Comparative safety study to assess the risk of anastomotic leakage of two-row versus three-row manual circular staplers in colorectal anastomosis

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1. LIST OF ABBREVIATIONS

Abbreviation	Definition
AL	Anastomotic Leak
ASD	Absolute Standardized Difference
CCI	Charlson Comorbidity Index
CHU	Complaint Handling Unit
CI	Confidence Interval
ICD	International Classification of Disease
PCS	Procedure Coding System
PHD	Premier Healthcare Database
PSW	Propensity Score Weighting
RR	Relative Risk
RWD	Real World Data
SD	Standard Deviation
US	United States

2. PROJECT TEAM

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3. MAJOR AMENDMENTS

Revision Number	Date	Section of study protocol	Amendment or update	Reason
1	January 06, 2023		Original	

4. RATIONALE AND BACKGROUND

Anastomotic leak (AL) after colorectal surgery is a serious complication, and can result in intra-abdominal abscess, wound infection, bowel obstruction, rupture of the operation wound, or require reoperation.[1-4] Male sex, low anterior resection, and patient comorbidity including malnutrition, obesity (body mass index >30 kg/m^2), and diabetes, are widely reported risk factors for AL. [5-8]

The use of circular stapling devices to facilitate colorectal anastomosis has been demonstrated to reduce the risk of AL vs hand sewn sutures and is widely used in colorectal anastomosis after left-sided colorectal surgery. Many circular staplers are characterized by two rows of staples fired under manual grip force, aimed to guarantee a high anastomotic resistance with reduced tissue damage. Among them are Ethicon manual circular staplers and Medtronic EEA™ Circular Stapler with DST Series™ Technology (device variants described in Table 1).

Technological advancements led to the introduction of the Tri-staple™ Technology of manual staples in the US Market in 2018 (Medtronic EEA™ circular stapler with Tri-Staple™ technology), which includes three staple lines and is thought to guarantee a higher resistance of the anastomotic site with less stress on tissue as compared to the two-row circular staplers.[9-11] Based on the results of two 2022 publications, 2-row manual circular staplers, including Ethicon manual circular staplers and Medtronic EEA™ Circular Stapler with DST Series™ Technology, may have a higher risk of AL, when compared to the Medtronic EEA™ circular stapler with Tri-Staple™ technology (3-row manual circular staplers).[8, 12] This evidence was reported from single-center retrospective studies conducted in Italy and Japan. Such settings have the potential for selection bias, and the estimates of AL risks are limited by the small sample size included in both studies and the variations in the diagnosis consensus to ascertain AL cases. A comparative analysis of the risk of AL among two-row versus three-row manual circular staplers in colorectal anastomosis using a nationally representative database has not been fully examined or demonstrated in the United States (US).

Health-care databases can be a useful source of data for safety surveillance of medical devices. Using data from a large U.S. health-care database, the current study is designed to estimate the risk of AL among patients who underwent a left-sided colorectal surgery with use of a 2-row manual circular stapler (Ethicon Manual Circular Staplers or Medtronic EEA™ Circular Stapler with DST™ technology) relative to use of a 3-row manual circular stapler (i.e., Medtronic EEA™ Circular Stapler with Tri-Staple™ technology).

A future study to estimate the risk of AL among patients who underwent a left-sided colorectal surgery with use of a 2-row powered circular stapler (Ethicon Powered Circular Stapler) relative to use of a 3-row manual circular stapler (i.e., Medtronic EEA™ Circular Stapler with Tri-Staple™ technology) is planned. The timing of this study execution will be based on sample size of the study devices of interest accumulated in the PHD and appropriate statistical power.

Table 1: Circular Staplers

Variant	Description / Image	Product Code
1) Ethicon Manual 2-row Circular Staplers		
Curved Circular Staplers	Legacy Curved Intraluminal Stapler (ILS) 	CDH21A CDH25A CDH29A CDH33A
	Ethicon Circular Stapler* (not available in US) 	CDH21B* CDH25B* CDH29B* CDH33B*
Endoscopic Circular Staplers	Legacy Endoscopic Intraluminal Stapler (ILS) 	ECS21A ECS25A ECS29A ECS33A
	Ethicon Circular Stapler, XL Sealed 	ECS21B ECS25B ECS29B ECS33B
2) Medtronic EEA™ Circular Stapler		
Medtronic EEA™ Circular Stapler with DST Series™ Technology (2-row)		EEA2135 EEA21 EEAXL2135 EEAXL21 EEA2535 EEA25 EEAXL2535 EEAXL25 EEA2835 EEA28 EEAXL2835 EEAXL28 EEA31 EEAXL31 EEA33 EEAXL33
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology (3-row)		TRIEEA28MT TRIEEA28XT TRIEEAXL28MT TRIEEAXL28XT TRIEEA31MT TRIEEA31XT TRIEEAXL31MT RIEEAXL31XT

*Ethicon Circular Stapler with product codes of CDH21B, CDH25B, CDH29B and CDH33B are not available in the US, hence not included in this study.

5. RESEARCH QUESTIONS AND OBJECTIVES

5.1 Research Question(s)

1) What is the risk of AL within 30 days post-index procedure where Ethicon Manual Circular Staplers, Medtronic EEA™ Circular Stapler with DST Series™ Technology, or Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology were used

2) What is the relative risk of AL within 30 days post-index procedure, in which Ethicon Manual Circular Staplers were used, in comparison to the Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology?

3) What is the relative risk of AL within 30 days post-index procedure, in which Medtronic EEA™ Circular Stapler with DST Series™ Technology was used, in comparison to the Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology?

5.2 Objectives

Among patients who underwent a left-sided colorectal surgery (i.e., the index procedure), such as hemicolectomy, sigmoid colectomy, or rectal resection, in which a study device (Ethicon Manual Circular Staplers, Medtronic EEA™ Circular Stapler with DST Series™ Technology, or Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology) was used:

5.2.1 Primary Objectives

1) To estimate the cumulative incidence and 95% confidence intervals (CI) of AL within 30 days post-index procedure stratified by study device, and by patient characteristics (including demographic, clinical, procedural, hospital, and provider characteristics).

2) To estimate the unadjusted and adjusted relative risk and 95% CIs of AL within 30 days post-index procedure for Ethicon Manual Circular Staplers compared to Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology.

3) To estimate the unadjusted and adjusted relative risk and 95% CIs of AL within 30 days post-index procedure for Medtronic EEA™ Circular Stapler with DST Series™ Technology compared to Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology.

5.2.2 Secondary Objectives

1) To estimate the unadjusted and adjusted relative risk and 95% CIs of AL within 30 days post-index procedure for Ethicon Manual Circular Staplers compared to Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology, separately in with and without a diverting stoma prior to or on the same day as a left-sided colorectal surgery during the index admission.

2) To estimate the unadjusted and adjusted relative risk and 95% CIs of AL within 30 days post-index procedure for Medtronic EEA™ Circular Stapler with DST Series™ Technology compared to Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology separately in with and without a diverting stoma prior to or on the same day as a left-sided colorectal surgery during the index admission.

6. RESEARCH METHODS

6.1 Data Source(s)

This study will use hospital billing records contained in the Premier Healthcare Database (PHD). The PHD contains complete clinical coding, hospital cost, and patient billing data from more than 1,041 hospitals throughout the United States (US). The PHD represents approximately 25% of inpatient hospital stays in the US, and it includes a wide variety of regions and most healthcare insurances in the US. Premier collects data from participating hospitals in its health care alliance. The Premier Alliance was formed to improve the quality of care. Participation in the Premier Alliance is voluntary. Although the database excludes federally funded hospitals (e.g., Veterans Affairs), the hospitals included are nationally representative. The database contains a date-stamped log of all billed items by cost-accounting department including medications; laboratory, diagnostic, and therapeutic services; and primary and secondary diagnoses for each patient's hospitalization. Identifier-linked enrollment files provide demographic and payor information. Detailed service level information for each hospital day is recorded; this includes details on medication and devices received.[13]

6.2 Study Design

A retrospective cohort study using electronic healthcare data will be conducted to compare the risk of AL between 2-row manual circular staplers (including Ethicon Manual Circular Stapler and Medtronic EEA™ Circular Stapler with DST Series™ Technology) and 3-row manual circular staplers (i.e., Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology), among patients who underwent a left-sided colorectal surgery.

With the absence of an International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code for AL, the risks and relative risks of AL will be estimated via surrogate diagnoses which usually occur concomitantly with a leak, e.g. an abscess, peritonitis, a fistula or a post-index surgery stoma formation — a surgical treatment for severe AL.

Three study cohorts, as defined below, will be identified between January 2019 (when Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology became available in the US) and June 2022 or most recent available data.

- Target cohort 1: Ethicon Manual Circular Staplers – this cohort will include patients who underwent a left-sided colorectal surgery in which the Ethicon Manual Circular Stapler was used. The product family of Ethicon Endo-Surgery (EES) Circular Staplers is comprised of four primary variants: Curved, Endoscopic, Straight, and Powered anastomotic staplers. Included in this study are two manual variants: Curved and Endoscopic Circular Staplers (see Table 1).

- Target cohort 2: Medtronic EEA™ Circular Stapler with DST Series™ Technology – this cohort will include patients who underwent a left-sided colorectal surgery in which the Medtronic EEA™ Circular Stapler with DST Series™ Technology was used (see Table 1).

- Comparison cohort: Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology – this

cohort will include patients in whom Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology was used during the index procedure of interest (see Table 1).

This study will include two head-to-head comparisons: Ethicon Manual Circular Stapler versus Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology; and Medtronic EEA™ Circular Stapler with DST™ Technology versus Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology. The index procedure will be defined as the initial procedure in which the device of interest was used. The index admission will include the time from admission to discharge. Propensity score weighting (PSW) will be used for confounding adjustment, followed by log-binomial regression for risk estimation.

Stoma creations during colorectal resection are reportedly to reduce the incidence of AL or the AL-related complications[14-16], secondary analyses will be conducted separately in those with and without a diverting stoma procedure prior to or on the same day as the index procedure (i.e., left-sided colorectal surgery) during the index admission.

6.3 Sample Selection

Inclusion Criteria

Patients who meet all of the following criteria will be included in this study:

1) Billing charges for a study device (Ethicon Manual Circular Stapler, Medtronic EEA™ Circular Stapler with DST Series™ Technology, or Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology) between January 1, 2019, and June 30, 2022 (or latest available data)

2) Undergoing a left-sided colorectal surgery (i.e., the index procedure), defined as presence of a qualifying procedure code for left-sided colorectal surgery (see Table A-1)

3) Aged 18 years or older at the index procedure.

Exclusion Criteria

Patients who meet any of the following criteria will be excluded:

1) Patient encounters where more than one study device (Ethicon Manual Circular Stapler, Medtronic EEA™ Circular Stapler with DST Series™ Technology, or Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology) was used in the same index procedure
2) Missing patient age or sex
3) Presence of an admission diagnosis indicating anastomotic leak (See ICD-10-CM in the **Table A- 2**) during the index admission noted as present on admission*

*Present on admission will be identified with “Yes” in the present on admission field in the PHD.

6.4 Primary Independent Variable (Exposure)

The study population will be classified into 3 groups based on exposure: 1) Ethicon Manual Circular Staplers; 2) Medtronic EEA™ Circular Stapler with DST Series™ Technology; and 3) Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology.

[redacted]

6.5 Dependent Variables (Outcomes)

Anastomotic leak within 30 days post-index procedure. AL will include all new AL cases identified during the index admission and those identified during a new admission within 30 days post-index procedure. A 30-day follow-up period is chosen as AL occurs at a median of 12 days (range, 3-30 days) after a colorectal procedure[14] and it is the standard post-operation follow-up study period for most studies assessing AL after stapled anastomosis.

As there is no specific diagnosis code for AL in the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) taxonomy, the cumulative incidence of AL can only be estimated via either surrogate diagnoses or procedures which usually occur concomitantly with a leak, e. g., an abscess, peritonitis, a fistula or a post-index surgery stoma formation — a surgical treatment for severe AL.

As such, the presence of an ICD-10-CM diagnosis code for anastomotic leak surrogate diagnoses, such as fistula of intestine, peritonitis, or peritoneal abscess during the index admission or re-admission within 30 days post-index procedure, or the presence of an ICD-10-Procedure Coding System (ICD-10-PCS) procedure code indicating a diverting stoma occurred within 1-30 days post-index procedure will be used to define AL in the PHD. A similar approach was used in other studies assessing the risk of AL using electronic health records (EHR), such as PHD[17] or Nationwide Inpatient Sample database[18]. The list of diagnosis codes is summarized in Table A- 2, and the list of ICD-10-PCS codes indicating diverting stoma is summarized in Table A- 3.

6.6 Other Variables

6.6.1 Patient Demographics/Clinical Characteristics

- Age: mean and category in years at index procedure (18-44; 45-64; 65-74; ≥75)
- Sex (Female or Male)
- Race (White, Black, Other, unknown)
- Comorbidity Index (Charlson Comorbidity Index: 0; 1-2; 3-4; ≥5).

  The Charlson Comorbidity Index (CCI) is a sum of weighted scores for 19 conditions. It represents the comorbidity burden and is commonly used for adjustment of comorbidities in observational studies.[19]

- Comorbid conditions: (Diagnosis code list for comorbid conditions is provided in Table A- 4).
  - Alcohol dependency
  - Cardiovascular diseases (CVD): CVD will be categorized based on ICD-10-CM diagnoses for cerebrovascular disease, congestive heart failure, ischemic heart disease, myocardial infarction, or peripheral artery disease.
  - Chronic obstructive pulmonary disease
  - Coagulation defects
  - Diabetes
  - Hypertension
  - Immunosuppression/Immunodeficiency
  - Kidney disease
  - Malnutrition
  - Obesity

6.6.2 Procedural Characteristics

- Surgical site (indication for product usage): primary organ involved in the index procedure as defined by the primary procedure code (See **Table A- 1**).
  - Rectum
  - Sigmoid
  - Descending colon
  - others
- Primary diagnosis: Primary ICD-10-CM discharge diagnosis code recorded during the index hospital admission will be used to designate indication for surgery (See **Table A-5**).
  - Malignant neoplasms
  - Benign neoplasm

- Diverticular disease or Diverticulitis
- Intestinal obstruction
- Others

- Diverting stoma (yes, no) occurred prior to or on the same day as the index procedure (i.e., left-sided colorectal surgery) during the index admission: defined as the presence of an ICD-10-PCS procedure code indicating diverting stoma (see **Table A- 3**) identified prior to or on the same day as the index procedure during the index admission

- Surgical approach:
  - Open
  - Laparoscopic
  - Robotic assisted
  - Unknown

  Surgical approach is determined by the primary and secondary procedure code. For a *primary* procedure code in ICD-10-PCS, the fifth character of the code explicitly identifies the surgical approach with '0' standing for an open procedure and characters other than '0' representing a laparoscopic approach, unless the presence of a *secondary* procedure code (i.e., ICD-10-PCS: 8E0W%CZ—Robotic Assisted Procedure of Trunk Region) indicating a robotic assistance procedure. Conversions from laparoscopic or unknown surgical approach to open surgical approach will be categorized as open surgery (the procedure code list for conversions is provided in **Table A- 6**).

- Year of index procedure

- Admission type during index procedure (elective admission; emergent or urgent admission): elective surgery was scheduled in advance, while urgent or emergency surgery was done because of an urgent medical condition. We assume an index encounter categorized as elective indicates a procedure scheduled in advance, while urgent or emergency index encounter admissions reflect an urgent medical condition.

6.6.3 Hospital and Provider Characteristics

- Hospital region (Midwest, northeast, south, west)
- Location (urban hospital; rural hospital)
- Hospital setting (inpatient; outpatient)
- Hospital bed size category (small, medium, large): modified from the bed size category definition using region of the U.S., the urban-rural designation of the hospital, in addition to the teaching status (https://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp)
- Teaching status (teaching hospital; non-teaching hospital)

- Surgeon specialty (colon/rectal surgeon, general surgeon, other, and unknown)

6.7 Subgroups/Stratification Variables

Whether a diverting stoma is an effective and safe procedure to prevent anastomosis leakage in colorectal resections remains controversial. Some studies have reported that the stoma creation reduced the incidence of AL or the AL-related complications, such as pelvic abscess.[14-16] To minimize the impact of an elective diverting stoma on the AL risk estimate, secondary analyses will be conducted separately in those with and without a diverting stoma procedure prior to or on the same day as the index procedure (i.e., left-sided colorectal surgery) during the index admission.

6.8 Sample Size and Study Power

A feasibility analysis identified more than 10,000 patients in PHD between 2019 and 2021 who were treated surgically with the use of Ethicon Manual Circular Stapler. Among those, approximately 6,000 patients had a left-sided colorectal surgery.

Among approximately 13,000 patients who were treated surgically with Medtronic EEA™ Circular Stapler with DST Series™ Technology, about 6,000 patients had a left-sided colorectal surgery in the PHD.

A similar analysis identified 623 patients in PHD between 2019 and 2021 who underwent surgical procedures where Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology was used. Among those, 526 underwent a left-sided colorectal surgery.

The final sample sizes for the study will vary based on applying the inclusion and exclusion criteria, as well as additional data beyond 2021 being available from PHD.

Power estimates assuming different combinations of relative risk, sample size, and the cumulative incidence of AL in the comparison cohort—Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology— are provided in Table 2

Table 2. The calculations assumed one-sided tests at a significance level of 0.025 (or type I error of 0.025). The estimated cumulative incidence of AL among patients who underwent a colorectal surgery with the use of Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology ranges from 2% to 3.5% in the literature. [8,12]

Table 2: Power estimation, by relative risk

Relative Risk	AL risk in the comparison cohort	Sample size in the target cohort	Sample size in the comparison cohort	Power
2.5	3%	6,000	500	0.995
2	3%	6,000	500	0.856
1.5	3%	6,000	500	0.324
2.5	2%	6,000	500	0.938
2	2%	6,000	500	0.642
1.5	2%	6,000	500	0.209

6.9 Data Analysis

6.9.1 Primary Descriptive analysis

6.9.1.1 Demographic, clinical, and procedural characteristics

Descriptive analyses will be first performed for demographic, clinical, and procedural characteristics of patients at the time of the index procedure where a study device was used. Descriptive statistics will be calculated for all study cohorts, including pre- and post- weighted patients by study device. Categorical variables will be summarized by frequencies and proportions and continuous variables will be summarized by means and standard deviations or medians and interquartile ranges. Balance is evaluated using absolute standardized differences (ASD). Nominal variables with more than two categories are summarized using a generalization of the absolute standardized difference for binary covariates. See the expected outputs in Table B- **1**, Table B- **2**, Table B- **3**, Table B- **4**, and Table B- **5**)

6.9.1.2 Unadjusted Cumulative incidence of AL

The number of new cases of AL within 30 days post-index procedure will be determined via surrogate diagnoses which usually occur concomitantly with a leak, e. g. an abscess, peritonitis or a fistula or the presence of a procedure code indicating diverting stoma— a surgical treatment for severe AL [defined in Section **6.5 Dependent Variables (Outcomes)**]. Unadjusted cumulative incidences [(number of new cases/number of patients at risk during the specified time period) x 100] and 95% CI will be calculated for all study cohorts. Cumulative incidences of AL and 95% CIs will also be stratified by key characteristics (including demographic, clinical, procedural, hospital, and provider characteristics). See the expected outputs in Table B- 6, Table B- 7 and Table B- 8.

6.9.2 Primary Comparative analysis

The goals of comparative analyses are to: 1) estimate the RR of AL for Ethicon Manual Circular Staplers compared to Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology; 2) estimate the RR of AL for the Medtronic EEA™ Circular Stapler with DST Series™ Technology compared to Medtronic EEA™ Circular Stapler with Tri-Staple™.

The primary analyses will be conducted separately for the comparison between Ethicon Manual Circular Stapler versus Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology and the comparison between Medtronic EEA™ Circular Stapler with DST™ Technology and Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology. See the expected outputs in Table B- 7 and Table B- 8.

A propensity score weighting (PSW) method will be used to control for potential confounders by balancing the distribution of baseline demographic, clinical, and procedural characteristics between the comparison groups. The following baseline variables will be considered in the propensity score model based on their clinical relevance to the safety of the device: patient demographics (age, sex, and race), clinical characteristics (CCI, comorbid conditions, diverting stoma occurred prior to or on the same day as the index procedure), procedural characteristics (procedure year, surgical site, primary diagnosis, surgical approach, and admission type), and hospital and provider

characteristics (hospital region, hospital location, hospital setting, hospital bed size, and surgeon specialty).

The weighting will be carried out for the comparator group to make it comparable in propensity score to the target group. Two propensity score weighting methods— untrimmed and trimed— can be used to balance the data to make the target group and the comparason group comparable on the measured confounders. The choice among the methods will be based on which provided the best balance. Propensity score methods that estimate the average treatment effect on the treated will be calculated and will be compared on the basis of covariate balance as measured by the absolute standardized difference (ASD), which is the difference in means or proportions expressed in pooled standard deviation units. We will compare the approaches on the basis of the number of variables with an ASD of >0.10 and the mean ASD, and the weighting approach with the fewest number of variables with covariate imbalance will be selected for analysis. If two methods achieve the same minimum number of variables with covariate imbalance, the method with the smallest ASD across all variables will be selected for outcome analysis. Notably, one data analyst will balance the data without access to the outcome data and a separate individual will perform the outcome analysis using the balanced data, thus removing the potential for bias resulting from repeated applications of covariate balancing to obtain a desired study outcome.

In the final PSW cohorts, covariate balanced cumulative incidences and 95% CI will be calculated for all device cohorts. A weighted (covariate balance weights) log-binomial regression outcome will be used with treatment as the only expalantory variable to estimate the covariate balanced RR (target group versus the comparator group for the study outcome of interest). A cluster robust standard error approach will be applied to calculate the variability in the estimate and to construct two-sided 95% confidence intervals. All variables included in the propensity score model are prespecified confounders of the relationship between the circular stapler and AL. If any of those variable don't balance well through propensity scores, it will be added as a covariate in the log-binomial regression model.

6.9.3 Secondary analysis

In the secondary analyese, all primary analyses will be repeated separately in those with and without a diverting stoma procedure prior to or on the same day as the index procedure (i.e., left-sided colorectal surgery) during the index admission. See the expected outputs from Table C- 1 and Table C- 12.

6.9.4 Sensitivity analysis

PHD is not a longitudinal patient database; rather, it is a longitudinal hospital database for the duration of continuous participation for each institution. The treatment pathway for each patient is not fully observed. Patients who receive care at another hospital after the index procedure, even within PHD, will be represented as a new patient. To minimize the potential impact of misclassification of study outcome resulting from the loss of follow-up, a sensitivity analysis will be conducted by repeating the primary analysis among patients from hospitals

with at least 30 days continuous enrollment in PHD after the patients' index procedure. See the expected outputs in Table B- 7, Table B- 8, Table C- 9, Table C- 10, Table C- 11, and Table C- 12.

7 QUALITY CONTROL

The study will be completed per the quality control guidance outlined in the Epidemiology, Medical Devices: Protocol Driven Research Study Checklist and its associated documents.

8 LIMITATIONS OF RESEARCH METHODS

The study is observational in nature and thus susceptible to limitations.

The first relates to the validity of the diagnosis of anastomotic leak. As with any other non-interventional database study using health insurance administrative claims or electronic health records (EHR), identification of medical events, such as anastomotic leak or co-morbidities, is limited to data that are captured as part of the medical record or claims, which are not primarily collected for research purposes, and will rely on appropriate diagnostic codes to detect these events. As there is no specific diagnosis code for anastomotic leak in the ICD-10-CM taxonomy, the anastomotic leak surrogate diagnoses, such as abscess of intestine, fistula of intestine, peritonitis, or peritoneal abscess, will be used to define AL in the PHD. Misclassification bias can result if study patients are not categorized correctly with regards to outcome, however, should be non-differential between the comparison groups.

Misclassifications due to the secondary use of billing data may also lead to under or overestimation of cohort size. For example, the search strategy designed in this study may underestimate the prevalence of products in the database if the search strategy missed any incorrectly coded entries for study devices such as misspellings leading to misclassification of the exposure. However, there is no evidence that the misclassification bias would be differential between the comparison groups.

Indication for product usage is not specifically stated in the PHD; it is being inferred based on the primary procedure codes recorded during the index hospitalization. Therefore, misclassification of indication in this study is possible but should be non-differential between the comparison groups.

Furthermore, PHD is not a longitudinal patient database; rather, it is a longitudinal hospital database for the duration of continuous participation for each institution. The treatment pathway for each patient is not fully observed. Patient records within a given institution are linked such that additional care at the same institution as the index procedure will be attributed to the same patient. However, patients who receive care at another hospital, even within PHD, will be represented as a new patient. This limitation may lead to underestimation of AL that occurred after the discharge from the index admission. To minimize the potential impact of misclassification of study outcome resulting from such loss of follow-up, a sensitivity analysis will be conducted by repeating our primary analysis among patients from hospitals with at least 30-day continuous enrollment in PHD after the patients' index procedure.

Finally, PHD represents data from hospitals that are part of the Premier healthcare performance improvement alliance of approximately 1,041 US hospitals from around the US but are not a random selection of US hospitals and under-represents hospital outpatient procedures. Although the database represents all regions and most payers, this characteristic of the database may affect the generalizability of the study results.

9 PROTECTION OF HUMAN SUBJECTS

This study will utilize a secondary source of de-identified data, the PHD.

The use of PHD was reviewed by the New England Institutional Review Board (IRB) and was determined to be exempt from broad IRB approval, as this research project did not involve human subjects research.

The PHD consists of de-identified healthcare records. In the US, retrospective analyses of the PHD data are considered exempt from informed consent and institutional review board (IRB) approval as dictated by Title 45 Code of Federal Regulations, Part 46 of the United States, specifically 45 CFR 46.101(b)(4).

Confidentiality of patient records will be maintained at all times. All study reports will contain aggregate data only and will not identify individual patients or physicians. At no time during the study will patients be requested with identifiable information, except when required by law.

10 MANAGEMENT AND REPORTING OF ADVERSE EVENTS AND ADVERSE REACTIONS

In this study, potential product complaints or safety signals may be identified. Thus, any potential combinations of specific product brand and safety outcomes will be reported to the operating company complaint handling unit (CHU) upon internal approval of the study report or manuscript or J&J receipt of the external data report. For all events that may be deemed product complaints, the data captured in the final study report, manuscript, or external report will constitute all clinical information known regarding these product complaints/adverse events. No follow-up on these potential adverse events or complaints can be conducted. The operating companies CHU is responsible for determining if they are actual product complaints and/or product-related adverse events. Communication of all potential Product Complaints to the appropriate operating company CHU must be done within 48 hours of internal approval of the final study report or manuscript or J&J receipt of an external study report using the Database RRA Potential Complaint Forwarding Form (100915839).

NOTE: For these studies, the date the final study report is approved, or the date the manuscript is internally approved, or the J&J receipt date for an external study report shall be considered the awareness date for the CHU.

11 DISSEMINATION PLAN

A final report will be created from study results and will be submitted for publication in a peer reviewed journal according to the J&J Publication Policy.

12 REFERENCES

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APPENDIX A: DIAGOSIS AND PROCEDURE CODES

Table A- 1: Procedure Codes (ICD-10-PCS) for Left-sided Colorectal Surgery

CODE	CODE DESCRIPTION
0DTG%	Resection, large intestine, left
0DTM%	Resection, Descending Colon
0DTN%	Resection, Sigmoid Colon
0DTP%	Resection, Rectum
0DBG%	Excision, large intestine, left
0DBM%	Excision, Descending Colon
0DBN%	Excision, Sigmoid Colon
0DBP%	Excision, Rectum
0DQM%	Repair, Descending Colon
0DQN%	Repair, Sigmoid Colon
0DQP%	Repair, Rectum

'%' at the end of the code denotes any value for subsequent characters.
'%' in the middle of the code denotes any valid value for a character in that specific position

Table A- 2: Diagnosis Codes (ICD-10-CM) Indicating Anastomotic Leak

CODE	CODE DESCRIPTION
K63.2	Fistula of intestine
K65.0	Generalized Peritonitis
K65.1	Peritoneal abscess
K91.89	Other postprocedural complications and disorders of digestive system
Y83.2	Surgical operation with anastomosis, bypass or graft as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure

Table A- 3: Procedure Codes (ICD-10-PCS) for Diverting Stoma

CODE	CODE DESCRIPTION
0D18%%4	Bypass Small Intestine to Cutaneous
0D1B%%4	Bypass Ileum to Cutaneous
0D1E%%4	Bypass large intestine to Cutaneous
0D1H%%4	Bypass Cecum to Cutaneous
0D1K%%4	Bypass Ascending Colon to Cutaneous,
0D1L%%4	Bypass Transverse Colon to Cutaneous
0D1M%%4	Bypass Descending Colon to Cutaneous
0D1N%%4	Bypass Sigmoid Colon to Cutaneous

'%' in the middle of the code denotes any valid value for a character in that specific position

Table A- 4: Diagnosis Codes (ICD-10-CM) for Comorbid Conditions

Comorbid conditions	CODE	DESCRIPTION
Alcohol dependency	F10.2%	Alcohol dependence
Cardiovascular diseases	G45%, G46%, I60%, I61%, I62%, I63%, , I65%, I66%, I67%, I68%, I69%, H34.0%	cerebrovascular disease
	I43, I50%, I09.9, I11.0, I13.0, I13.2, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9	congestive heart failure
	I20%, I23%, I24%, I25%	ischemic heart disease
	I21%, I22%	myocardial infarction
	I70%, I71%, I73.1, I73.8%, I73.9, I77.1, Z95.8%, Z95.9	peripheral artery disease
Chronic obstructive pulmonary disease	J44.0, J44.1, J44.9	Chronic obstructive pulmonary disease
Coagulation defects	D65, D66, D67, D68.0, D68.1, D68.2, D68.3%, D68.4, D68.5%, D68.6%, D68.9	Coagulation defects
Diabetes	E11.%, E10.%, E13.%, O24.%, E08.%, Z79.4, Z79.84	Diabetes mellitus, Gestational diabetes, Secondary diabetes, long term (current) use of insulin/oral antidiabetic drugs
Hypertension	I10, I11%, I12%, I13%, I15%	Hypertension
Immunodeficiency/immunosuppression	D80%, D81%, D82%, D83%, D84%	immunodeficiencies
	Z92.25	Personal history of immunosuppression therapy
	Z79.52	Long term (current) use of systemic steroids
	B20	AIDS/HIV
Kidney disease	N18%, N19, I12.0, I13.1%, N03.2, N03.3, N03.4, N03.5, N03.6, N03.7, N05.2, N05.3, N05.4, N05.5, N05.6, N05.7, N25.0, Z49.0%, Z94.0, Z99.2	Renal diseases
Malnutrition	E41, E42, E43, E44%, E46, E63%	Malnutrition, nutritional deficiencies
Obesity	E66.0%, E66.1, E66.2, E66.8, E66.9, Z68.3%, Z68.4%	Obesity, body mass index (BMI) 30-39, BMI 40 or greater

'%' at the end of the code denotes any value for subsequent characters.

Table A- 5: Diagnosis Codes (ICD-10-CM) for Indications of Surgery

PRIMARY DIAGNOSIS	CODE	CODE DESCRIPTION
Malignant neoplasms	C18.6	Malignant neoplasm of descending colon
	C18.7	Malignant neoplasm of sigmoid colon
	C18.8	Malignant neoplasm of overlapping sites of colon
	C18.9	Malignant neoplasm of colon, unspecified
	C19	Malignant neoplasm of rectosigmoid junction
	C20	Malignant neoplasm of rectum
Benign neoplasm	D12.4	Benign neoplasm of descending colon
	D12.5	Benign neoplasm of sigmoid colon
	D12.6	Benign neoplasm of colon, unspecified
	D12.7	Benign neoplasm of rectosigmoid junction
	D12.8	Benign neoplasm of rectum
Diverticular disease or Diverticulitis	K57.2%	Diverticulitis of large intestine
	K57.3%	Diverticular disease of large intestine
	K57.8%	Diverticulitis of intestine, part unspecified
	K57.9%	Diverticular disease of intestine, part unspecified
Intestinal obstruction	K56.2	Volvulus
	K56.6%	Other and unspecified intestinal obstruction

'%' at the end of the code denotes any value for subsequent characters.

Table A- 6: Diagnosis Codes (ICD-10-CM) for Conversion of Minimally Invasive Procedure to Open Procedure

CODE	CODE DESCRIPTION
Z53.31	Laparoscopic surgical procedure converted to open procedure
Z53.32	Thoracoscopic surgical procedure converted to open procedure
Z53.33	Arthroscopic surgical procedure converted to open procedure
Z53.39	Other specified procedure converted to open procedure

APPENDIX B: MOCK-UP TABLES—Primary Analysis

Table B- 1: Study cohort attrition

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with DST™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology	
Criteria	**N**	**% Retained**	**N**	**% Retained**	**N**	**% Retained**
Include all patients having billing charges for either study device of interest between January 1, 2019 and June 30, 2022						
Include patients with a left-sided colorectal surgery, during the same episode of admission as the billing charge for device of interest						
Include patients aged 18 years or older at the index procedure						
Exclude patients with use of both a target device and comparator device in the index procedure						
Exclude patients with missing age or sex						
Exclude patients with an admission diagnosis indicating anastomotic leak during the same episode of admission as the billing charge for device of interest						
Number of patients with a diverting stoma prior to or at the same day as the index procedure during the index admission						
Number of patients without a diverting stoma prior to or at the same day as the index procedure during the index admission						

Table B- 2: Patient Characteristics at the Index Admission before Propensity Score Weighting: Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q1-Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Diverting stoma occurred prior to or on the same day as the index procedure					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Peripheral Artery Disease					
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table B- 3: Patient Characteristics at the Index Admission before Propensity Score Weighting: Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Diverting stoma occurred prior to or on the same day as the index procedure					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Peripheral Artery Disease					
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital (yes)					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table B- 4: Patient Characteristics at the Index Admission after Propensity Score Weighting: Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q1-Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Diverting stoma occurred prior to or on the same day as the index procedure					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Peripheral Artery Disease					
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table B- 5: Patient Characteristics at the Index Admission after Propensity Score Weighting: Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Diverting stoma occurred prior to or on the same day as the index procedure					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Peripheral Artery Disease					
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital (yes)					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table B- 6: Cumulative Incidence (95% Confidence Interval) of Anastomotic Leak, by Study Device and Key Characteristics

	Ethicon Manual Circular Staplers			Medtronic EEA™ Circular Stapler with DST™ Technology			Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		
	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)
Overall									
Sex									
Male									
Female									
Age									
18-<45 years									
45-<65 years									
65-<75 years									
75 years or older									
Race									
White									
Black									
Other									
Unknown									
Surgical site									
Rectum									
Sigmoid									
Descending colon									
Others									
Primary diagnosis									
Malignant neoplasms									
Benign neoplasm									
Diverticular disease or Diverticulitis									
Intestinal obstruction									
Others									
Diverting stoma occurred prior to or on the same day as the index procedure									

	Ethicon Manual Circular Staplers			Medtronic EEA™ Circular Stapler with DST™ Technology			Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		
	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)
Yes									
No									
Cardiovascular Diseases - Overall									
Yes									
No									
Cerebrovascular Disease									
Yes									
No									
Congestive Heart Failure									
Yes									
No									
Ischemic Heart Disease									
Yes									
No									
Myocardial Infarction									
Yes									
No									
Peripheral Artery Disease									
Yes									
No									
Chronic Obstructive Pulmonary Disease									
Yes									
No									
Coagulation Defects									
Yes									
No									
Diabetes									
Yes									

	Ethicon Manual Circular Staplers			Medtronic EEA™ Circular Stapler with DST™ Technology			Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		
	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)
No									
Hypertension									
Yes									
No									
Immunodeficiency/ Immunosuppression									
Yes									
No									
Kidney Disease									
Yes									
No									
Malnutrition									
Yes									
No									
Obesity									
Yes									
No									
Surgical approach									
Open									
Laparoscopic									
Robotic assisted									
Unknown									
Admission type									
Elective									
Urgent/emergency									
Hospital region									
Midwest									
Northeast									
South									
West									
Hospital setting									

	Ethicon Manual Circular Staplers			Medtronic EEA™ Circular Stapler with DST™ Technology			Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		
	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)	Number of patients	Number of events	Cumulative incidence (95% CI)
Inpatient									
Outpatient									

CI=Confidence Interval

Table B- 7: Risk Estimates for Anastomotic Leak— Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Number of Patients	Number of Events	Cumulative Incidence (95% CI)	Risk Ratio (95% CI)
1) Primary analysis				
Before Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
2) Sensitivity analysis (30-day continuous enrollment requirement)				
Before Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				

CI=Confidence Interval

Table B- 8: Risk Estimates for Anastomotic Leak — Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Number of Patients	Number of Events	Cumulative Incidence (95% CI)	Risk Ratio (95% CI)
1) Primary analysis				
Before Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
2) Sensitivity analysis (30-day continuous enrollment requirement)				
Before Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				

CI=Confidence Interval

APPENDIX C: MOCK-UP TABLES—Secondary Analysis

Table C- 1: Patient Characteristics at the Index Admission **with diverting stoma** prior to or at the same day as the index procedure before Propensity Score Weighting: Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q1-Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Peripheral Artery Disease					
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 2: Patient Characteristics at the Index Admission **with diverting** stoma prior to or at the same day as the index procedure before Propensity Score Weighting: Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					
Peripheral Artery Disease					

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital (yes)					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 3: Patient Characteristics at the Index Admission **with diverting stoma** prior to or at the same day as the index procedure after Propensity Score Weighting: Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q1-Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					
Peripheral Artery Disease					

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 4: Patient Characteristics at the Index Admission **with diverting stoma** prior to or at the same day as the index procedure after Propensity Score Weighting: Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					
Peripheral Artery Disease					

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital (yes)					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 5: Patient Characteristics at the Index Admission **without diverting stoma** prior to or at the same day as the index procedure before Propensity Score Weighting: Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology:

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q1-Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					
Peripheral Artery Disease					

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 6: Patient Characteristics at the Index Admission **without diverting stoma** prior to or at the same day as the index procedure before Propensity Score Weighting: Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					
Peripheral Artery Disease					

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital (yes)					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 7: Patient Characteristics at the Index Admission **without diverting stoma** prior to or at the same day as the index procedure after Propensity Score Weighting: Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q1-Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					
Peripheral Artery Disease					

	Ethicon Manual Circular Staplers		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 8: Patient Characteristics at the Index Admission **without diverting stoma** prior to or at the same day as the index procedure after Propensity Score Weighting: Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
N					
Sex: Male					
Age					
Mean (Standard Deviation)					
18-<45 years					
45-<65 years					
65-<75 years					
75 years or older					
Race					
White					
Black					
Other					
Unknown					
Procedure year					
2019					
2020					
2021					
2022, Q2					
Surgical site					
Rectum					
Sigmoid					
Descending colon					
Others					
Primary diagnosis					
Malignant neoplasms					
Benign neoplasm					
Diverticular disease or Diverticulitis					
Intestinal obstruction					
Others					
Surgical approach					
Open					
Laparoscopic					
Robotic assisted					
Unknown					
Cardiovascular Diseases - Overall					
Cerebrovascular Disease					
Congestive Heart Failure					
Ischemic Heart Disease					
Myocardial Infarction					
Peripheral Artery Disease					

	Medtronic EEA™ Circular Stapler with DST Series™ Technology		Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology		Absolute Standardized Difference
	n	%	n	%	
Chronic Obstructive Pulmonary Disease					
Coagulation Defects					
Diabetes					
Hypertension					
Immunodeficiency/ Immunosuppression					
Kidney Disease					
Malnutrition					
Obesity					
Admission type: Elective					
Hospital setting: Inpatient					
Location: Urban hospital					
Teaching hospital (yes)					
Hospital region					
Midwest					
Northeast					
South					
West					
Hospital size					
Large					
Medium					
Small					
Surgeon specialty					
General surgeon					
Colon/Rectal surgeon					
Other/Unknown					
Charlson Comorbidity Index Scores					
0					
1-2					
3-4					
5+					

Table C- 9: Risk Estimates for Anastomotic Leak among patients who had diverting stoma prior to or at the same day as the index procedure during the index admission — Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Number of Patients	Number of Events	Cumulative Incidence (95% CI)	Risk Ratio (95% CI)
1) Primary analysis				
Before Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
2) Sensitivity analysis (30-day continuous enrollment requirement)				
Before Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				

CI=Confidence Interval

Table C- 10: Risk Estimates for Anastomotic Leak among patients who had diverting stoma prior to or at the same day as the index procedure during the index admission — Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Number of Patients	Number of Events	Cumulative Incidence (95% CI)	Risk Ratio (95% CI)
1) Primary analysis				
Before Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
2) Sensitivity analysis (30-day continuous enrollment requirement)				
Before Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				

CI=Confidence Interval

Table C- 11: Risk Estimates for Anastomotic Leak among patients who did not have diverting stoma prior to or at the same day as the index procedure during the index admission — Ethicon Manual Circular Staplers vs. Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology

	Number of Patients	Number of Events	Cumulative Incidence (95% CI)	Risk Ratio (95% CI)
1) Primary analysis				
Before Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
2) Sensitivity analysis (30-day continuous enrollment requirement)				
Before Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Ethicon Manual Circular Staplers				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				

CI=Confidence Interval

Table C- 12: Risk Estimates for Anastomotic Leak among patients who did not have diverting stoma prior to or at the same day as the index procedure during the index admission—Medtronic EEA™ Circular Stapler with DST Series™ Technology vs. Tri-Staple™ Technology

	Number of Patients	Number of Events	Cumulative Incidence (95% CI)	Risk Ratio (95% CI)
1) Primary analysis				
Before Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
2) Sensitivity analysis (30-day continuous enrollment requirement)				
Before Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				
After Propensity Score Weighting				
Medtronic EEA™ Circular Stapler with DST Series™ Technology				
Medtronic EEA™ Circular Stapler with Tri-Staple™ Technology				

CI=Confidence Interval