64-1.22	0.5
Disease Duration (years)	1.02	1.00-1.03	0.012
Disease Location			
Crohn's colitis	REF	REF	
Crohn's ileitis	0.51	0.28-0.95	0.030
Crohn's ileocolitis	0.99	0.58-1.75	>0.9
UC Proctitis	0.38	0.06-1.48	0.2
UC Left-Sided	0.52	0.20-1.22	0.15
UC Extensive	0.62	0.35-1.14	0.12
Upper GI Tract CD	1.41	0.62-2.95	0.4
Perianal CD	1.38	0.84-2.19	0.2
IBD Disease Behavior			
Non-stricturing, nonpenetrating	REF	REF	
Stricturing	1.13	0.76-1.66	0.6
Penetrating	1.56	0.93-2.55	0.084
Stricturing and Penetrating	0.88	0.53-1.42	0.6
History of bowel resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without bowel resection	0.94	0.56-1.55	0.8
Prior bowel resection	2.38	1.67-3.40	<0.001
Current smoker	2.14	1.33-3.40	0.001
ASA Status			
1-2	REF	REF	
3-5	1.60	1.16-2.22	0.004
Body Mass Index	1.04	1.01-1.07	0.019
Weight Loss >10% Body Weight	0.80	0.48-1.30	0.4
Pre-Op LOS (days)	1.02	0.97-1.05	0.5
Outside Hospital Transfer	1.20	0.50-2.56	0.7
Prior hospital admission within 30 days	1.35	0.89-2.00	0.15
Associated Comorbidity			
Anemia or other blood disease	1.56	1.10-2.20	0.013
Depression	1.91	1.29-2.81	0.001
Hypertension	1.58	1.00-2.47	0.046
Osteoarthritis/Degenerative arthritis	1.30	0.75-2.16	0.3
Heart disease	2.26	1.10-4.43	0.021
Rheumatoid Arthritis	2.35	1.14-4.65	0.016
Diabetes	3.08	1.49-6.17	0.002
Kianey disease	1.22	0.48-2.75	0.6
History of cancer	1.54	0.63-3.38	0.3
	0.83	0.24-2.23	0.7
Liver disease	1.31	0.42-3.40	0.6
Siomach disease	1.23	0.07-2.10	0.0
Genetic hypercoagulability disorder	1.78	0.50-4.8/	0.3
History of pulmonary ombolies	1.09	0.02-2.00	0.0
Solf Administered Compensities Search	1.42	1 12 1 12	0.0 40 001
Pro On Discasso Easturge/Interview	1.27	1.13-1.43	<0.001
TPN	2.07	1,11-3,71	0.018

Supplementary Table 3. Univariable logistic regression for risk factors associated with any infection

Fever	1.36	0.56-2.93	0.5
Clostridium difficile infection	1.20	0.43-2.84	0.7
Non-abdominal infection	2.51	1.30-4.70	0.005
Abscess	0.87	0.49-1.48	0.6
Abscess drainage	0.80	0.32-1.72	0.6
Toxic meracolon or free perforation	2.03	0.86-4.44	0.087
Cutomagalavirua Infaction	2.00	0.21 6 10	0.007
	1.41	0.21-0.19	0.7
Pre-Op Hemoglobin (g/dL)	0.94	0.87-1.01	0.10
Pre-Op White Blood Cells (/mm ³)	1.00	1.00-1.00	0.7
Pre-Op Platelets (/mm ³)	1.00	1.00-1.00	0.7
Pre-Op Albumin (a/dL)	0.96	0.74-1.26	0.8
Pre-On creatinine (mg/dL)	0.86	0 56-1 10	0.3
Bro On Medication Exposures	0.00	0.00 1.10	0.0
Pie-Op Medication Exposures	0.44	0 22 0 80	0.012
Budesonide	0.44	0.22-0.80	0.013
Corticosteroids	1.36	0.98-1.89	0.061
Stress dose corticosteroids	0.95	0.68-1.34	0.8
Thiopurines	1.18	0.81-1.69	0.4
Methotrexate	1.49	0.84-2.54	0.2
Natalizumab	1.39	0.07-10.9	0.8
Cyclosporine	1.04	0.16-4.20	>0.9
Listekinumah	2.13	0.80-5.19	0.11
Vedelizumeh	0.02	0.57 1 47	0.11
	0.93	0.57-1.47	0.0
Opioid pain medications	1.59	1.14-2.21	0.000
Antibiotics	1.04	0.75-1.44	0.8
Pre-Op antibiotics	1.04	0.75-1.44	0.8
Surgery duration (min)	1.00	1.00-1.00	0.024
Surgical timing			
Flective/Staged	REF	REF	
Semi-Lirgent	1 23	0.81-1.84	0.3
Urgent/Emergent	2.22	1 09 0 70	0.020
	3.32	1.06-9.70	0.029
Surgical Approach		5	
Laparoscopic	REF	REF	
Laparoscopic converted to open	1.85	1.14-2.94	0.010
Open	1.40	0.95-2.03	0.082
Bowel prep used	0.78	0.56-1.10	0.2
Bowel prep used Surgical wound protector used	0.78	0.56-1.10	0.2
Bowel prep used Surgical wound protector used Bowel Resection Performed	0.78 0.90 0.87	0.56-1.10 0.61-1.35 0.43-1.97	0.2 0.6
Bowel prep used Surgical wound protector used Bowel Resection Performed	0.78 0.90 0.87	0.56-1.10 0.61-1.35 0.43-1.97	0.2 0.6 0.7
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created	0.78 0.90 0.87 0.92	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29	0.2 0.6 0.7 0.6
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type	0.78 0.90 0.87 0.92	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29	0.2 0.6 0.7 0.6
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None	0.78 0.90 0.87 0.92 REF	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF	0.2 0.6 0.7 0.6
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn	0.78 0.90 0.87 0.92 REF 0.87	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37	0.2 0.6 0.7 0.6 0.5
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled	0.78 0.90 0.87 0.92 REF 0.87 0.95	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35	0.2 0.6 0.7 0.6 0.5 0.8
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25	0.2 0.6 0.7 0.6 0.5 0.8 0.5
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50	0.2 0.6 0.7 0.6 0.5 0.8 0.5 0.5 >0.9
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Daugh grapted	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 4.28	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.24	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 0.10	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 4 50 7.02	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.2
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 >0.9
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91173	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Inscienced action and determined	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.40.000	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.9 0.03 0.05 0.05 0.2 0.05 0.05 0.2 0.05 0.05 0.2 0.05 0.05 0.2 0.05 0.05 0.05 0.2 0.05 0.05 0.05 0.2 0.05 0.05 0.2 0.05 0.05 0.05 0.2 0.05 0.05 0.05 0.2 0.05 0.05 0.2 0.05 0.05 0.2 0.05 0.2 0.05 0.05 0.2 0.05 0.05 0.05 0.05 0.2 0.05 0.05 0.05 0.2 0.05 0.05 0.05 0.05 0.2 0.05 0.08 0.02 0.03 0.05 0.03 0.05 0.08 0.05 0.08 0.05 0.02 0.03 0.05 0.0
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.281 0.4 0.9 >0.9 0.035 0.2 0.035
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL ≤ 50 mL 51-250	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035 0.091
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL ≤ 1-250 > 250 mL	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035 0.2 0.035 0.2 0.035
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units)	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035 0.091 0.017
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035 0.2 0.091 0.017
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.09 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.2 0.035 0.091 0.091 0.017 0.4
Bowel prep usedSurgical wound protector usedBowel Resection PerformedAnastomosis createdAnastomosis typeNoneHand-SewnStapledIleocolic resectionSegmental small bowel only or colon resection onlyColectomyPouch createdGenitourinary Fistula RepairInternal Fistula RepairCutaneous Fistula RepairSurgical abscess drainageStricturoplasty performedStoma formed or revisedIncidental appendectomySurgical blood loss ≤ 50 mLS1-250> 250 mLPeri-operative blood transfusion (units)01-3> 4	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24 7.08	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.09 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.2 0.035 0.091 0.091 0.017 0.4 0.5 0.4 0.5 0.5 0.5 0.5 0.5 0.5 0.8 0.5 0.5 0.9 0.5 0.9 0.5 0.9 0.2 0.0 0.5 0.9 0.5 0.9 0.5 0.9 0.0 0.0 0.0 0.0 0.0 0.0 0.0
Bowel prep usedSurgical wound protector usedBowel Resection PerformedAnastomosis createdAnastomosis typeNoneHand-SewnStapledIleocolic resectionSegmental small bowel only or colon resection onlyColectomyPouch createdGenitourinary Fistula RepairInternal Fistula RepairCutaneous Fistula RepairSurgical abscess drainageStricturoplasty performedStoma formed or revisedIncidental appendectomySurgical blood loss \leq 50 mL $51-250$ > 250 mLPeri-operative blood transfusion (units)01-3 \geq 4	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70 0.90	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24-7.98 0.70 - 0.00	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.2 0.035 0.2 0.091 0.091 0.017 0.4 0.5 0.5
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70 0.99	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24-7.98 0.70-1.39	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035 0.091 0.017 0.4 0.5 >0.9
Bowel prep usedSurgical wound protector usedBowel Resection PerformedAnastomosis createdAnastomosis typeNoneHand-SewnStapledIleocolic resectionSegmental small bowel only or colon resection onlyColectomyPouch createdGenitourinary Fistula RepairInternal Fistula RepairSurgical abscess drainageStricturoplasty performedStoma formed or revisedIncidental appendectomySurgical blood loss< 50 mL	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70 0.99 1.00	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24-7.98 0.70-1.39 0.99-1.01	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.2 0.091 0.091 0.017 0.4 0.5 >0.9 0.2 0.091 0.017
Bowel prep usedSurgical wound protector usedBowel Resection PerformedAnastomosis createdAnastomosis typeNoneHand-SewnStapledIleocolic resectionSegmental small bowel only or colon resection onlyColectomyPouch createdGenitourinary Fistula RepairInternal Fistula RepairSurgical abscess drainageStricturoplasty performedStoma formed or revisedIncidental appendectomySurgical blood loss≤ 50 mL51-250> 250 mLPeri-operative blood transfusion (units)01-3≥ 4Intra-Operative hypotensionHighest Intra-Operative Heart rateUreteral Stent Placed	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70 0.99 1.00 2.22	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24-7.98 0.70-1.39 0.99-1.01 1.43-3.39	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.2 0.035 0.091 0.091 0.017 0.4 0.5 >0.9 0.7 <0.001
Bowel prep usedSurgical wound protector usedBowel Resection PerformedAnastomosis createdAnastomosis typeNoneHand-SewnStapledIleocolic resectionSegmental small bowel only or colon resection onlyColectomyPouch createdGenitourinary Fistula RepairInternal Fistula RepairCutaneous Fistula RepairSurgical abscess drainageStricturoplasty performedStoma formed or revisedIncidental appendectomySurgical blood loss ≤ 50 mL $51-250$ > 250 mLPeri-operative blood transfusion (units)01-3 ≥ 4 Intra-Operative hypotensionHighest Intra-Operative Heart rateUreteral Stent PlacedPost-Op Blood Sugar ≥ 200 mg/dL	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70 0.99 1.00 2.22 1.79	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24-7.98 0.70-1.39 0.99-1.01 1.43-3.39 0.91-3.37	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.2 0.035 0.2 0.091 0.091 0.091 0.017 0.4 0.5 >0.9 0.7 <0.001 0.080
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension Highest Intra-Operative Heart rate Ureteral Stent Placed Post-Op Blood Sugar ≥ 200 mg/dL Foley Catheter > 24 brs Post-Operatively	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70 0.99 1.00 2.22 1.79 1.34	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24-7.98 0.70-1.39 0.99-1.01 1.43-3.39 0.91-3.37 0.97-1.87	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 0.2 0.035 0.2 0.091 0.091 0.017 0.4 0.5 >0.9 0.7 <0.001 0.080 0.078
Bowel prep used Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension Highest Intra-Operative Heart rate Ureteral Stent Placed Post-Op Blood Sugar ≥ 200 mg/dL Foley Catheter > 24 hrs Post-Operatively	0.78 0.90 0.87 0.92 REF 0.87 0.95 0.90 1.01 1.04 1.38 3.43 0.53 1.41 0.95 0.97 1.25 0.67 REF 1.35 1.81 REF 1.34 1.70 0.99 1.00 2.22 1.79 1.34	0.56-1.10 0.61-1.35 0.43-1.97 0.66-1.29 REF 0.54-1.37 0.66-1.35 0.64-1.25 0.67-1.50 0.74-1.45 0.78-2.34 1.50-7.66 0.24-1.03 0.55-3.21 0.49-1.72 0.36-2.24 0.91-1.73 0.46-0.96 REF 0.95-1.93 1.10-2.91 REF 0.64-2.61 0.24-7.98 0.70-1.39 0.99-1.01 1.43-3.39 0.91-3.37 0.97-1.87	0.2 0.6 0.7 0.6 0.5 0.8 0.5 >0.9 0.8 0.2 0.003 0.081 0.4 0.9 >0.9 >0.9 0.2 0.035 0.091 0.017 0.4 0.5 >0.9 0.7 <0.001 0.080 0.078 0.44 0.5 >0.9 0.7 <0.001 0.080 0.078 0.44 0.5 >0.9 0.7 <0.9 0.7 0.8 0.9 0.15 0.9 0.2 0.035 0.2 0.09 0.2 0.09 0.2 0.09 0.2 0.091 0.017 0.4 0.5 >0.9 0.7 0.003 0.091 0.017 0.4 0.5 0.5 0.9 0.0 0.0 0.0 0.0 0.0 0.0 0.0

OR – Odds Ratio; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; CD – Crohn's disease; UC – ulcerative colitis; GI – gastrointestinal; IBD – inflammatory bowel disease; LOS – length of stay; ASA – American Society of Anesthesiologists physical status classification; Pre-Op – Preoperative; TPN – total parenteral nutrition

Supplementary Table 4. Multivariable analysis of risk factors for any infection postoperatively using serum TNFi exposure with undetectable defined as below commercial assay lower limit of quantitation threshold, never on a TNFi, or no TNFi within 180 days of surgery

Predictor	OR Any	95% CI	p-value
	Infection		P
Serum TNFi			
Undetectable (n=544)	REF	REF	
Detectable (n=213)	1.261	0.794-1.985	0.32
Age	1.015	1.001-1.030	0.030
Male gender	0.891	0.590-1.348	0.58
Pre-Op Corticosteroids	1.747	1.140-2.684	0.011
Pre-Op Budesonide	0.482	0.212-1.004	0.057
UC/Indeterminate colitis	0.819	0.500-1.323	0.42
Prior Bowel Resection			.
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	0.644	0.315-1.247	0.21
Yes bowel resection	2.226	1.388-3.605	<0.001
Pre-Op Non-Abdominal Infection	3.032	1.321-6.731	0.007
Ureteral Stent	2.470	1.408-4.278	0.001
Rheumatoid Arthritis	3.280	1.179-8.732	0.019
ASA Status			
1-2	REF	REF	
3-5	1.357	0.897-2.054	0.15
Diabetes	2.666	1.096-6.325	0.027
Genitourinary Fistula	2.804	0.952-7.915	0.054
Depression	1.867	1.110-3.094	0.017

OR – Odds Ratio; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; Pre-Op – Preoperative; UC – ulcerative colitis; ASA – American Society of Anesthesiologists physical status classification

Supplementary Table 5. Multivariable analysis of risk factors for any infection postoperatively using serum TNFi exposure with undetectable defined as level = $0 \mu g/mL$, never on a TNFi, or no TNFi within 180 days of surgery

Predictor	OR Any	95% CI	p-value
	Infection		-
Serum TNFi			
Undetectable (n=513)			
Detectable (n=244)	1.123	0.718-1.743	0.61
Age	1.015	1.001-1.030	0.032
Male gender	0.896	0.593-1.354	0.60
Pre-Op Corticosteroids	1.754	1.144-2.697	0.010
Pre-Op Budesonide	0.483	0.214-1.002	0.058
UC/Indeterminate colitis	0.806	0.492-1.301	0.38
Prior Bowel Resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	0.649	0.318-1.255	0.21
Yes bowel resection	2.205	1.375-3.571	0.001
Pre-Op Non-Abdominal Infection	3.015	1.314-6.685	0.007
Ureteral Stent	2.448	1.397-4.234	0.001
Rheumatoid Arthritis	3.224	1.156-8.592	0.021
Diabetes	2.662	1.095-6.315	0.027
Genitourinary Fistula	2.737	0.934-7.685	0.058
ASA Status			
1-2	REF	REF	
3-5	1.360	0.899-2.059	0.14
Depression	1.868	1.111-3.096	0.016
Anemia or other Blood Disorder	1.708	1.094-2.653	0.018

OR – Odds Ratio; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; Pre-Op – Preoperative; UC – ulcerative colitis; ASA – American Society of Anesthesiologists physical status classification

Supplementary Table 6. Multivariable analysis of risk factors for any infection postoperatively using Serum TNF quartile analysis with undetectable defined as level = 0 μ g/mL, never on a TNFi, or no TNFi within 180 days of surgery

Predictor	OR Any	95% CI	p-value
	Infection		
Serum TNFi			
1 st quartile (undetectable) (n=513)	REF	REF	
2 nd quartile (0.1-4.4 µg/mL) (n=82)	0.983	0.456-1.984	0.96
3 rd quartile (4.5-11.7 µg/mL) (n=81)	1.087	0.510-2.187	0.82
4 th quartile (>11.7 μg/mL) (n=81)	1.051	0.463-2.230	0.90
Age	1.017	1.002-1.033	0.025
Male gender	0.925	0.589-1.456	0.74
Pre-Op Corticosteroids	1.840	1.148-2.957	0.011
Pre-Op Budesonide	0.630	0.277-1.306	0.24
UC/Indeterminate colitis	0.841	0.486-1.430	0.53
Prior Bowel Resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	0.663	0.304-1.360	0.28
Yes bowel resection	2.155	1.285-3.656	0.004
Pre-Op Non-Abdominal Infection	3.735	1.530-8.916	0.003
Ureteral Stent	1.979	1.091-3.527	0.022
Rheumatoid Arthritis	5.387	1.920-15.02	0.001
Surgical Timing			
Elective/Staged	REF	REF	
Semi-urgent	1.200	0.666-2.106	0.53
Urgent/emergent	7.045	1.674-31.29	0.007
Diabetes	3.569	1.494-8.442	0.004
Genitourinary Fistula	3.496	1.135-10.37	0.025
Anemia or other Blood Disorder	1.509	0.924-2.446	0.10

OR – Odds Ratio; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; Pre-Op – Preoperative; UC – ulcerative colitis

Predictor	OR SSI	95% CI	p-value
TNFi use within 12 weeks of surgery	0.95	0.64-1.41	0.8
TNFi use within 12 weeks of surgerv			
Naïve	REF	REF	REF
Past	1.02	0.612-1.689	0.948
Current	0.98	0.592-1.615	0.930
Serum TNFi detectable (>commercial assav lower	2.13	0.92-5.44	0.091
limit of quantitation threshold)	2.10	0.02 0.44	0.001
Sorum TNEi detectable (S0 µg/mL)	1.08	0 78 5 06	0.202
	1.90	0.70-3.90	0.202
1 st quartile (undetectable)	KEF 0.00		
2^{rd} quartile (0.1-4.4 µg/mL)	0.92	0.03-5.12	0.921
3^{rd} quartile (4.5-11.7 µg/mL)	1.05	0.49-1.25	0.823
4 ^{···} quartile (>11.7 μg/mL)	1.09	0.70-1.59	0.711
Detectable antibodies to IFX or ADA	0.587	0.14-2.54	0.48
Ulcerative colitis	0.69	0.44-1.06	0.10
Age	1.01	1.00-1.03	0.02
Male Gender	1.08	0.73-1.60	0.7
Disease Duration (years)	1.01	1.00-1.03	0.10
Disease Location			
Crohn's colitis	REF	REF	
Crohn's ileitis	0.67	0.33-1.42	0.3
Crohn's ileocolitis	1.09	0.58-2.20	0.8
UC Proctitis	0.34	0.02-1.91	0.3
UC Left-Sided	0.58	0.18-1.66	0.3
UC Extensive	0.70	0.34-1.47	0.3
Lipper GLTract CD	1 15	0 39-2 78	0.8
Porianal CD	1.10	1 00 2 10	0.0
	1.07	1.08-3.10	0.019
IBD Disease Benavior	DEE		
Non-stricturing, nonpenetrating	KEF 4.40		0.5
Stricturing	1.18	0.73-1.90	0.5
Penetrating	2.18	1.23-3.80	0.006
Stricturing and Penetrating	0.82	0.43-1.49	0.5
Prior abdominal surgery			
No prior abdominal surgery	REF	REF	
Abdominal surgery without bowel resection	1.08	0.56-1.99	0.8
Prior bowel resection	2.67	1.74-4.13	<0.001
Current smoker	2.44	1.42-4.06	<0.001
ASA Status			
1-2	REF	REF	
3-5	1.29	0.87-1.90	0.2
Body Mass Index	1.03	1.00-1.07	0.071
Weight Loss >10% Body Weight	0.78	0.41-1.39	0.4
Pre-Op LOS (davs)	1.01	0.96-1.06	0.6
Outside Hospital Transfer	0.88	0 26-2 28	0.8
Prior hospital admission within 30 days	1 24	0 75-1 98	0.4
Associated Comorbidity		0.10 1.00	V. 1
Anemia or other blood discose	1.66	1 10-2 /0	0.015
Depression	1.00	1.10-2.45	0.013
	2.10	1.00-2.01	0.032
Appendension	2.12	1.20-3.45	0.003
	1.29	0.07-2.34	0.4
	1.7.50	1.00-4.81	0.035
Rheumatoia Arthritis	1.00	0 54 0 40	
Diabetes	1.39	0.51-3.19	0.5
	1.39 3.64	0.51-3.19 1.66-7.51	0.5 <0.001
Kidney disease	1.39 3.64 1.38	0.51-3.19 1.66-7.51 0.46-3.38	0.5 <0.001 0.5
Kidney disease History of cancer	1.39 3.64 1.38 1.81	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26	0.5 < 0.001 0.5 0.2
Kidney disease History of cancer Lung disease	1.39 3.64 1.38 1.81 0.30	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45	0.5 < 0.001 0.5 0.2 0.2
Kidney disease History of cancer Lung disease Liver disease	1.39 3.64 1.38 1.81 0.30 1.19	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45 0.27-3.57	0.5 < 0.001 0.5 0.2 0.2 0.8
Kidney disease History of cancer Lung disease Liver disease Stomach disease	1.39 3.64 1.38 1.81 0.30 1.19 1.33	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45 0.27-3.57 0.64-2.52	0.5 <0.001 0.5 0.2 0.2 0.8 0.4
Kidney disease History of cancer Lung disease Liver disease Stomach disease Genetic hypercoagulability disorder	1.39 3.64 1.38 1.81 0.30 1.19 1.33 1.56	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45 0.27-3.57 0.64-2.52 0.36-4.86	0.5 <0.001 0.5 0.2 0.2 0.8 0.4 0.5
Kidney disease History of cancer Lung disease Liver disease Stomach disease Genetic hypercoagulability disorder History of deep vein thrombosis	1.39 3.64 1.38 1.81 0.30 1.19 1.33 1.56 1.08	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45 0.27-3.57 0.64-2.52 0.36-4.86 0.44-2.30	0.5 <0.001 0.5 0.2 0.2 0.8 0.4 0.5 0.9
Kidney disease History of cancer Lung disease Liver disease Stomach disease Genetic hypercoagulability disorder History of deep vein thrombosis History of pulmonary embolus	1.39 3.64 1.38 1.81 0.30 1.19 1.33 1.56 1.08 1.81	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45 0.27-3.57 0.64-2.52 0.36-4.86 0.44-2.30 0.51-5.05	0.5 <0.001 0.5 0.2 0.8 0.4 0.5 0.9 0.3
Kidney disease History of cancer Lung disease Liver disease Stomach disease Genetic hypercoagulability disorder History of deep vein thrombosis History of pulmonary embolus Self-Administered Comorbidity Score	1.39 3.64 1.38 1.81 0.30 1.19 1.33 1.56 1.08 1.81 1.24	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45 0.27-3.57 0.64-2.52 0.36-4.86 0.44-2.30 0.51-5.05 1.08-1.42	0.5 <0.001 0.5 0.2 0.8 0.4 0.5 0.9 0.3 0.002
Kidney disease History of cancer Lung disease Liver disease Stomach disease Genetic hypercoagulability disorder History of deep vein thrombosis History of pulmonary embolus Self-Administered Comorbidity Score Pre-Op Disease Features/Intervention	1.39 3.64 1.38 1.81 0.30 1.19 1.33 1.56 1.08 1.81 1.24	0.51-3.19 1.66-7.51 0.46-3.38 0.66-4.26 0.02-1.45 0.27-3.57 0.64-2.52 0.36-4.86 0.44-2.30 0.51-5.05 1.08-1.42	0.5 <0.001 0.5 0.2 0.8 0.4 0.5 0.9 0.3 0.002

Supplementary Table 7. Univariable logistic regression for risk factors associated with surgical site infection

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Fever	1.60	0.59-3.72	0.3
Clostridium difficile infection	1.64	0.54-4.09	0.3
Non-abdominal infection	1.62	0.68-3.40	0.2
Abscess	0.90	0.44-1.67	0.8
Abscess drainage	0.93	0.31-2.20	0.9
Toxic megacolon or free perforation	1.19	0.34-3.15	0.8
Cytomegalovirus Infection	1.04	0.06-5.91	>0.9
Pre-On Hemoglobin (g/dl.)	0.96	0.87-1.05	03
Pre-Op White Blood Cells (/mm ³)	1.00	1 00-1 00	0.8
Pro On Plotolete (/mm ³)	1.00	1.00-1.00	0.0
	1.00	1.00-1.00	>0.9
Pre-Op Albumin (g/dL)	1.08	0.79-1.50	0.6
Pre-Op creatinine (mg/dL)	0.91	0.56-1.18	0.6
Pre-Op Medication Exposures			
Budesonide	0.54	0.23-1.07	0.10
Corticosteroids	1.56	1.06-2.30	0.025
Stress dose corticosteroids	0.87	0.58-1.31	0.5
Thionurines	0.80	0 49-1 26	0.4
Methotrevate	1 42	0.71-2.63	0.3
Notolizumoh	1.42	0.12.19.7	0.5
Natalizumad	2.37	0.12-10.7	0.5
Cyclosporine	1.78	0.27-7.23	0.5
Ustekinumab	2.93	1.03-7.38	0.029
Vedolizumab	0.72	0.38-1.28	0.3
Opioid pain medications	1.60	1.08-2.37	0.019
Antibiotics	0.90	0.61-1.34	0.6
Surgery duration (min)	1.00	1 00-1 00	0.13
Surgical timing		1.00 1.00	0.1.0
Elective/Staged	DEE	DEE	
Semi-Orgent	1.02	0.60-1.67	>0.9
Urgent/Emergent	2.90	0.78-8.88	0.077
Surgical Approach			
Laparoscopic	REF	REF	
Laparoscopic converted to open	2.63	1.53-4.42	<0.001
Open	1.68	1.07-2.63	0.023
Rowel propused	0.62	0.41-0.94	0.023
Bowei bieb useu	0.02	0.41-0.34	0.023
Surgical wound protector used	0.81	0.52-1.32	0.4
Surgical wound protector used	0.81	0.52-1.32	0.4
Surgical wound protector used Bowel Resection Performed Apastomocia created	0.81	0.52-1.32 0.28-1.38 0.67-1.49	0.4
Surgical wound protector used Bowel Resection Performed Anastomosis created	0.81 0.58 0.99	0.52-1.32 0.28-1.38 0.67-1.49	0.4 0.2 >0.9
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type	0.81 0.58 0.99	0.52-1.32 0.28-1.38 0.67-1.49	0.4 0.2 >0.9
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None	0.81 0.58 0.99 REF	0.52-1.32 0.28-1.38 0.67-1.49 REF	0.4 0.2 >0.9
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn	0.81 0.58 0.99 REF 0.82	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44	0.4 0.2 >0.9 0.5
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled	0.82 0.81 0.58 0.99 REF 0.82 1.07	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64	0.4 0.2 >0.9 0.5 0.7
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection	0.81 0.58 0.99 REF 0.82 1.07 1.05	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58	0.4 0.2 >0.9 0.5 0.7 0.8
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44	0.4 0.2 >0.9 0.5 0.7 0.8 0.6
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy	0.02 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created	0.02 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 4.26	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.205 66	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.50	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.92 4.00	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.9
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.2
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.6 0.2 0.6 0.2 0.6 0.2 0.5 0.7 0.9 0.5 0.7 0.9 0.5 0.9 0.5 0.9 0.5 0.7 0.9 0.5 0.7 0.9 0.5 0.7 0.9 0.5 0.7 0.9 0.5 0.7 0.8 0.9 0.5 0.7 0.9 0.5 0.7 0.8 0.9 0.12 0.5 0.7 0.2 0.5 0.7 0.9 0.12 0.6 0.2 0.12 0.5 0.7 0.2 0.12 0.5 0.7 0.2 0.12 0.5 0.7 0.2 0.12 0.5 0.7 0.2 0.12 0.15 0.2 0.12 0.15 0.2 0.12 0.15 0.2 0.15 0.2 0.12 0.15 0.2 0.15 0.2 0.12 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.12 0.15 0.2 0.15 0.2 0.12 0.6 0.2 0.15 0.2 0.15 0.2 0.2 0.15 0.2 0.15 0.2 0.2 0.12 0.6 0.2 0.15 0.2 0.2 0.12 0.6 0.2 0.15 0.2 0.2 0.12 0.6 0.2 0.2 0.15 0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.2
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.09 0.6 0.2 0.7 0.8 0.2 0.9 0.5 0.7 0.9 0.5 0.7 0.8 0.9 0.5 0.7 0.8 0.9 0.5 0.7 0.8 0.9 0.5 0.7 0.8 0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.7 0.7 0.8 0.12 0.6 0.2 0.12 0.15 0.7 0.12 0.15 0.7 0.12 0.15 0.7 0.12 0.15 0.7 0.12 0.15 0.7 0.12 0.15 0.7 0.15 0.7 0.12 0.15 0.9 0.12 0.15 0.9 0.15 0.7 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.9 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.12 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.15 0.2 0.2 0.2 0.15 0.2 0.2 0.2 0.2 0.2 0.2 0.2 0.2
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood lose	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.66 0.2 0.75 0.9 0.75 0.9 0.75 0.9 0.75 0.9 0.6 0.2 0.72
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 PEE	0.41-0.34 0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 DEE	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.72
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss \$ 50 mL	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 4.07	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.62-1.62	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.072
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.072 0.3 0.3 0.3
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.072
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL \$250 mL Peri-operative blood transfusion (units)	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.66 0.2 0.15 0.9 0.6 0.2 0.3 0.2
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss \leq 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.3 0.2
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss \leq 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.12
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81 2.97	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.48-2.07 0.48-2.07 0.48-2.07 0.48-2.07 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-14.00	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.072 0.3 0.2 0.12 0.3 0.2 0.12 0.2 0.3 0.2
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4	0.82 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81 2.97 1.15	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-14.00 0.76-1.73	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.72 0.5 0.7 0.5 0.7 0.5 0.5 0.7 0.5 0.7 0.8 0.9 0.12 0.5 0.2 0.15 0.2 0.5 0.7 0.5 0.7 0.5 0.7 0.5 0.7 0.8 0.9 0.12 0.5 0.7 0.5 0.7 0.5 0.7 0.8 0.9 0.12 0.6 0.2 0.15 0.2 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL Stricturoplasty blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension Higheet Intra-Operative Heart rate	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81 2.97 1.15 1.00	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-14.00 0.76-1.73 0.99-1.01	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.072 0.3 0.2 0.12 0.3 0.2 0.5 0.6
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss \leq 50 mL Peri-operative blood transfusion (units) 0 1-3 \geq 4 Intra-Operative hypotension Highest Intra-Operative Heart rate Unstent Stant Blace d	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81 2.97 1.15 1.00 2.00	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-1.400 0.76-1.73 0.99-1.01 4.25.2.02	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.072 0.3 0.2 0.12 0.5 0.6 0.2 0.5 0.6
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension Highest Intra-Operative Heart rate Ureteral Stent Placed	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81 2.97 1.15 1.00 2.09	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-14.00 0.76-1.73 0.99-1.01 1.25-3.39	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.72 0.3 0.2 0.12 0.5 0.6 0.9 0.6 0.72
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension Highest Intra-Operative Heart rate Ureteral Stent Placed Post-Op Blood Sugar ≥ 200 mg/dL	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.81 2.97 1.15 1.00 2.09 1.43	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-14.00 0.76-1.73 0.99-1.01 1.25-3.39 0.60-3.01	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.72 0.3 0.2 0.5 0.6 0.9 0.4
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Cutaneous Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension Highest Intra-Operative Heart rate Ureteral Stent Placed Post-Op Blood Sugar ≥ 200 mg/dL Foley Catheter > 24 hrs Post-Operatively	0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81 2.97 1.15 1.00 2.09 1.43 1.02	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-14.00 0.76-1.73 0.99-1.01 1.25-3.39 0.60-3.01 0.68-1.52	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.9 0.12 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.072 0.3 0.2 0.5 0.6 0.2 0.5 0.6 0.2 0.3 0.2 0.5 0.6 0.9 0.4 >0.9
Surgical wound protector used Bowel Resection Performed Anastomosis created Anastomosis type None Hand-Sewn Stapled Ileocolic resection Segmental small bowel only or colon resection only Colectomy Pouch created Genitourinary Fistula Repair Internal Fistula Repair Surgical abscess drainage Stricturoplasty performed Stoma formed or revised Incidental appendectomy Surgical blood loss ≤ 50 mL 51-250 > 250 mL Peri-operative blood transfusion (units) 0 1-3 ≥ 4 Intra-Operative hypotension Highest Intra-Operative Heart rate Ureteral Stent Placed Post-Op Blood Sugar ≥ 200 mg/dL Foley Catheter > 24 hrs Post-Operatively Study site	0.81 0.81 0.58 0.99 REF 0.82 1.07 1.05 0.89 0.97 1.63 1.36 0.58 1.99 1.05 0.73 1.31 0.66 REF 1.27 1.42 REF 1.81 2.97 1.15 1.00 2.09 1.43 1.02	0.52-1.32 0.28-1.38 0.67-1.49 REF 0.45-1.44 0.70-1.64 0.71-1.58 0.53-1.44 0.64-1.45 0.85-2.93 0.39-3.66 0.22-1.26 0.72-4.72 0.48-2.07 0.17-2.09 0.89-1.94 0.42-1.02 REF 0.83-1.93 0.77-2.52 REF 0.80-3.69 0.42-14.00 0.76-1.73 0.99-1.01 1.25-3.39 0.60-3.01 0.68-1.52	0.4 0.2 >0.9 0.5 0.7 0.8 0.6 0.9 0.12 0.6 0.2 0.15 0.9 0.6 0.2 0.15 0.9 0.6 0.2 0.072 0.3 0.2 0.12 0.3 0.2 0.72 0.3 0.2 0.12 0.072

OR – Odds Ratio; SSI – surgical site infection; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; CD – Crohn's disease; UC – ulcerative colitis; GI – gastrointestinal; IBD – inflammatory bowel disease; LOS – length of stay; ASA – American Society of Anesthesiologists physical status classification; Pre-Op – Preoperative; TPN – total parenteral nutrition

Supplementary Table 8. Multivariable analysis of risk factors for Surgical Site Infection postoperatively using serum TNFi exposure with undetectable defined as below commercial assay lower limit of quantitation threshold, never on a TNFi, or no TNFi within 180 days of surgery

Predictor	OR SSI	95% CI	p-value
Serum TNF			
Undetectable (n=544)	REF	REF	
Detectable (n=213)	1.623	0.920-2.829	0.090
Age	1.021	1.002-1.040	0.028
Male gender	1.260	0.753-2.124	0.380
Pre-Op Corticosteroids	2.339	1.371-4.028	0.002
UC/Indeterminate colitis	0.608	0.237-1.651	0.310
Prior Bowel Resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	1.058	0.449-2.349	0.890
Yes bowel resection	2.749	1.506-5.132	0.001
Diabetes	2.856	1.065-7.347	0.032
IBD Disease Behavior			
Neither stricturing or penetrating	REF	REF	
Penetrating only	2.322	0.885-6.454	0.094
Stricturing only	0.835	0.346-2.163	0.700
Stricturing and penetrating	0.428	0.146-1.252	0.120
Hypertension	1.853	0.865-3.840	0.100
Ureteral Stent	2.331	1.192-4.429	0.011
Current smoking	2.346	1.083-4.828	0.024
Anemia or other Blood Disorder	1.541	0.870-2.688	0.130

OR – Odds Ratio; SSI – surgical site infection; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; Pre-Op – Preoperative; UC – ulcerative colitis; IBD – inflammatory bowel disease

Supplementary Table 9. Multivariable analysis of risk factors for Surgical Site Infection postoperatively using serum TNFi exposure with undetectable defined as level = 0 μ g/mL, never on a TNFi, or no TNFi within 180 days of surgery

Predictor	OR SSI	95% CI	p-value
Serum TNFi			
Undetectable (n=513)			
Detectable (n=244)	1.393	0.801-2.396	0.230
Age	1.020	1.002-1.039	0.033
Male gender	1.272	0.761-2.143	0.360
Pre-Op Corticosteroids	2.346	1.375-4.041	0.002
UC/Indeterminate colitis	0.594	0.233-1.606	0.290
Prior Bowel Resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	1.086	0.463-2.402	0.840
Yes bowel resection	2.735	1.498-5.105	0.001
Diabetes	2.880	1.080-7.370	0.030
IBD Disease Behavior			
Neither stricturing or penetrating	REF	REF	
Penetrating only	2.275	0.871-6.291	0.100
Stricturing only	0.838	0.348-2.165	0.700
Stricturing and penetrating	0.436	0.149-1.270	0.120
Hypertension	1.839	0.858-3.809	0.110
Ureteral Stent	2.276	1.164-4.322	0.014
Current smoking	2.312	1.067-4.759	0.027
Anemia or other Blood Disorder	1.523	0.861-2.654	0.140

OR – Odds Ratio; SSI – surgical site infection; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; Pre-Op – Preoperative; UC – ulcerative colitis; IBD – inflammatory bowel disease

Supplementary Table 10. Multivariable analysis of risk factors for Surgical Site Infection postoperatively using Serum TNF quartile analysis with undetectable defined as level = 0 μ g/mL, never on a TNFi, or no TNFi within 180 days of surgery

Predictor	OR SSI	95% CI	p-value
Serum TNFi			
1 st quartile (undetectable) (n=513)	REF	REF	
2 nd quartile (0.1-4.4 µg/mL) (n=82)	1.327	0.582-2.805	0.480
3 rd quartile (4.4-11.7 µg/mL) (n=81)	1.221	0.508-2.676	0.630
4 th quartile (>11.7 μg/mL) (n=81)	1.375	0.580-2.981	0.440
Age	1.017	0.999-1.036	0.064
Male gender	1.173	0.713-1.942	0.530
Pre-Op Corticosteroids	1.969	1.179-3.306	0.010
UC/Indeterminate colitis	0.701	0.291-1.790	0.440
Prior Bowel Resection			
No prior abdominal surgery	REF	REF	
Abdominal surgery without resection	1.065	0.471-2.287	0.880
Yes bowel resection	2.689	1.446-5.083	0.002
IBD Disease Behavior			
Neither stricturing or penetrating	REF	REF	
Penetrating only	1.753	0.685-4.708	0.250
Stricturing only	0.712	0.305-1.767	0.440
Stricturing and penetrating	0.432	0.155-1.209	0.110
Ureteral Stent	2.331	1.234-4.301	0.008
Anemia or other Blood Disorder	1.851	1.100-3.090	0.019
Current smoking	2.354	1.158-4.603	0.014
Diabetes	2.905	1.111-7.271	0.025
Pre-Op Opioid use	1.531	0.912-2.558	0.100
Hypertension	1.674	0.817-3.315	0.150
Surgical Approach			
Laparoscopic	REF	REF	
Laparoscopic convert to open	2.000	1.005-3.898	0.044
Open	0.922	0.477-1.749	0.810

OR – Odds Ratio; SSI – surgical site infection; 95% CI – 95% Confidence Interval; REF – Reference; TNFi – tumor necrosis factor inhibitor; Pre-Op – Preoperative; UC – ulcerative colitis; IBD – inflammatory bowel disease