The Uptake of Laparoscopic Rectal Cancer Surgery: 2004-2014

by

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ABSTRACT

Background: Colorectal cancer is the second most common malignancy in Canadian males, and third most common malignancy in Canadian females; approximately thirty percent of colorectal cancers are tumors of the rectum (rectal cancer). Surgery is the cornerstone of treatment for most patients with rectal cancer, often combined with adjuvant or neoadjuvant chemotherapy and/or radiation. Traditionally, surgery was accomplished through an **open** approach with a midline abdominal incision (open surgery or OS). Over the past decade, success with laparoscopic colon cancer surgery has led to the introduction of minimally invasive rectal cancer surgery. **Laparoscopic** rectal cancer surgery (LS) has some clear advantages over OS, including decreased patient morbidity and decreased length of hospital stay. Randomized data has also demonstrated equivalent disease-free survival, overall survival and rates of local recurrence between LS and OS. The use of LS for rectal cancer has increased internationally. Currently, the uptake of LS for rectal cancer in Canada is unknown.
Objectives: The overall objective of this study was to describe and better understand the uptake of LS for rectal cancer in Canada. Specific objectives included: 1) To describe the national and provincial uptake of LS for rectal cancer Canada, as defined by the proportion of rectal cancer surgeries performed laparoscopically, from fiscal years 2004-2014; 2) To identify geographic, patient, surgeon and hospital characteristics associated with the use of LS; and 3) To describe the content and timing of provincial policies regarding financial remuneration for LS, and to correlate these with provincial uptake of LS for rectal cancer. **Methods**: This was a retrospective cohort study using the Discharge Abstract Database held by the Canadian Institute for Health Information. All patients 18 or older with a Canadian postal code who underwent surgery for rectal cancer between 2004-2014 in Canada (except Quebec) were identified. Patients who were pregnant, underwent emergency surgery or a complex resection were excluded. The annual provincial and national uptake of LS was calculated. Univariable and multivariable logistic regression models were created to estimate the effects of geographic, patient, surgeon and hospital factors on the uptake of LS. Province-specific figures graphing the proportion of LS over time were created, with the year of financial incentive indicated**. Results:** We identified 28,455 patients with rectal cancer who underwent radical rectal resection; 17.6% underwent LS and 82.4% OS. The use of LS for rectal cancer increased in Canada from 5.9% in 2004 to 34.0% in 2014. There was significant interprovincial variation in the use of LS over time. In 2014, uptake of LS was highest in PE, ON and BC. On multivariable analysis, age-category, sex, comorbidity score, urban/rural status, surgeon/hospital volume, type of surgical resection, year and province were associated with the uptake of LS. Year and province were the strongest predictors of LS. Financial incentive appeared to be associated with the uptake of LS in ON and BC, but not NS. **Conclusion**: There is marked interprovincial variation in the use of LS for rectal cancer. We have identified several geographic, patient, surgeon and hospital factors associated with the use of LS for rectal cancer. This study provides the first pan-Canadian description of the use of LS for rectal cancer and has identified potential targets for further implementation of LS.

LIST OF ABBREVIATIONS USED

LS	Laparoscopic Surgery
OS	Open Surgery
CCI	Charlson Comorbidity Index
NL	Newfoundland
PE	Prince Edward Island
NB	New Brunswick
NS	Nova Scotia
ON	Ontario
MB	Manitoba
SK	Saskatchewan
AB	Alberta
BC	British Columbia
RCT	Randomized Controlled Trial
LAR	Low anterior resection
APR	Abdominoperineal resection
HP	Hartmann's procedure
TME	Total Mesorectal excision
BMI	Body mass index
DAD	Discharge Abstract Database
CIHI	Canadian Institute for Health Information
ICD	International Classification of Disease

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Chapter 1: Background and Rationale

Colorectal cancer is one of the most common malignancies, affecting approximately 6% of the Canadian population.[1] In Nova Scotia, an estimated 416 males and 420 females were diagnosed with colorectal cancer in 2017.[2] Colorectal cancer is the second leading cause of cancer death for males and the third most common cause of cancer death in females; approximately 12% of all cancer deaths in Canada can be attributed to colorectal cancer.[2] However, the death rate is declining in both sexes, a trend that is likely associated with the implementation of population-based screening.[3]

Approximately thirty percent of colorectal cancers are tumors of the rectum (rectal cancer).[4] Surgery is the cornerstone of treatment for most patients with rectal cancer, often combined with adjuvant or neoadjuvant chemotherapy and/or radiation. In general, surgery includes radical resection of part/all of the rectum with adequate margins and lymph node harvest. Recently, as with other surgery, there has been an interest in performing rectal surgery with a minimally invasive (laparoscopic) approach. Laparoscopic rectal cancer surgery has emerged as a novel way to apply oncological surgical principles with smaller incisions and reduced patient morbidity. To date, the overall uptake of this surgical approach in Canada is unknown.

1.1 Rectal cancer surgery

1.1.1 Basic principles

The rectum is a tube-like structure that extends from sigmoid colon to the anus, approximately 12 to 15 cm in length, and is located within the pelvis. It lies within close proximity to important neurovascular structures which supply reproductive organs and above the sphincter muscles that are responsible for continence.

The choice of surgical resection of the rectum depends on the size and location of the primary rectal tumor and is most commonly achieved by two different procedures. An abdominal perineal resection (APR) is complete excision of the rectum and anus, which includes an approach through both the abdomen and perineum, with a permanent colostomy. In general, this procedure is indicated when there is a very low rectal cancer that involves, or is extremely close to, the anal sphincters. A low anterior resection (LAR) involves the removal of the rectum through an abdominal approach alone with preservation of the anus. Intestinal continuity is established with a colo-rectal or colo-anal anastomosis. For excisions of low rectal tumors, a temporary proximal diverting ileostomy is often created to divert stool away from the healing anastomosis when LAR is performed.[5] For patients requiring emergency surgery due to obstruction, bleeding or perforation or those with severe co-morbidities a Hartmann's procedure (HP) may be performed with LAR to avoid the potential morbidity of anastomosis complications and decrease operative time.[5] Broadly, rectal cancer surgery can be divided into three groups: LAR, LAR with loop ileostomy and APR.

The goal of rectal cancer surgery, as with other cancer surgery, is to remove the diseased organ with adequate margins of healthy tissue. To optimize survival and prevent local recurrence, surgery must remove all of the microscopic and macroscopic disease. Total mesorectal excision (TME) is a surgical technique described by Heald in 1986[6] that involves an en bloc removal of the rectum, blood supply, lymphatics, and mesorectal envelope of the rectum. TME is the standard of care for middle and lower rectal cancers, and its principles can be applied to both APR and LAR. Incomplete TME is associated with increased rates of local recurrence and decreased survival.[7,8] Circumferential resection margin (CRM) refers to the radial spread of the tumor. Similar to an incomplete TME, a positive CRM is associated with a significant increase in local recurrence rates.[9] A complete TME and negative CRM are important prognostic factors for rectal cancer outcomes.

The surgical treatment of rectal cancer should achieve an adequate oncologic resection while minimizing the associated morbidity. Careful consideration of tumor and patient characteristics will help determine which surgical approach will provide the best chance of cure, maintain post-operative quality of life and minimize complications.

1.1.2 Open and laparoscopic approach

Traditionally, surgery for rectal cancer was performed as **open** surgery (OS)- with a long midline incision and all steps of the operation performed through this incision (or combined with a perineal incision in APR). Recently, a minimally invasive approach has been adopted for rectal surgery. **Laparoscopic surgery** (LS) is achieved by placing ports in the abdominal wall to gain access to the peritoneal cavity, insufflating the abdomen with carbon dioxide and using a camera and long instruments to carry out the procedure. In a laparoscopic LAR, a small incision is made to remove the specimen. In a laparoscopic APR, the specimen is removed through the anus.[4] (see Figure 1)

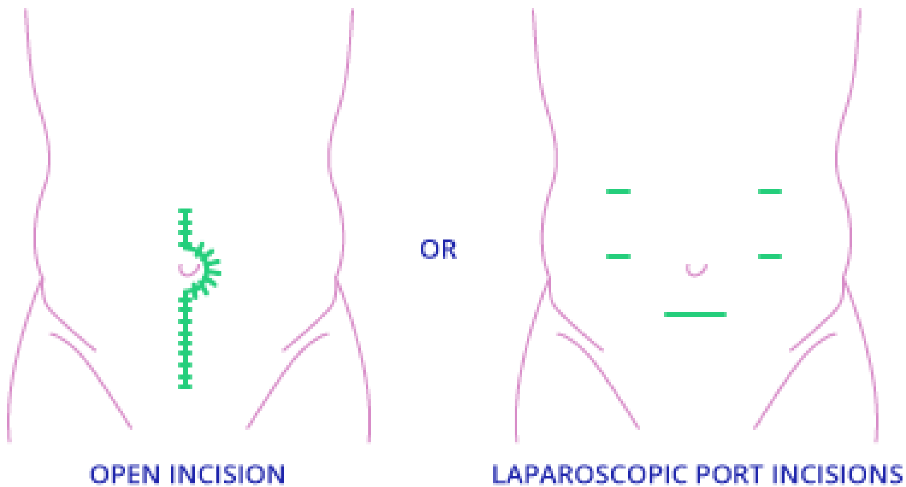

Figure 1.Incisions for open and laparoscopic rectal surgery [10]

The proposed benefits of LS include smaller incisions (and improved cosmesis), decreased postoperative pain, decreased morbidity and shorter length of stay. However, for LS for rectal cancer to safely be employed, it must achieve oncologic results similar to the traditional OS.

1.1.3 LS vs. OS for colon cancer

The role of LS for rectal cancer cannot be completely understood without first discussing LS for colon cancer. Surgery for colon cancer is technically easier than for rectal cancer in both OS and LS. The colon is easily accessible, and colectomy does not generally require dissection in the pelvis which is technically challenging. For these reasons and others, LS for colon cancer was investigated earlier than LS for rectal cancer, and consequently, the evidence supporting laparoscopic colectomy for colon cancer is more robust. Three multicenter randomized control trials (RCT) published in 2004-2008 compared overall survival, local recurrence rate and disease-free survival between OS and LS for colon cancer. The COST, MRC CLASICC, and COLOR trial all found that LS was non-inferior to OS for colon cancer regarding these oncologic outcomes.[11-15] A subsequent Cochrane review on the long-term outcomes of patients with colon cancer undergoing LS identified 33 RCTs published on this topic and found equivalent recurrence rates and long-term outcomes between OS and LS.[16]

Laparoscopic colectomy is also equivalent or superior to OS when comparing morbidity and other clinical outcomes. The COST and COLOR trial found patients had a shorter length of stay and used less narcotics when their surgery was performed laparoscopically.[11,12] Laparoscopic colectomy has also been associated with a quicker return of bowel function, improved pulmonary function, decreased surgical site infection and decreased total morbidity when compared to OS.[17-23]

Based on the aggregate of these data, clear uptake of LS for colon cancer has been observed in the developed world. The proportional uptake of LS for colon cancer has increased dramatically in recent years, comprising approximately half of all resections in the US[24], England[25] and Canada.[26]

1.2 LS for rectal cancer

The anatomic location of the rectum within the bony pelvis and its close proximity to important structures increases the technical difficulty of rectal surgery compared to colon surgery. However, despite the challenges of rectal cancer surgery, the success of LS in colon cancer has stimulated interest and investigation of LS for rectal cancer; several recent RCTs have compared LS and OS for rectal cancer. The endpoints of these trials included traditional oncologic outcomes such as overall survival, disease-free survival, and local recurrence. Given the importance of pathologic quality as surrogate outcomes in rectal cancer, several trials have also included pathology-related endpoints such the circumferential radial margin (CRM), completeness of TME and distal negative margin.

1.2.1 Oncologic outcomes

Similar to colon cancer, three multi-center, non-inferiority RCTs comparing LS and OS for rectal cancer have established equivalent oncologic outcomes between the two surgical approaches. The MRC CLASICC, COREAN, and COLOR II found no difference in overall survival, disease-free survival, and recurrence between LS and OS.[13,27-29] In addition, there are also many non-randomized comparative studies that support the findings of these RCTs. [30-34]

Despite the consistency in these trials, recent evidence has demonstrated some concerning findings regarding LS for rectal cancer in relation to surrogate pathology outcomes. The Australasian Laparoscopic Cancer of the Rectum Trial (ALaCaRT), a non-inferiority RCT that compared LS and OS for rectal cancer [35] used a composite pathological outcome- including negative circumferential margin, complete TME, and a clear distal margin to define a "successful resection". This was achieved in 82% of patients in the LS group and 89% of patients in the OS group. The margin of non-inferiority was not excluded, and a post-hoc test for superiority favored the OS group. Moreover, a subgroup analysis suggested that adverse pathologic outcomes with LS were particularly marked in patients who had neoadjuvant chemoradiotherapy, large tumors, or a high body mass index (BMI).[35]

Similar to ALaCaRT, the ACOSOG Z6051 trial also used composite pathological endpoints of distal margin, circumferential radial margin, and complete TME to define complete surgical excision.[36] This was achieved in 86.9% of the OS group compared to 81.7% of the LS group; LS did not meet criteria for non-inferiority compared to OS. Based on these results, the authors concluded that the routine use of LS for patients with stage II or stage III rectal cancer could not be supported.

These somewhat concerning pathology-focused findings (ALaCaRT and ACOSOG) contrast the results of MRC CLASICC, COREAN and COLOR II, all which demonstrated equivalent oncologic outcomes between LS and OS for rectal cancer. These conflicting results are likely related to a fundamental difference in the study characteristics and endpoints examined.

Although the ALaCaRT and ACOSOG trials failed to demonstrate non-inferiority of LS when compared to OS, the overall quality of surgery was high and better than earlier RCTs. For example, the COLOR II trial reported an overall CRM positivity rate of 10%, and 25% in those patients who underwent APR.[29] Similarly, the MRC CLASSIC reported 16% of patients undergoing LS had a positive CRM, and 12% among those patients undergoing laparoscopic APR (compared to 6% in the open group).[37] Despite the high rate of CRM positivity in patients who underwent LS in these trials, there were no differences in rates of local recurrence and survival between open and LS.[14,27,29] This suggests that potential inferior pathological outcomes with LS (as found in ALaCaRT and ACOSOG) may not translate into a difference in survival data, a more meaningful outcome for patients and providers. Finally, the impact of additional treatment received by many patients with rectal cancer (chemoradiation) may mitigate the impact of worrisome pathologic findings on eventual oncologic outcomes. The impending publication of long-term oncologic outcomes of ALaCaRT and ACOSOG will hopefully provide clarity in the near future.

1.2.2 Morbidity and other outcomes

LS for rectal cancer has favorable short-term outcomes when compared to OS.[38-44] Randomized data have consistently demonstrated reduced blood loss, less narcotic use and quicker return of bowel function among patients undergoing LS.[13,28,45] For all patients undergoing elective rectal surgery, LS is associated with a 40% decrease in postoperative complications when compared to OS.[46]

1.2.3 Summary

LS for rectal cancer has equivalent survival and recurrence outcomes with significant benefit in terms of short-term outcomes and morbidity when compared to OS. There remains some concern related to pathological endpoints, suggesting that tumor excision may be less complete when compared to OS, although to date no clear detrimental impact on recurrence or survival has been demonstrated.

1.3 The uptake of LS for rectal cancer

There are limited data summarizing the uptake of LS for rectal cancer at a population level. After the publication of the COST trial, LS for colorectal resection increased in the United States. It is estimated the uptake of LS for rectal cancer has increased from 2.1% in 2004 to 13.2% in 2009.[47] Another study from the United States found that approximately 53% of patients with early rectal cancer had LS in 2004-2011, while more recent research has demonstrated that by 2015, over half (55.3%) of patients with rectal cancer had LS in the US[48,49] Similarly in Italy, the majority of patients with rectal cancer underwent LS in 2014 (52.5%).[50] In Australia the rate of LS for rectal cancer has increased from 0.6% in 2000 to 15.5% in 2008, while England has observed an increase in the uptake of LS from 0% in 1996 to 21.7% in 2006.[51] [52]

In Canada, Simunovic *et al.* investigated the uptake of LS for colorectal cancer in Ontario from 2002-2009 and found that the rate of LS for rectal cancer increased from 4.8% to 19.6%. [53] A similar study published by Musselman *et al.* found an increase in the annual rate of LS from 0.60 per 100,000 in 2003 to 2.24 per 100,000 in 2008 in Ontario.[54] Currently, there is a lack of national-level data exists on the uptake of LS for rectal cancer in Canada.

1.3.1 Potential factors associated with uptake of LS for rectal cancer: patient factors

The difficulty of LS for rectal cancer is associated with certain patient factors. Laparoscopy can be challenging in obese patients due to difficulty gaining entry into the abdomen and distortion of anatomy from intra-abdominal adipose tissue. This technical challenge contributes to the high rate of conversion from LS to OS in obese patients undergoing LS.[55,56] Therefore, body mass index (BMI) is likely associated with the uptake of LS.

Other patient characteristics may influence uptake. In general, males have a narrower bony pelvis than females, which increases the difficulty of pelvic dissection. Male gender and narrow pelvis are independent predictors of longer operative time and increased technical difficulty in LS for rectal cancer.[57,58] Tumor characteristics also influence the feasibility of LS. Large, bulky rectal tumors are challenging to resect successfully, and tumor size is an independent predictor for conversion, increased operative time and morbidity in patients undergoing LS for rectal cancer. [57,58] Moreover, patients with large rectal tumors are more likely to have a positive CRM.[59] The location of the tumor can also impact the technical difficulty of LS for rectal cancer[41] [28,60] Low tumors that necessitate APR require less manipulation of the rectum in the pelvis because there is no anastomosis, making a laparoscopic APR technically easier than a laparoscopic LAR. Low rectal tumors amenable to LAR are likely the most challenging rectal tumors to resect, and low anastomoses are the most likely to leak postoperatively, prompting many surgeons to perform a loop ileostomy at the time of resection to divert stool away from the healing anastomosis. Therefore, tumor size and type of surgery (LAR, LAR with loop ileostomy, or APR) are likely associated with the uptake of LS.

In general, LS is performed more often in younger patients.[61] Age-related differences in physiology may explain the decreased utilization of laparoscopy in elderly patients. Although LS is generally safe, insufflation of carbon dioxide into the abdomen can lead to severe physiologic derangements such as hypercarbia, and decreased cardiopulmonary function.[62,63] The effects of pneumoperitoneum may be more pronounced in elderly patients, or those with co-morbidities.[62,64] Additional concerns with the use of LS for rectal cancer in elderly patients include prolonged operative times and extreme positioning required for exposure.[65] However, recent evidence has demonstrated that age is not an independent risk factor for postoperative morbidity after LS for rectal cancer[22,66] and that elderly patients may actually benefit from LS in terms of shorter length of stay and return of gastrointestinal function.[67] Therefore, the influence of age on the uptake of LS for rectal cancer remains unclear. This relationship is important to define, as increasing age is a well-established risk factor for rectal cancer.[4]

Important medical comorbidities are defined as conditions that are present on admission, not directly related to the admission diagnosis, that increase the likelihood of poor outcomes or increased intensity of resource utilization.[68] Patients with severe medical comorbidities may have increased susceptibility to the adverse effects of pneumoperitoneum and Trendelenburg positioning (head-down) during LS for rectal cancer[69], which could lead to increased rates of postoperative complications. An American Society of Anesthesiologists (ASA) score of 3 or greater is associated with increased postoperative morbidity in patients undergoing LS for rectal cancer, after controlling for age.[66] Consequently, patients with multiple medical conditions may be denied LS. However, recent evidence suggests that these "high-risk" patients may actually benefit the most from LS in terms of decreased morbidity, intra-operative blood loss, postoperative pain and length of stay.[70-72] Similar to age, the influence of patient co-morbidity on the uptake of LS for rectal cancer is currently unknown and should be further defined.

1.3.2 Potential factors associated with uptake of LS for rectal cancer: surgeon/hospital volume and setting

Surgeon volume is described as the number of cases performed in one year (annual) or over a certain time-period (cumulative). Patients who have surgery for rectal cancer (both LS and OS) have improved early postoperative outcomes, decreased mortality and lower permanent stoma and CRM positivity rates when treated by a high volume surgeon.[73-77] Laparoscopic LAR is one of the most technically difficult colorectal procedures[78], with a learning curve estimated to be between 50-200 cases.[79 80] Outcomes after LS for rectal cancer are influenced by surgeon experience and volume such that oncologic outcomes, complication rates, and length of hospital stay all decrease as the experience of the surgeon increases.[81,82] Therefore, surgeon volume may influence the uptake of LS for rectal cancer.

The use of LS for rectal cancer is likely influenced by hospital characteristics. Urban teaching hospitals are more likely to utilize LS than rural, nonteaching hospitals.[83] There has been extensive research on the impact of hospital volume on outcomes in rectal cancer. For patients undergoing surgery (both LS and OS), those who have surgery in a high volume center have lower mortality rates, higher overall survival, and less CRM positivity than those treated in low volume centers.[84-86] Currently, the difference in use of LS between high and low volume hospitals in Canada is unknown.

1.3.3 Potential factors associated with uptake of LS for rectal cancer: surgeon financial reimbursement

In Canada, most physicians are paid on a fee-for-service basis, although newer models with individually negotiated salaries are becoming more common. Physician reimbursement method can influence the delivery of care to patients with cancer.[87] In Ontario, the physician-billing schedule was updated to give surgeons a 25% premium if they initiated colon surgery using a laparoscopic approach.[53] This financial incentive was associated with a significant increase in uptake of LS for colon cancer in Ontario.[53] The Ontario government did not implement a financial incentive for LS for rectal cancer at this time. It is possible that since the publication of the COST, COREAN and COLOR II trials that some provincial governments may have changed physician reimbursement for rectal cancer surgery; the impact of such changes is unclear.

1.3.4 Potential factors associated with uptake of LS for rectal cancer: Geography urban/rural status and province

Geographic variation in medical practices is multifactorial, and is likely related to many of the previously discussed patient, surgeon and hospital characteristics.[88] In the United States, patients with similar rectal tumors can expect different surgical management depending on where they live. The proportion of patients given a permanent colostomy for rectal cancer significantly varies among counties located within the same state.[89] The distribution of LS and OS for rectal cancer also varies by geographic region in the United States, where the overwhelming majority of LS are performed on patients living in metropolitan/urban areas.[90] In Canada, a survey of surgeons who treat rectal cancer revealed a regional variation in care[91], however, this difference may be attributed to a difference in the distribution of practicing specialists between regions.

Given the results of this survey, and the geographic trends observed in the United States, it is possible that geographic factors influence the uptake of LS for rectal cancer in Canada, and that variation exists among provinces.

1.4 Overall summary

LS for rectal cancer has acceptable oncological and long-term outcomes when compared to OS, and offers short-term outcome advantages. However, resection of mid and lower rectal cancer is technically demanding, especially with large tumors in a narrow male pelvis. These technical challenges may contribute to inferior pathological outcomes. As surgeons become more familiar with LS for rectal cancer, these issues may resolve.

Currently, the adoption of LS for rectal cancer in Canada is unknown. This study will describe the uptake of this technique, and explore which geographic, patient, surgeon and hospital factors are associated with its use. This information will help fill a gap in the literature, describing the use of LS for rectal cancer in Canada. Additionally, the variation in uptake among provinces will be described, and potential targets for innovation implementation will be identified.

1.5 Objectives

1.5.1 Overall objective

To describe and better understand the uptake of LS for rectal cancer in Canada.

1.5.2 Hypothesis

We hypothesize that, in Canada:

1. The uptake of LS for rectal cancer has increased over the past decade and differs across provinces.
2. The uptake of LS for rectal cancer is associated with specific geographic, patient, surgeon, and hospital factors.
3. The uptake of LS for rectal cancer is higher in provinces with policies that provide incentive for LS when compared to provinces without these policies.

1.5.3 Specific objectives

1. To describe the unadjusted and age-adjusted uptake of LS for rectal cancer, as defined by the proportion of rectal cancer surgeries performed laparoscopically in Canada, from fiscal years 2004-2014, both nationally and at a provincial level.
2. To identify geographic, patient, surgeon and hospital characteristics associated with the use of LS for rectal cancer.
3. To describe the content and timing of provincial policies regarding financial remuneration for LS for rectal cancer, and to correlate with provincial uptake.

Chapter 2: Materials and Methods

2.1 Cohort selection

This population-based retrospective cohort study utilized the Discharge Abstract Database (DAD) held by the Canadian Institute for Health Information (CIHI) to identify all rectal resections performed for rectal cancer in Canada, excluding Quebec, from April 1, 2004, to March 31, 2015. The DAD is a national administrative database that contains clinical and demographic information on hospital discharges, deaths, sign-outs, and transfers. Hospitals in all provinces, except Quebec, are required to provide CIHI with data for the DAD.

We included all adult patients with a valid Canadian postal code and a diagnosis of rectal cancer who underwent radical rectal resection. In an attempt to capture only those patients who would be eligible for either LS or OS, pregnant patients, emergency surgery and complex, multi-visceral resections were excluded. Emergency surgery in the setting of rectal cancer is often performed for perforation, obstruction or bleeding and is generally performed via an open approach. Similarly, those patients with locally advanced rectal cancer who require resection of adjacent organs (bladder, small bowel, abdominal wall, etc.) are generally not candidates for LS due to the complexity of the resection. Both emergency procedures and complex resections were exclusion criteria in recent randomized trials of LS versus OS for rectal cancer.[11,15,60,92,93]

Potential cases were identified using the International Classification of Disease, Tenth Revision, Canada (ICD-10-CA) to capture any patient with a diagnosis of rectal cancer. Surgical procedures were identified using the Canadian Classification of Health Intervention (CCI) coding system (see Table 1 and 2 for specific ICD and CCI codes). Patients were assigned to the year of admission for rectal resection.

2.2 Variables

Geographic variables included urban/rural status and province. Urban/rural status was captured using the forward sortation area (FSA)- the first three characters of the postal code recorded in the DAD. Urban/rural status is identified using the second character, 1-9 indicates urban postal code and 0 indicates a rural postal code.[94]

Patient variables included age, sex, surgery type and comorbidity. Age at time of admission was categorized as 18-50, 51-65, 66-80 and >80, and analyzed as a categorical variable. Sex was analyzed as a binary variable (male/female). Surgery type was grouped into three categories (LAR, LAR with loop ileostomy, and APR). Specific procedure codes are listed in Table 2. Specific codes for partial excision of rectum without anastomosis (colostomy and closure of rectal stump) were included in the APR group, although this description more accurately defines a Hartmann's procedure (HP). In the setting of rectal cancer, an elective (planned) HP is generally used for patients who do not require APR but have severe co-morbidities or impaired sphincter function (incontinence) to avoid the potential morbidity of anastomosis complications or worsening incontinence.[95,96] The proportion of patients undergoing rectal cancer surgery who undergo HP is low, ranging from 1.6%-13.9%.[97,98] This number is likely lower among patients undergoing elective rectal cancer surgery, as HP is commonly used to treat obstructing colorectal tumors in an emergency setting. Therefore, in our cohort of patients who underwent elective rectal cancer surgery (admissions via the emergency department excluded), we estimated that the proportion of patients undergoing a HP would be exceedingly low. An exploratory analysis to confirm this hypothesis was conducted, and the proportion of patients undergoing a HP was higher than expected, while the number of APRs was lower than expected. Given the similarity between these two procedures (both include permanent colostomy and resection of the rectum), those patients with the procedure code for partial excision of rectum without anastomosis (colostomy and closure of rectal stump) were included in our APR group. Further sensitivity analyses were conducted to ensure there were no systematic differences between this group of patients and the rest of the cohort.

Comorbidity was defined according to the Charlson Comorbidity Index, which uses categorized comorbidities of patients based on the ICD diagnostic codes in administrative databases. It consists of 17 comorbidities, which are weighted from 1 to 6 and then summed to form the total comorbidity score. This index has been validated to measure mortality risk and burden of disease in a wide range of patient populations.[99] In Canada, the reported in-hospital mortality for patients with a Charlson comorbidity index of 0 is 1.5%, compared to 28.3% for those with a score of ≥6.[100]The Charlson comorbidity index has been validated in many different patient cohorts, including the elderly,[101] patients with colorectal cancer,[102-104]and others.[100,105-107] Using the ICD-10 coding algorithm constructed by Quan *et al.*,[108] any Charlson comorbidity (except the primary diagnosis of rectal cancer) present prior to admission was identified and used to create the Charlson Comorbidity Index. There is a lack of consistency in the categorization of Charlson comorbidity scores for assessment of rectal cancer outcomes.[3,72,102,103,109-111] However, most studies use a score of 0 as single category.[3,100,102,103]Given the significant increase in in-hospital mortality associated with Charlson comorbidity scores ≥6[100]and the use of >6 as a category in previous studies of LS for rectal cancer,[72] we chose to categorize Charlson comorbidity index as 0, 1-6, and >6.

The mean annual number of rectal cancer surgeries was calculated for each hospital and surgeon, including only years in which at least one rectal cancer surgery was performed. Average annual volumes were categorized into quartiles and dichotomized into high and low, with high volume defined as above the 75^{th} quartile.

The presence of a province-specific financial incentive for LS was elicited using review of provincial billing codes and associated documentation. Any code describing financial remuneration for the use of laparoscopy with LAR or APR was considered a financial incentive for LS.

2.3 Objective-specific methodology and data analysis

<u>Objective 1:</u> *To describe the unadjusted and age-adjusted uptake of LS for rectal cancer, as defined by the proportion of rectal cancer surgeries performed laparoscopically in Canada, from fiscal years 2004-2014, both nationally and at a provincial level.*

The total number and unadjusted proportion of LS and OS for rectal cancer were reported at a national and provincial level from April 2004-March 2015. The annual proportion of LS was described according to age category, sex, province, urban/rural status, comorbidity score, surgery type, and surgeon/hospital volume.

The age-adjusted proportion of LS for each sex was calculated using direct-standardization and reported on a provincial and national level.

<u>Objective 2:</u> *To identify geographic, patient, surgeon and hospital characteristics associated with the use of LS for rectal cancer.*

The distributions of demographic, patient, surgeon, and hospital variables were compared between LS and OS groups using Chi-squared test for categorical variables and Student's t-test for continuous variables.

The association between geographic variables (urban/rural status, province), patient factors (age, sex, surgery type), year, surgeon volume and hospital volume with the uptake of LS was estimated using multiple logistic regression. As these variables were believed to potentially be associated with the use of LS for rectal cancer *a priori*, all were included in both univariable and multivariable analyses. Interaction terms were not used, as the purpose of this study was to describe the association between specific factors and use of LS, not to create a complex predictive model.

Sensitivity analyses were performed in three specific sub-cohorts. The first sub-cohort excluded patients of surgeons who did not perform any LS for rectal cancer during the study period. This sensitivity analysis will systematically reduce the influence of surgeon practice on the estimation of the uptake of LS for rectal cancer. The second sensitivity analysis was performed excluding any patient who underwent partial excision of the rectum with end colostomy and rectal stump (HP) to determine if our inclusion of these patients in the APR category was valid (see Methods 2.2 Variable Definition). The final sensitivity analysis was performed on patients with "rectosigmoid" tumors identified by the C19 ICD code. Tumors high in the rectum, or at rectosigmoid junction, are technically easier to resect than low rectal cancers and patients with rectosigmoid tumors may be treated more like those with colon cancer in that neoadjuvant chemoradiotherapy is not part of the treatment pathway. In order to determine if the predictors of LS were different in this group, we created model 4 to estimate the association between demographic, patient, surgeon and hospital factors with the uptake of LS among patients with rectosigmoid tumors.

Objective 3: *To describe the content and timing of provincial policies regarding financial remuneration for LS for rectal cancer, and to correlate with provincial uptake*.

The relationship between provincial policies and uptake of LS for rectal cancer was investigated by first describing any province's financial remuneration LS that differed from OS, as described in provincial billing code documents.

Province-specific figures depicting the proportion of LS over time were created with the year of financial incentive implementation marked. The slope of uptake over time was calculated before and after financial incentive implementation and compared among provinces.

2.4 Data Analysis

All statistical analysis was conducted using STATA 14 StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP. For statistical testing, a P value of < 0.05 was deemed statistically significant. For logistic regression analysis, associations were reported as odds ratios (OR) and 95% confidence intervals (CI).

Table 1. ICD-10-CA codes for rectal cancer

ICD-10-CA Code	Diagnosis
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum

Table 2 CCI codes for LS and OS for rectal cancer

	CCI Code	Description
Lower anterior resection (LAR)		
Open	1.NQ.87.RD	Partial excision of rectum with colo-rectal anastomosis
	1.NQ.89.SF	Total excision of rectum with colo-anal anastomosis
	1.NQ.89.KZ	Total excision of rectum with transanal sphincter-sparing TME and colo-anal anastomosis
Laparoscopic	1.NQ.87.DE * **1.NQ.87.DF ***	Partial excision of rectum with colorectal anastomosis
	1.NQ.89.GV	Total excision of rectum with laparoscopic abdominal approach and transanal sphincter-sparing TME and colo-anal anastomosis
LAR with loop ileostomy	Any LAR code + 1.NK.77.	Concomitant ileostomy formation
Abdominal perineal resection (APR)		
Open	1.NQ.89.RS	Total excision of rectum with stoma formation and distal closure (anterior approach)
	1.NQ.89.LH	Total excision of rectum with stoma formation and distal closure
	1.NQ.87.TF	Partial excision of rectum without anastomosis (colostomy and closure of rectal stump)
Laparoscopic	1.NQ.89.AB	Total excision of rectum with stoma formation and distal closure
	1.NQ.87.DX	Partial excision of rectum without anastomosis (colostomy and closure of rectal stump)

* The CCI code for laparoscopic LAR with colorectal anastomosis changed in 2009

Table 3. Definition of variables

Variable name	**Description**
Province	Submitting province 1 Newfoundland 2 Prince Edward Island 3 Nova Scotia 4 New Brunswick 0 Ontario 5 Manitoba 6 Saskatchewan 7 Alberta 8 British Columbia
Year	Fiscal year of admission
Rural/urban status	Place of residence rural or urban Postal code truncated to forward sortation area (FSA) First 3 characters of postal code, second character defines geographic area: 0 rural, 1-9 urban
Age	Age in years at time of admission, categorized as 18-50, 51-65, 66-80 and >80
Comorbidity score	Charlson comorbidity index (0: reference, 1-6, >6)
Sex	Male or female
Surgeon volume	High volume >75th percentile of average annual surgeon volume
Hospital volume	High volume >75th percentile of average annual hospital volume
Surgery type	LAR with or without ileostomy, APR (see Table 2)

Chapter 3: Results

3.1 Cohort Composition and Patient Population

Our initial Discharge Abstract Database inquiry identified 38,010 patients with a diagnosis of rectal cancer who underwent a radical rectal resection (Figure 2). Ninety-one patients did not have a valid Canadian postal code. Exclusion criteria were met in four patients who were pregnant at the time of admission, 2,341 patients who were admitted via the emergency department and 7,119 patients who underwent a complex multi-visceral resection (see Table 4 for procedure descriptions and frequencies for complex resections), leaving a final cohort of 28,455 patients.

The distribution of geographic, patient, surgeon and hospital factors among all patients within our study cohort, stratified by LS and OS, are presented in Table 5. Patients who underwent LS were more likely to be in a younger age-category ($p<0.001$), female ($p<0.001$), and have a lower Charlson comorbidity score ($p<0.001$) compared to the OS group. Additionally, there were a higher proportion of LS patients who were operated on by a high-volume surgeon (31.8% vs. 23.5%, respectively; $p<0.001$) and in a high-volume hospital (31.4% vs. 23.0%, respectively; p=<0.001). In terms of surgery type, APR was less common in the LS group compared to OS (20.4% vs. 42.8%, respectively; $p<0.001$). More patients in the LS group resided in an urban area compared the OS group (83.2% vs. 76.9%, respectively; $p<0.001$).

3.2 Objective 1: *To describe the unadjusted and age-adjusted uptake of LS for rectal cancer, as defined by the proportion of rectal cancer surgeries performed laparoscopically in Canada, from fiscal years 2004-2014, both nationally and at a provincial level.*

3.2.1 Pan-Canadian uptake of LS

Over the entire 11-year period of our study, 17.6% of our cohort underwent LS, and 82.4% underwent OS (Figure 3). The annual number of rectal cancer surgeries in Canada remained relatively stable over time, with an increase in the number of LS cases and a corresponding decrease in OS cases (Figure 4). The pan-Canadian uptake of LS for rectal cancer increased from 5.9% in 2004 to 34.0% in 2014. Conversely, the use of OS for rectal cancer decreased from 94.1% in 2004 to 66.0% in 2014 (Figure 3).

In general, the unadjusted and age-adjusted uptake for LS in Canada was similar. Nationally, the age-adjusted proportion of males undergoing LS for rectal cancer increased from 5.1% in 2004 to 31.8% (Figure 5). Similarly, the age-adjusted proportion of females undergoing LS for rectal cancer in Canada increased from 6.9% in 2004 to 37.8% (Figure 5). For both sexes, the unadjusted and age-adjusted uptake of LS increased at a relatively constant rate.

3.2.2 Provincial Uptake of LS

Not surprisingly, there were significant differences between provinces regarding the number of rectal cancer surgeries performed, given differences in provincial populations (Figure 6). Prince Edward Island (PE) had the lowest number of rectal cancer surgeries (175), representing only 0.6% of the total cohort. Conversely, Ontario (ON) performed almost half of all rectal cancer surgeries (43.9%), with 12,943 cases. Following ON, British Columbia (BC) and Alberta (AB) had the second and third highest number of rectal cancer surgeries, respectively. Approximately 78% of cases were performed in these three provinces.

The overall (Table 5) and annual proportional use of LS for rectal cancer varied among provinces (Figure 7). From 2004-2014, the greatest proportional increase in LS was observed in PE, ON, and BC. All provinces had a statistically significant increase in the uptake of LS for rectal cancer over the study period except Newfoundland (NL).

The annual change in percent of uptake varied among provinces (Table 6). In NL, Nova Scotia (NS), Manitoba (MB) and Saskatchewan (SK), the largest annual increase in uptake of LS occurred early in the study period (2006-2009), while PE, New Brunswick (NB), ON, AB and BC experienced the largest increase in annual percent between 2011-2014. The largest single annual change in percentage of LS occurred in PE from 2012-2013 with a 28.6% increase.

Overall, each province had a relatively unique experience with the use of LS from 2004-2014. The following provides a brief summary of each province's uptake of LS over time.

NL was the only province that did not experience a statistically significant increase in the use of LS (Figure 8). There were 886 rectal cancer resections (3.1% of the Canadian total) performed from 2004-2014, ranging from 67-94 per year. Uptake of LS increased from 0% in 2004 to 1.3% in 2014. The sex-specific age-standardized use of LS in NL was higher than the unadjusted rates, most notably in 2009 for males (14.9%) and 2010 for females (19.5%). For both unadjusted and adjusted rates, use of LS declined after peaking in 2009-2010.

PE performed the fewest number of rectal cancer surgeries (175) but had highest proportional use of LS by 2014 (52.4%) (Figure 9). From 2004-2012 there was only one LS performed; in 2013 and 2014 six (28.6%) and 11 (52.4%) laparoscopic cases were performed respectively. The sex-specific age-adjusted use of LS was higher among females compared to males. In 2014, over 60.0% of females undergoing rectal cancer resection had LS compared to 45.9% of males.

In **NS**, there were 1,358 rectal cancer resections performed from 2004-2014. Use of LS increased from 2.6% in 2004 to 13.8% in 2014 (Figure 10). The largest annual increase in uptake occurred between 2007 and 2008, and the highest proportional use was in 2011 (16.8%). After adjusting for age distribution, annual proportions of LS remained similar to unadjusted rates.

The use of LS for rectal cancer in **NB** was low (Figure 11). Between 2004-2014, the annual proportional use of LS ranged from 4.5%-10.0%. The highest proportional use of LS occurred in 2012, when 12.2% of rectal surgeries were done laparoscopically. In general, use of LS was higher in the last three years of the study compared to 2004-2012. After adjusting for age, uptake of LS among females in NB was higher than the unadjusted uptake. The opposite was true among males, where there was a decrease in uptake of LS after direct standardization.

Between 2004-2014 almost half of the rectal cancer resections in Canada were performed in **ON** (12,943). The increase in proportional use of LS in ON was the second highest in the country, where rates increased from 7.2% in 2004 to 42.0% in 2014 (Figure 12). The largest annual increase in uptake occurred between 2013 (31.8%) and 2014 (42.0%). Age-adjusted rates were higher in females compared to unadjusted rates, and lower in males.

There were 1,497 rectal cancer resections in **MB** between 2004-2014, representing 5.3% of the total cohort. Uptake of LS increased from 5.1% to 17.7% over the 11 years of this study (Figure 13). The largest increase in uptake occurred between 2006 (7.8%) and 2007 (17.4%). After 2007 there was no consistent trend in uptake until 2012 where rates declined consistently until the end of the study. Age-adjusted rates were similar to unadjusted rates.

SK performed 4.4% of the rectal cancer surgeries in Canada between 2004-2014 (1,250). The uptake of LS in 2004 was higher in SK compared to other provinces (10.7%), however, in 2014 SK had the 3rd lowest proportional use of LS (11.8%) (Figure 14). Overall, the uptake of LS remained stable in SK except for a brief increase in 2008. Age-adjusted rates among females were higher than unadjusted rates, and lower among males.

AB had the 4th highest proportional use of LS for rectal cancer in 2014. A total of 3,519 rectal cancer surgeries were done in AB, representing 12.4% of the national total. Uptake increased from 3.3% to 32.0% (Figure 15). Overall, the annual change in uptake of LS was inconsistent prior to 2011, after which it consistently increased. The largest annual increase in use of LS occurred in the last year of the study from 22.3% in 2013 to 32.0% in 2014. Age-adjusted rates were higher in females compared to unadjusted rates, while both rates were similar in males.

Approximately 20% (5,792) of all rectal cancer resections were performed in **BC**. The use of LS in BC increased fairly consistently during this study (Figure 16), with the largest increase between 2012-2013 (29.0% to 36.1%). Uptake increased from 5.7% in 2004 to 39.1% in 2014, representing the 3rd highest use of LS in Canada. The uptake of LS in BC did not change significantly after adjusting for age.

Overall, trends in the provincial uptake of LS were similar before and after age-adjustment. Importantly, marked interprovincial variation in uptake persisted after calculation of sex-specific age adjusted rates, indicating that the variation in use of LS among provinces is not completely explained by differences in age distributions (Figure 17 and 18).

3.3 Objective 2: *To identify geographic, patient, surgeon and hospital characteristics associated with the use of LS for rectal cancer*

3.3.1 Patient, geographic, surgeon and hospital factors associated with the uptake of LS

The uptake of LS varied among patients of different age-categories, comorbidity score, and sex. Patients □50 and 51-65 experienced the largest increase in uptake between 2004-2014 (~29%) compared to older age-groups (Figure 19), while those >80 had the smallest increase (22.2%). The use of LS for rectal cancer increased over time more dramatically in females than males (Figure 20), and uptake was consistently higher in females during the entire study period. In terms of comorbidity score, use of LS over time increased among all three categories of the

Charlson Comorbidity Index (CCI), with the greatest increase observed in patients with a CCI score of >6, where uptake increased from 3.6% to 33.3% (Figure 21). Interestingly, uptake of LS was initially low in this group of comorbid patients, but between 2011-2014 the uptake increased markedly each year.

Use of LS in 2004 was similar in patients with rural and urban residences (4.7% in rural and 6.3% urban), however the increase in uptake over time was significantly higher in the urban group such that 36.4% of had LS in 2014 (compared to 25.2% in rural group) (Figure 22).

Uptake of LS varied between high and low volume surgeons, high and low volume hospitals, and by type of surgical resection. High volume surgeons, who performed an average of 10-28 rectal cancer surgeries/year, had an increased uptake of LS from 4.8%-39.8% (Figure 23). Similarly, use of LS for rectal cancer in high volume hospitals increased from 9.5%-39.6% (Figure 24). Use of laparoscopic LAR increased over time more dramatically compared to laparoscopic APR (9.1%-42.0% LAR and 1.3%-22.8% APR) (Figure 25). Uptake of LS was consistently higher among patients undergoing LAR compared to LAR with ileostomy and APR, for all years of the study.

Geographic, patient, surgeon and hospital variables were identified *a priori* as potential factors associated with the uptake of LS for rectal cancer and were included in our multiple logistic regression models.

The results of the univariate and multivariable logistic regression (model 1) can be found in Table 7. On multivariable analysis, age-category, sex, comorbidity score, residence, surgeon/ hospital volume, type of surgical resection, year and specific province were all significantly associated with the use of LS.

Year and specific province were the strongest predictors of the uptake of LS for rectal cancer. The probability of LS increased annually between 2004-2014, and the odds of LS in 2014 were 9.63 times the odds in 2004. Compared to Ontario, NL and NB had the lowest odds of LS. High surgeon volume and hospital volume were also strong predictors of LS. APR was a negative predictor of LS, whereby patients undergoing APR had a 66% decrease in the odds of LS compared to LAR.

The results of a sensitivity analysis on a sub-cohort of patients who had been treated by a surgeon who performed at least one LS for rectal cancer between 2004-2014 are presented in Table 8. This sub-cohort included 21,173 patients treated by 650 surgeons and had a similar distribution of patient, geographic, surgeon and hospital variables to our original cohort. Volume-statistics were recalculated and dichotomized above and below sixteen rectal cancer procedures per year (surgeon volume) and 45 rectal cancer procedures per year (hospital volume).

Significant predictors of LS were the same in model 2 as model 1 but magnitudes of association differed. Year, surgeon/hospital volume became weaker predictors of LS, while APR and LAR with ileostomy were more negatively associated with LS, compared to model 1.

Our second subgroup analysis (model 3) excluded patients who underwent HP (partial excision of the rectum with colostomy and closure of rectal stump). There were 4,233 patients who underwent HP, comprising 14.9% of the entire study cohort. Exploratory analysis did not demonstrate any systematic, clinically significant differences between groups. Importantly, the distribution of Charlson Comorbidity scores was similar; the proportion of patients with a comorbidity score >6 was 7.3% in patients who underwent HP compared to 5.8% in those who did not have HP. Age distribution was also similar between the HP group and the rest of the cohort, with a mean age of 67 and 66, respectively. Although these differences are statistically significant (chi-square $p<0.001$), they are unlikely to be clinically significant.

The results of model 3 are presented in Table 9. Predictors of LS for rectal cancer were the same before and after exclusion of HP. In general, magnitudes of association were similar between model 1 and model 3, with the exception of surgery type. APR became a stronger negative predictor of LS after removing HP (OR 0.27). Overall, the results of this sensitivity analysis suggest that the incorporation of HP patients in the APR group will not result in systematic misclassification or bias.

Our final sensitivity analysis (model 4) included 10,846 patients with rectosigmoid tumors. The annual uptake of LS increased from 7.8% in 2004 to 40.2% in 2014 in this subcohort. Predictors of LS included younger age, female sex, less comorbidity, urban residence, high surgeon and hospital volume, LAR, specific province, and year. Overall, significant predictors of LS among patients with rectosigmoid cancer were not different than predictors of our entire cohort, suggesting that predictors of LS are not different in patients with rectosigmoid tumors compared to other tumors of the rectum.

3.4 Objective 3: *To describe the content and timing of provincial policies regarding financial remuneration for LS for rectal cancer, and to correlate with provincial uptake*.

An inquiry of provincial fee-code documents revealed that NS, ON, and BC were the only provinces with financial incentives for LS (Table 10). In NS there is a 5% increase in remuneration for laparoscopic LAR, but there is no specific laparoscopic APR fee-code. ON has a 25% premium for LS, including both APR and LAR. In BC, an 11% increase in remuneration is provided for a laparoscopic APR compared to an open APR, and a 25% increase for laparoscopic LAR.

The NS laparoscopic LAR fee-code was introduced in March 2012. On average, uptake of LS increased by 1.2%/year before and 0.8%/year after financial incentive implementation, suggesting that this policy was not associated with a change in the uptake of LS (Figure 25).

In ON, a 25% increase for laparoscopic LAR/APR was introduced in October 2009. There was an average increase in the uptake of LS from 2.5%/year before to 4.4%/year after implementation (Figure 26). Similarly, there was an increase in the average annual increase in uptake of LS from 2.9%/year to 4.3%/year after the 2011 introduction of a financial incentive in BC (Figure 27).

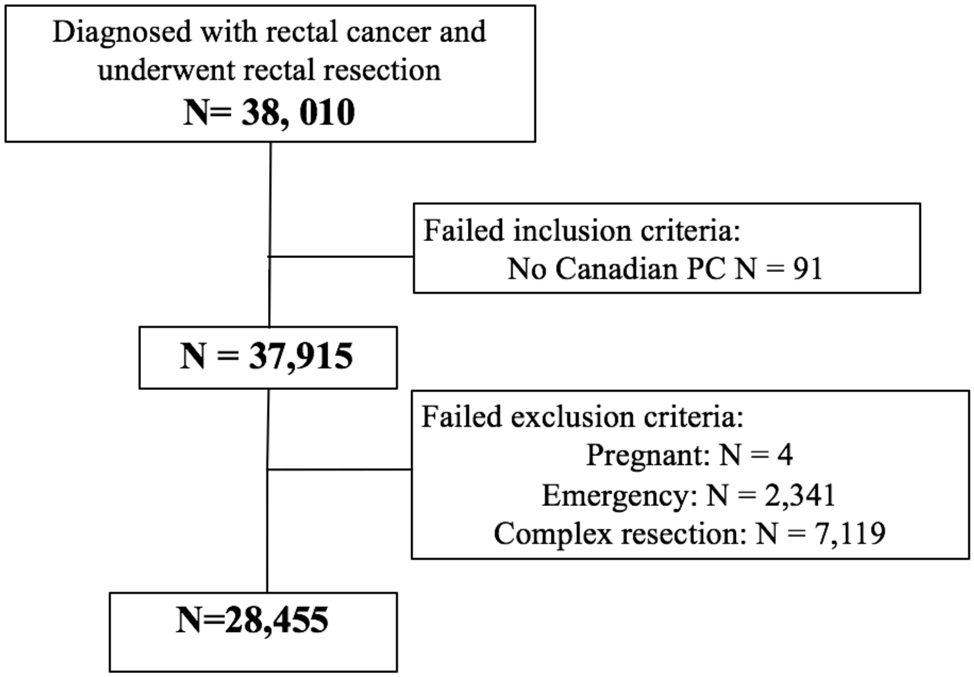

Figure 2. Flow diagram of cohort creation

Table 4. Description and frequency of complex surgical procedures used as exclusion criteria in creation of study cohort

Code	Description	# Removed
1MG87	Excision partial, lymph nodes intra-abdominal	8
1MG89	Excision total, lymph nodes intra-abdominal	0
1NF87	Excision partial, stomach	4
1NF89	Excision total, stomach	0
1NM87	Excision partial, large intestine	586
1NM89	Excision total, large intestine	12
1NP86	Closure of fistula, small and large intestine	45
1OA87	Excision partial, liver	149
1OB87	Excision partial, spleen	8
1OB89	Excision total, spleen	51
1OJ87	Excision partial, pancreas	7
1OK87	Excision partial, pancreas with duodenum	3
1OT07	Hyperthermy, abdominal cavity	11
1OT35	Pharmacotherapy, local abdominal cavity	15
1OT52	Drainage abdominal cavity	276
1OT72	Release, abdominal cavity	1312
1OT87	Excision partial, abdominal cavity	177
1OT91	Excision radical, abdominal cavity	39

Code	Description	# Removed
1OW	Therapeutic interventions on surgically constructed sites in digestive and biliary tract	71
1PB87	Excision partial, adrenal gland	2
1PB89	Excision total, adrenal gland	7
1PC87	Excision partial, kidney	14
1PC89	Excision total, kidney	17
1PC91	Excision radical, kidney	40
1PG72	Release, ureter	212
1PG80	Repair, ureter	131
1PG82	Reattachment ureter	2
1PG87	Excision partial, ureter	82
1PG89	Excision total, ureter	9
1PM87	Excision partial, bladder	280
1PM89	Excision total, bladder	1
1PM90	Excision total bladder, with reconstruction	8
1PM91	Excision radical, bladder	32
1PM92	Excision radical bladder, with reconstruction	127
1PV	Therapeutic intervention on surgically created sites in urinary tract	3
1RB87	Excision partial, ovary	86
1RB89	Excision total, ovary	188
1RD89	Excision total, ovary with fallopian tube	1017
1RM87	Excision partial, uterus and surrounding structures	111
1RM89	Excision total, uterus and surrounding structures	447
1RM91	Excision radical, uterus and surrounding structures	113
1RS87	Excision partial, vagina	401
1RS89	Excision total, vagina	77
1SF87	Excision partial, sacrum and coccyx	72
1SF89	Excision total, sacrum and coccyx	35
1SF91	Excision radical, sacrum and coccyx	17
1SH	Therapeutic interventions on soft tissue of back	2
1SQ87	Excision partial, pelvis	3
1SQ91	Excision radical, pelvis	1
1SW	Therapeutic interventions on the pubis	2
1SY58	Procurement, muscles of the chest and abdomen	54
1SY72	Release, muscles of the chest and abdomen	1
1SY80	Repair, muscles of the chest and abdomen	2139
1SY84	Construction or reconstruction, muscles of the chest and abdomen	3
1SY87	Excision partial, muscles of the chest and abdomen	6
1SZ87	Excision partial, soft tissue of the chest and abdomen	44
1YS87	Excision partial, skin of abdomen and trunk	43

Table 5. Geographic, patient, surgeon and hospital characteristics of patients undergoing LS and OS for rectal cancer in Canada from 2004-2014

	Laparoscopic (N=5,002)		**Open (N=23,453)**		**p-value**
	N	%	N	%	
Age (years)					<0.001
□50	582	11.6	2,168	9.2	
51-65	1,870	37.4	8,499	36.2	
66-80	1,975	39.5	9,9910	42.3	
>80	575	11.5	2,876	12.3	
Gender					<0.001
Female	1,912	38.2	7,351	31.3	
Male	3,090	61.8	16,102	68.7	
Charlson Comorbidity Index					<0.001
0	3,034	60.7	13,326	56.8	
1-6	1,733	34.6	8,640	36.8	
□7	235	4.7	1,487	6.3	
Residence					<0.001
Rural	841	16.8	5,419	23.1	
Urban	4,161	83.2	18,034	76.9	
Surgeon volume					<0.001
High	1,591	31.8	5,506	23.5	
Low	3,411	68.2	17,947	76.5	
Hospital volume					<0.001
High	1,569	31.4	5,391	23.0	
Low	3,433	68.6	18,062	77.0	
Surgery type					<0.001
LAR	3,207	64.1	10,647	45.4	
LAR + ileostomy	625	18.4	2,766	11.8	
APR	1,170	20.4	10,040	42.8	
Year of surgery					<0.001
2004	151	3.0	2,388	10.2	
2005	217	4.3	2,513	10.7	
2006	281	5.6	2,312	9.9	
2007	344	6.9	2,215	9.4	
2008	399	7.9	2,192	9.3	
2009	439	8.8	2,310	9.9	
2010	463	9.3	2,095	8.9	
2011	556	11.1	1,969	8.4	
2012	622	12.4	1,989	8.5	
2013	673	13.5	1,809	7.7	
2014	857	17.1	1,661	7.1	
Province					<0.001
NL	27	0.5	859	3.7	

	Laparoscopic (N=5,002)		**Open (N=23,453)**		**p-value**
	N	%	N	%	
PE	18	0.4	157	0.7	
NS	148	3.0	1,210	5.2	
NB	55	1.1	980	4.2	
ON	2,775	55.5	10,168	43.3	
MB	214	4.3	1,283	5.5	
SK	136	2.7	1,114	4.8	
AB	470	9.4	3,049	13.0	
BC	1,159	23.1	4,633	19.8	

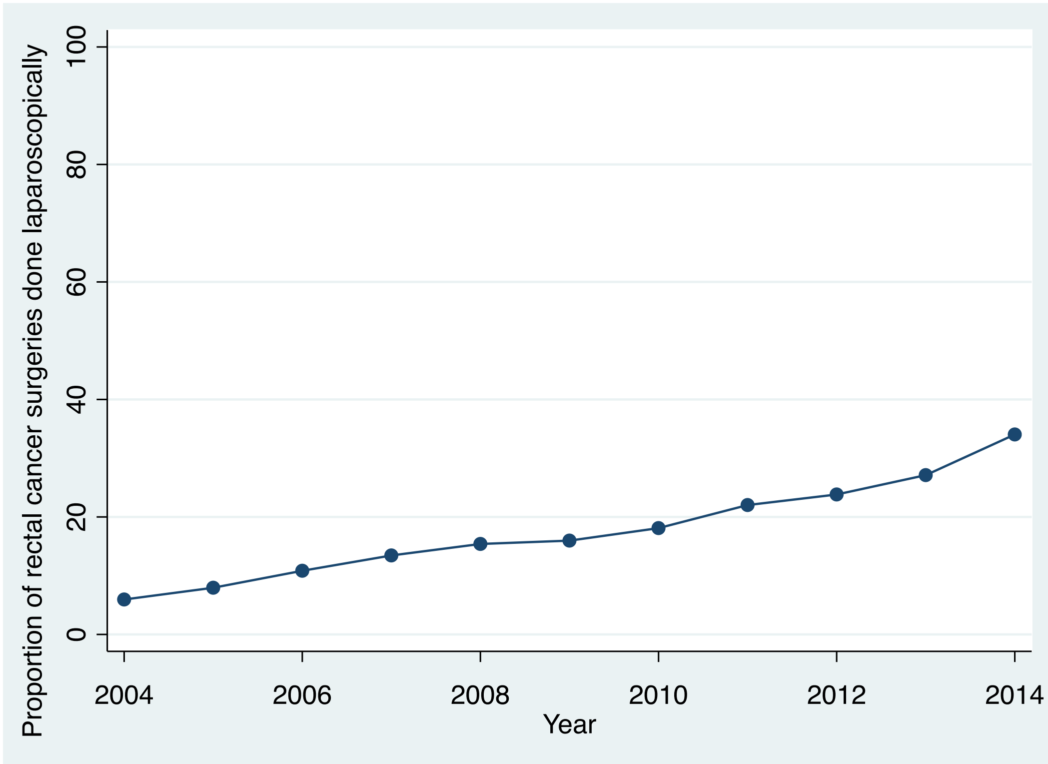

Figure 3. The uptake of LS for rectal cancer in Canada from 2004-2014

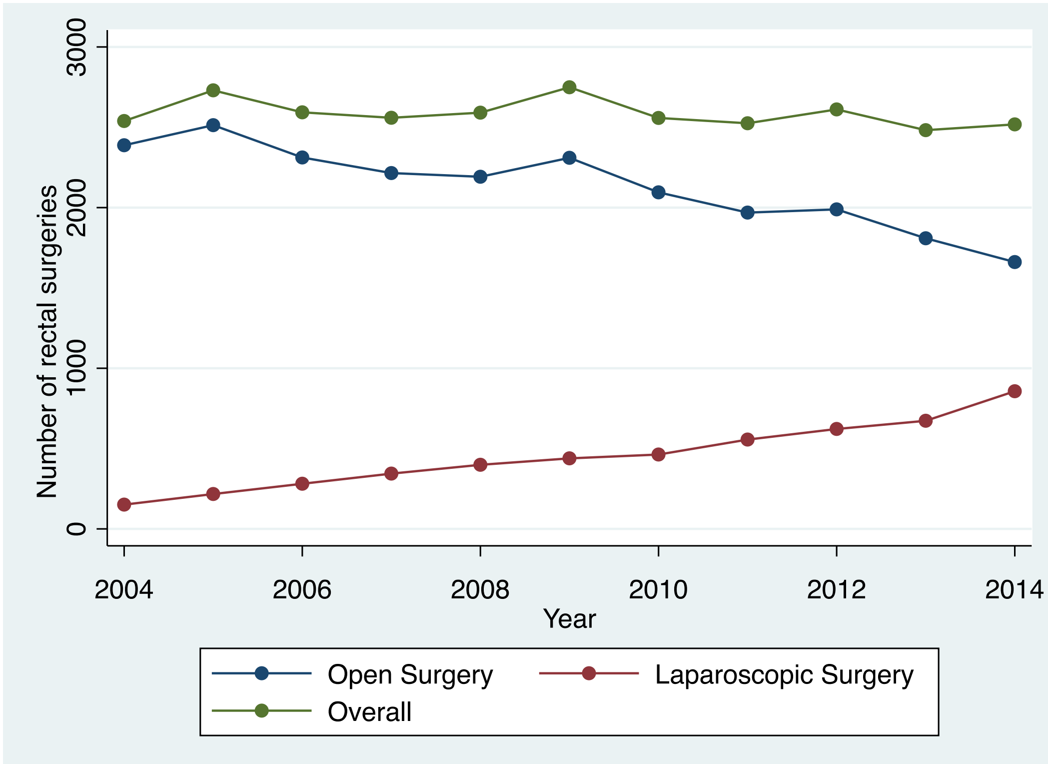

Figure 4. Total number of rectal cancer surgeries performed in Canada 2004-2014

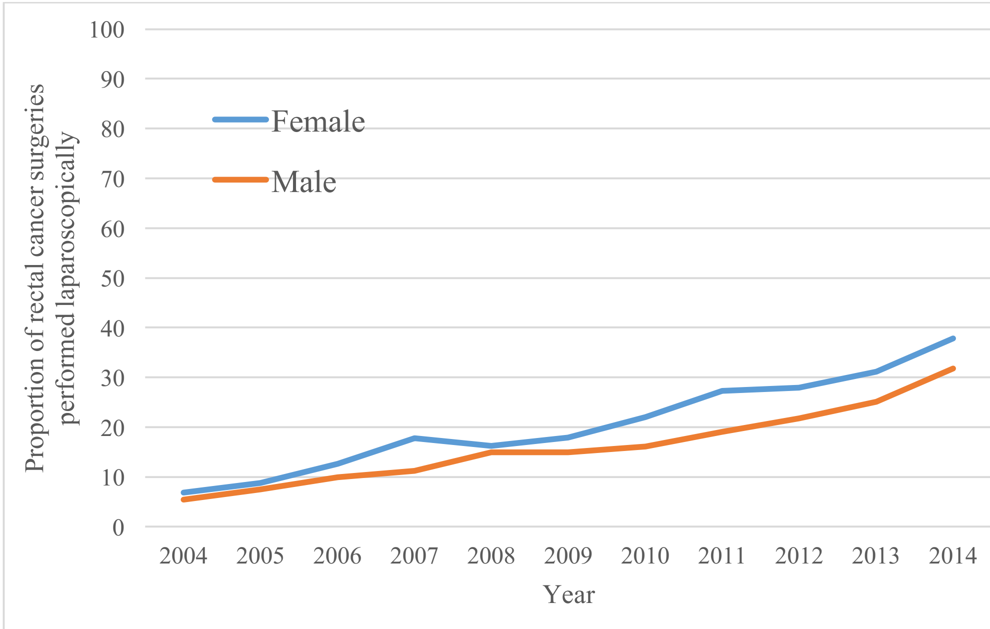

Figure 5. Age-adjusted proportions of rectal cancer surgeries performed laparoscopically among males and females in Canada from 2004-2014

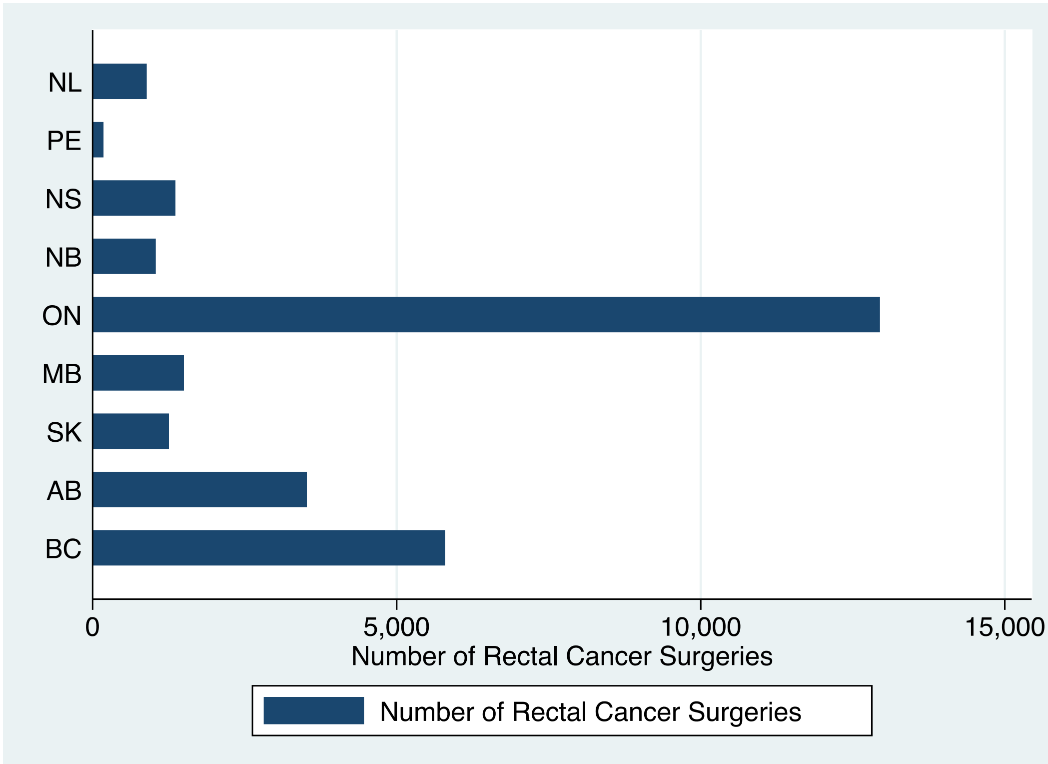

Figure 6. Total number of rectal cancer surgeries performed for cancer in each province, 2004-2014

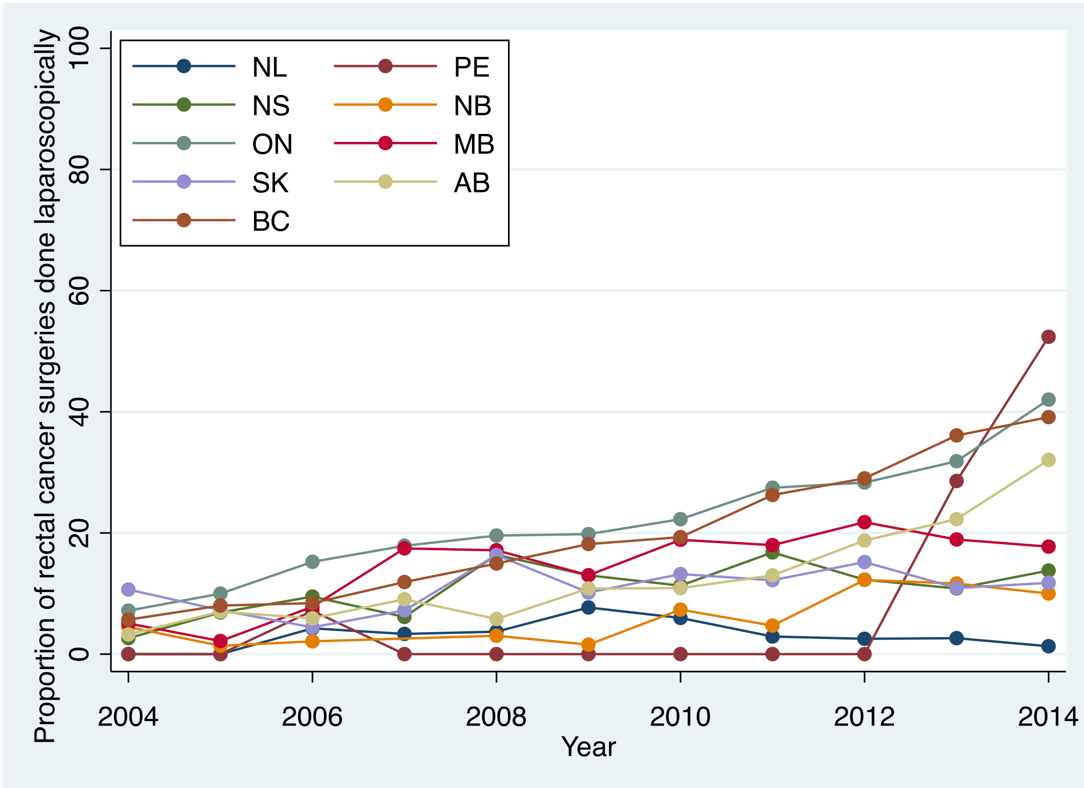

Figure 7. The uptake of LS for rectal cancer among provinces in Canada from 2004-2014

Table 6. Change in the annual proportion of LS for rectal cancer among provinces, 2004-2014

	04-05	**05-06**	**06-07**	**07-08**	**08-09**	**09-10**	**10-11**	**11-12**	**12-13**	**13-14**
NL	0	2.26	-0.93	0.37	3.99	-1.72	-3.08	-0.36	0.1	-1.33
PE	0	7.14	-7.14	0	0	0	0	0	28.57	23.81
NS	4.24	2.62	-3.35	10.23	-3.37	-1.7	5.49	-4.51	-1.45	2.96
NB	-3.11	0.74	-2.11	3.03	-1.47	5.78	-2.64	7.53	-0.59	-1.65
ON	2.81	5.25	2.65	1.68	0.23	2.9	4.76	0.85	3.53	10.17
MB	-1.91	5.65	9.64	-0.3	-4.13	5.86	-0.89	3.79	-2.85	-1.17
SK	-3.4	-2.84	2.8	9.14	-6.19	3.04	-1.01	3.00	-4.30	0.86
AB	3.76	-1.1	3.16	-3.26	5.01	0.08	2.11	5.75	3.53	9.76
BC	2.32	0.41	3.48	3.04	3.23	1.14	6.35	2.75	7.08	3.03
CAN	2.00	2.89	2.60	1.96	0.57	2.13	3.92	1.80	3.30	6.92

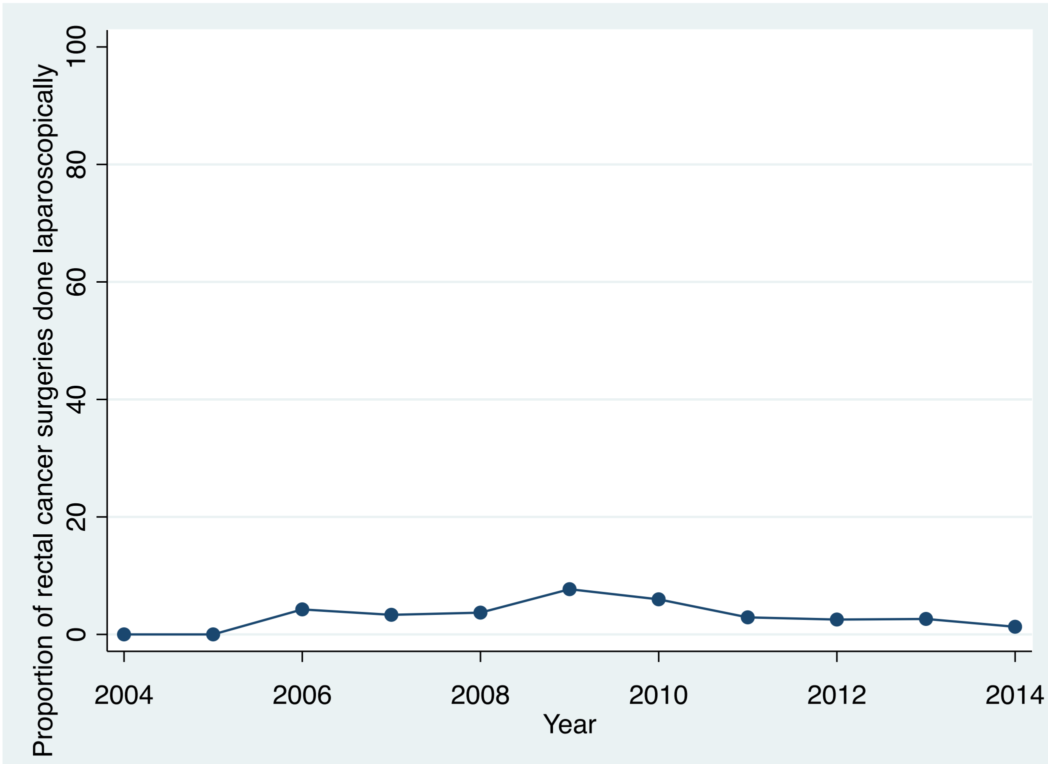

Figure 8. The uptake of LS for rectal cancer in Newfoundland from 2004-2014

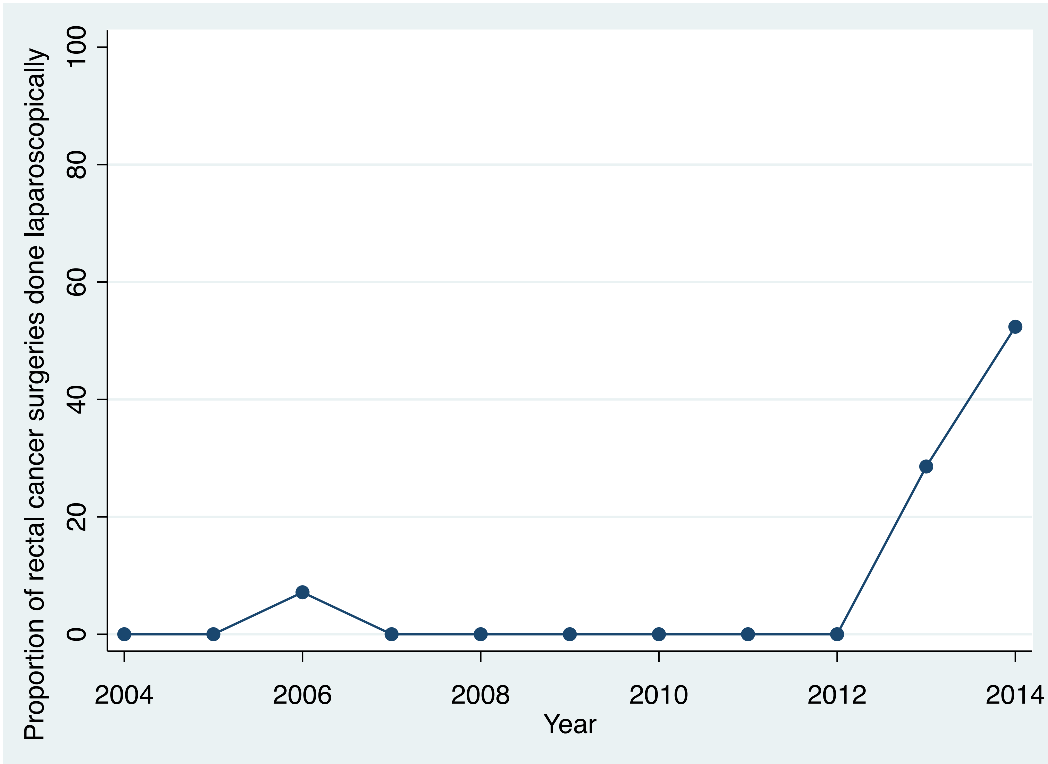

Figure 9. The uptake of LS for rectal cancer in Prince Edward Island from 2004-2014

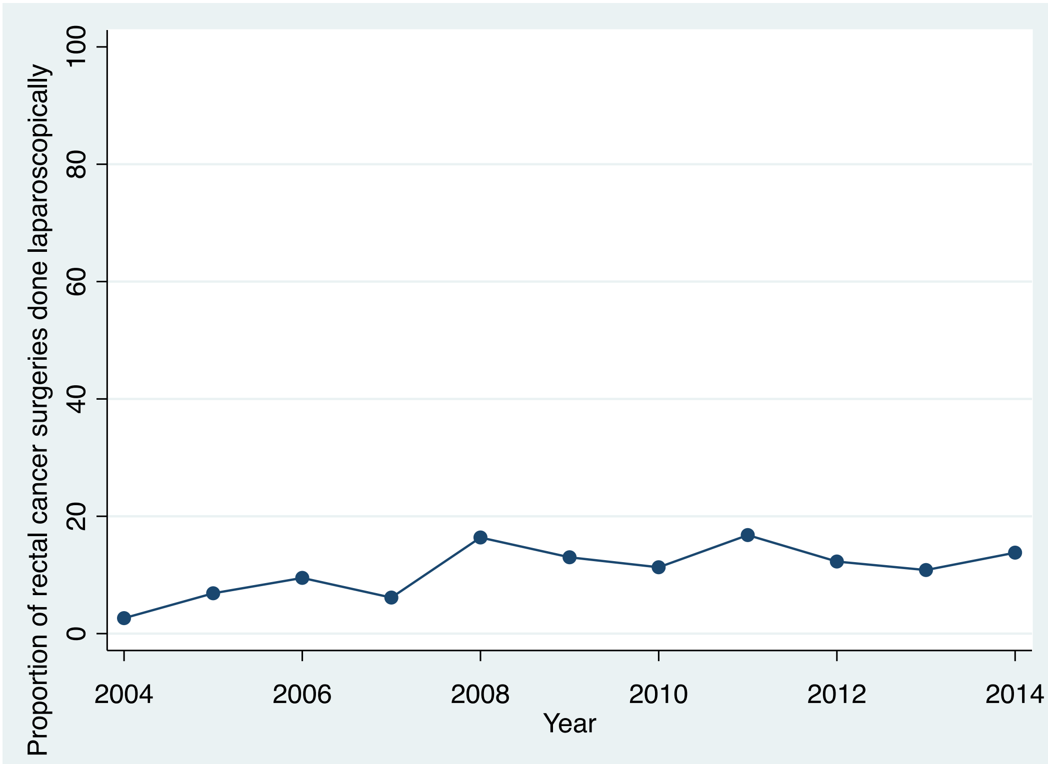

Figure 10. The uptake of LS for rectal cancer in Nova Scotia from 2004-2014

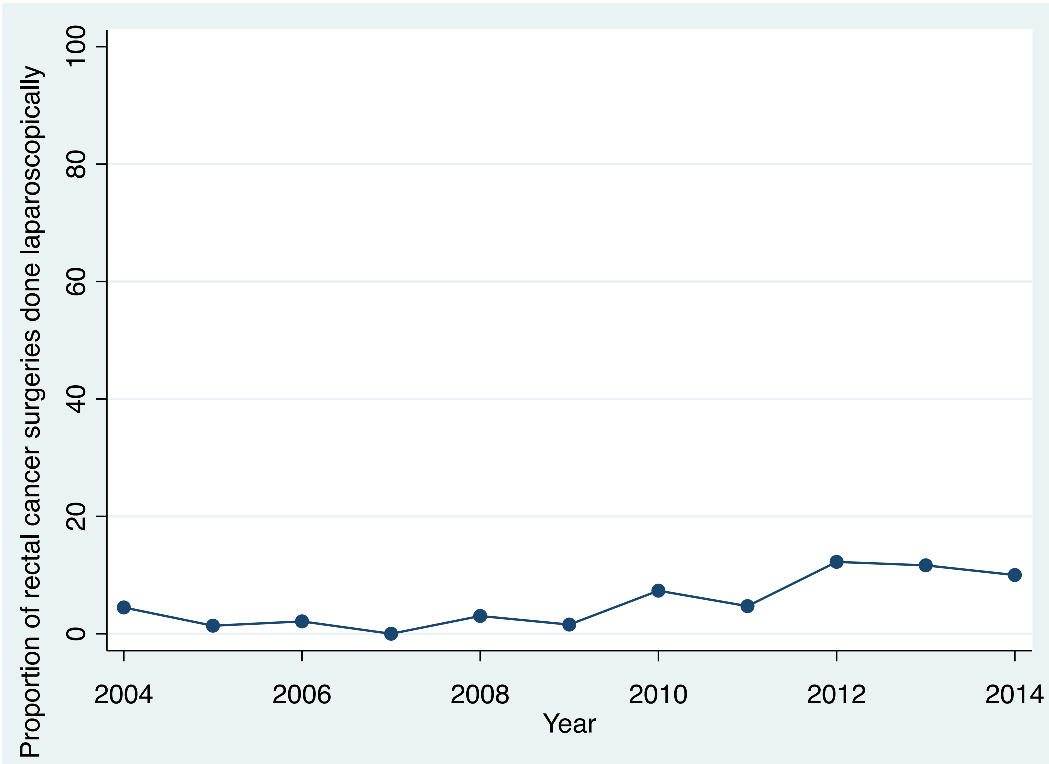

Figure 11. The uptake of LS for rectal cancer in New Brunswick from 2004-2014

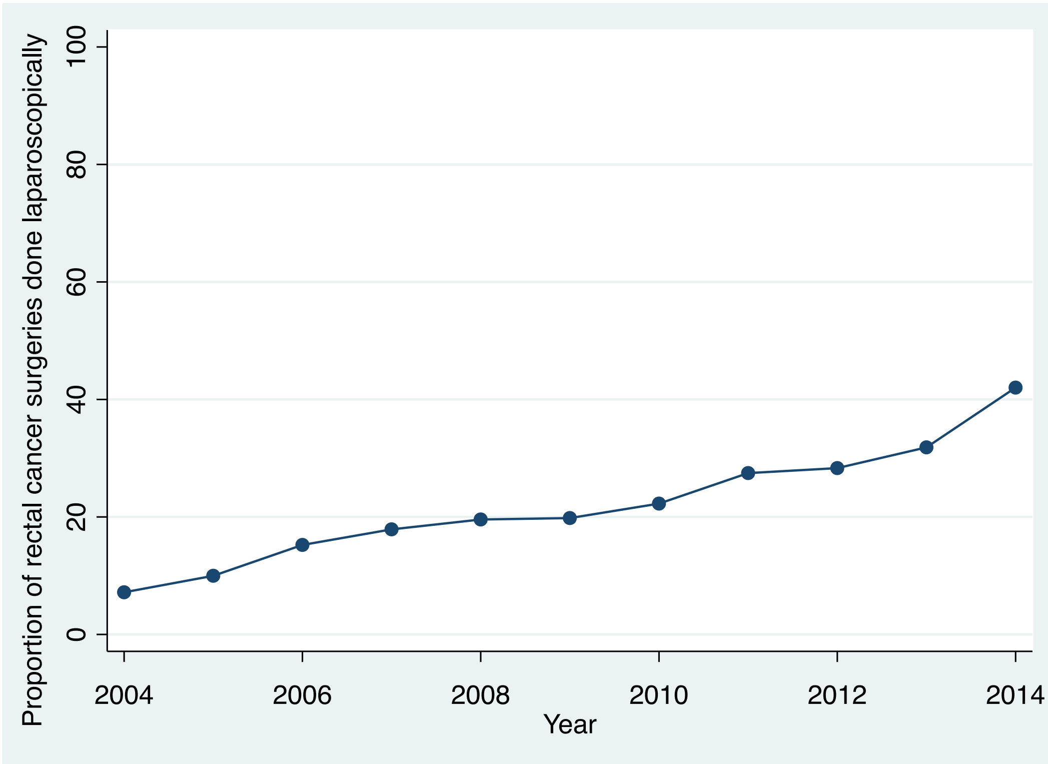

Figure 12. The uptake of LS for rectal cancer in Ontario from 2004-2014

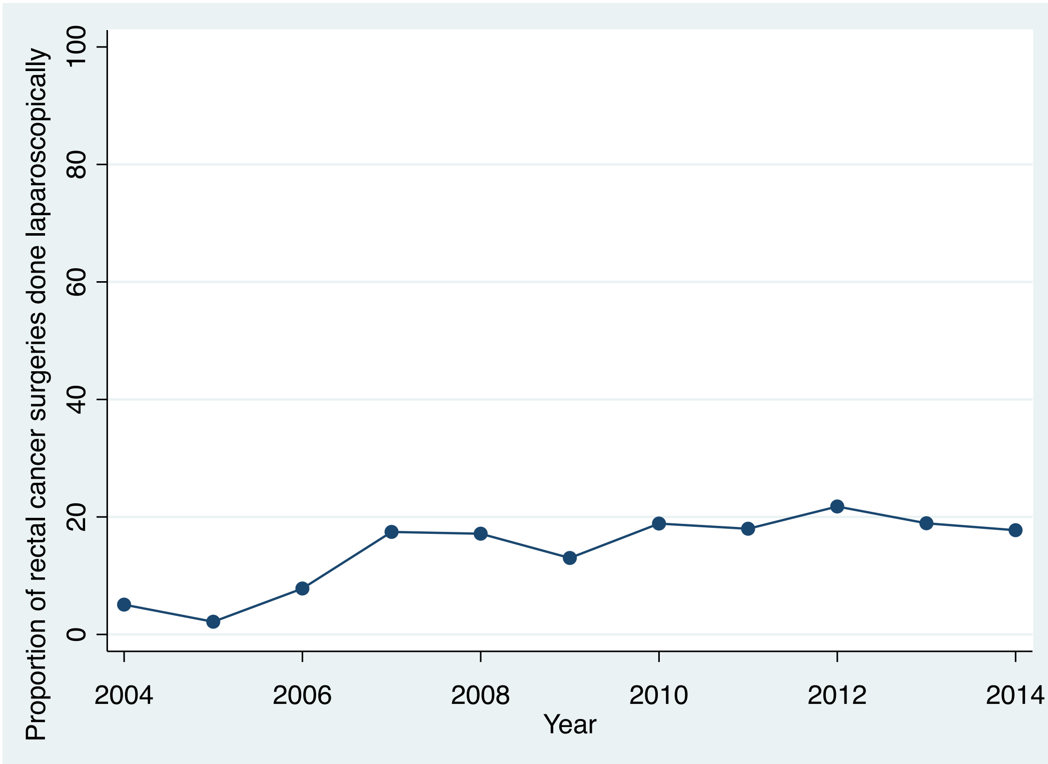

Figure 13. The uptake of LS for rectal cancer in Manitoba from 2004-2014

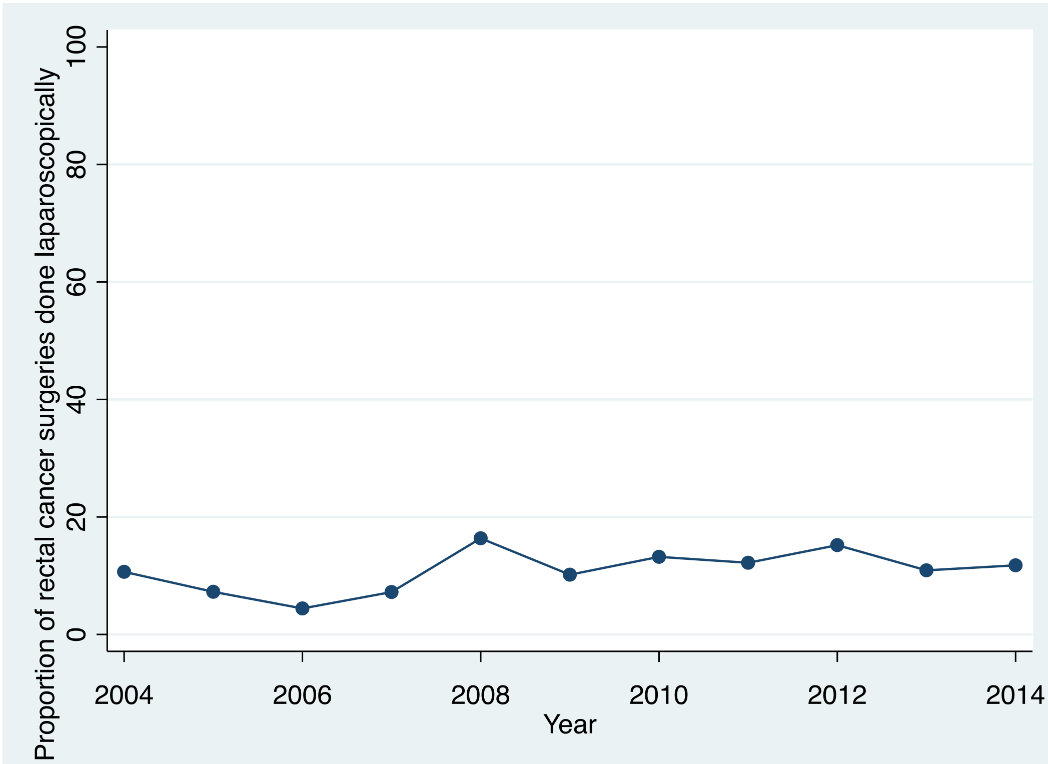

Figure 14. The uptake of LS for rectal cancer in Saskatchewan from 2004-2014

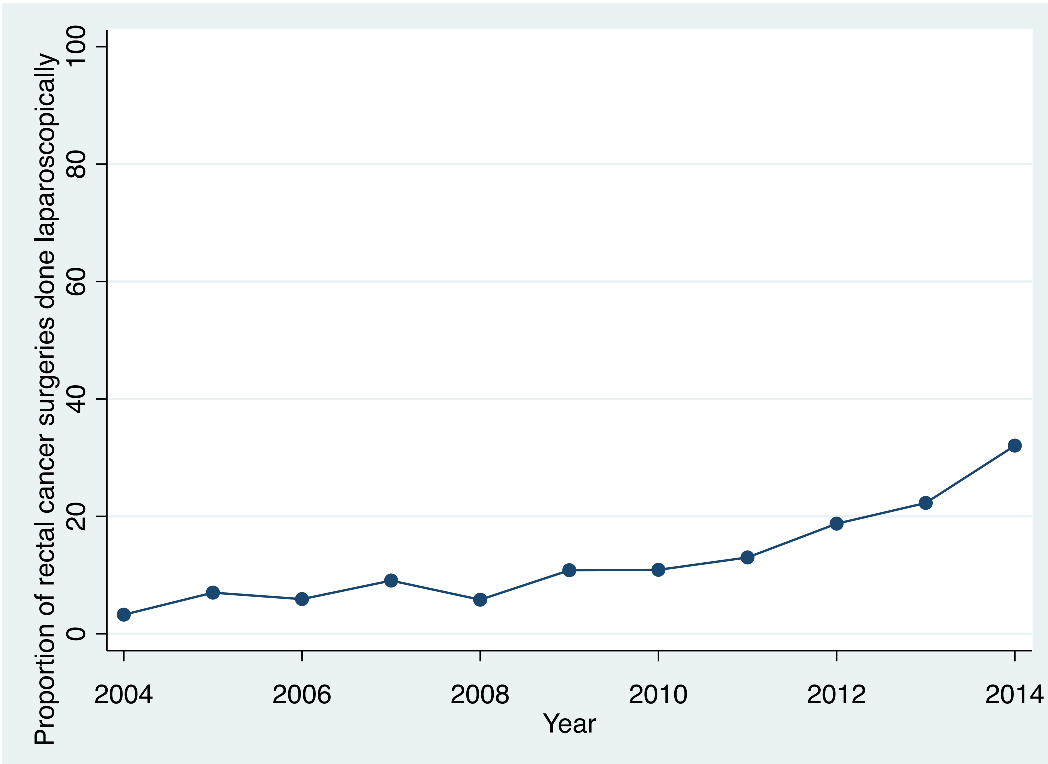

Figure 15. The uptake of LS for rectal cancer in Alberta from 2004-2014

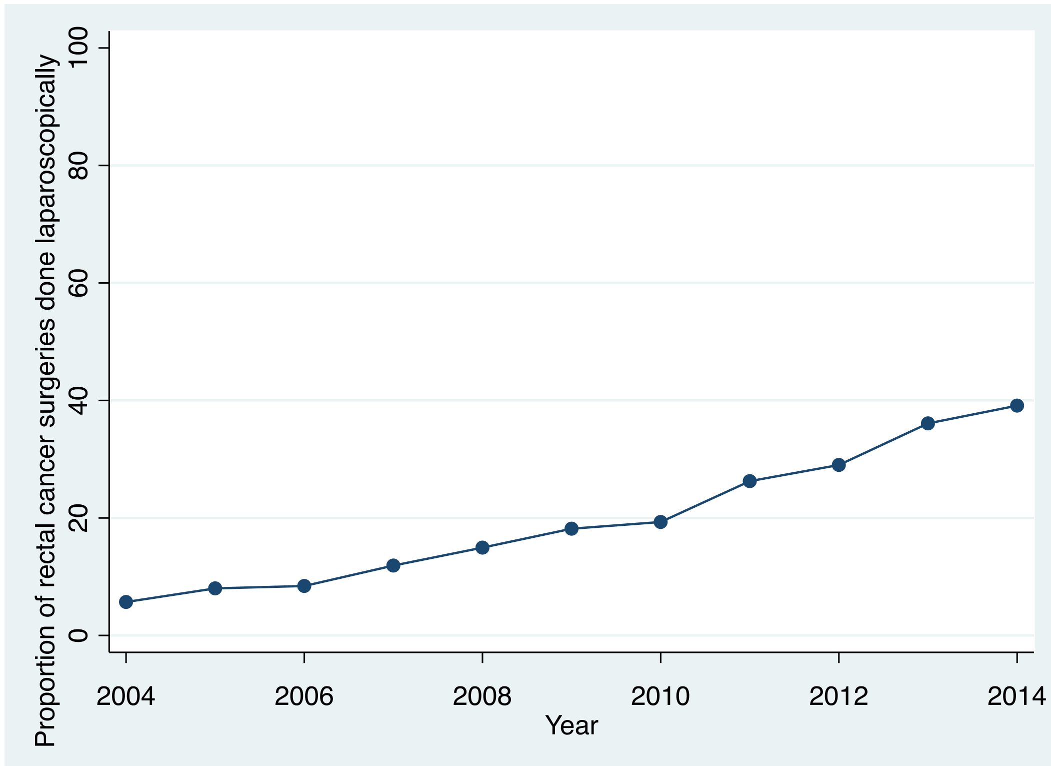

Figure 16. The uptake of LS for rectal cancer in British Columbia from 2004-2014

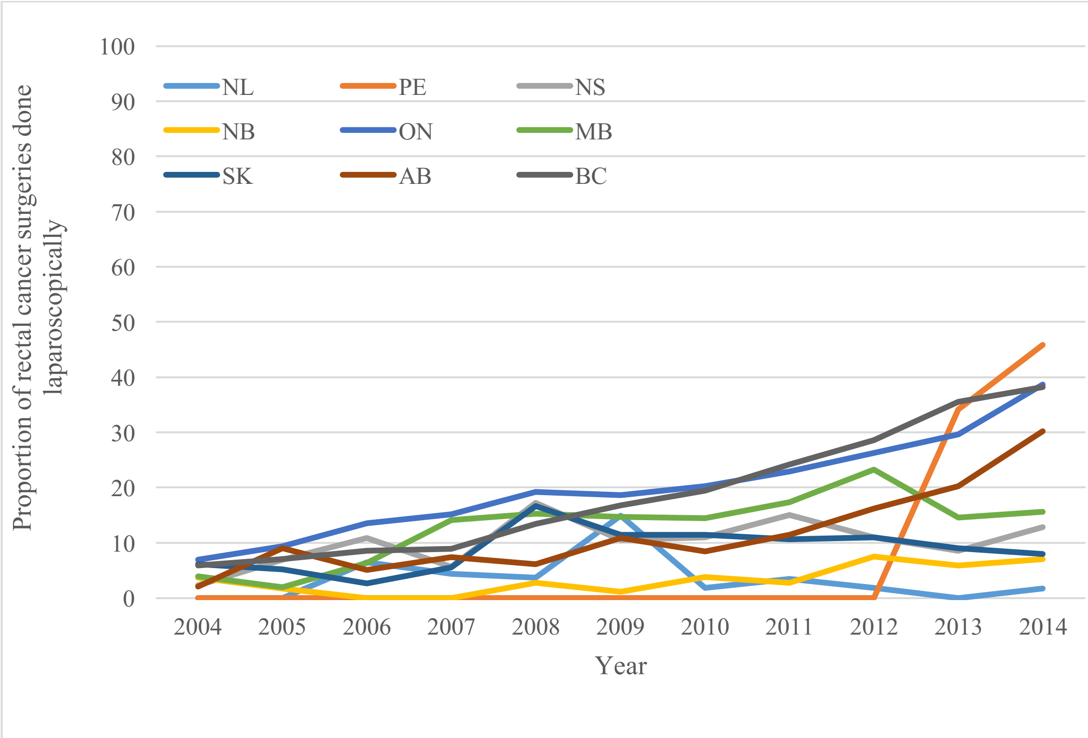

Figure 17. Age-adjusted proportions of rectal cancer surgery done laparoscopically among males in Canada from 2004-2014

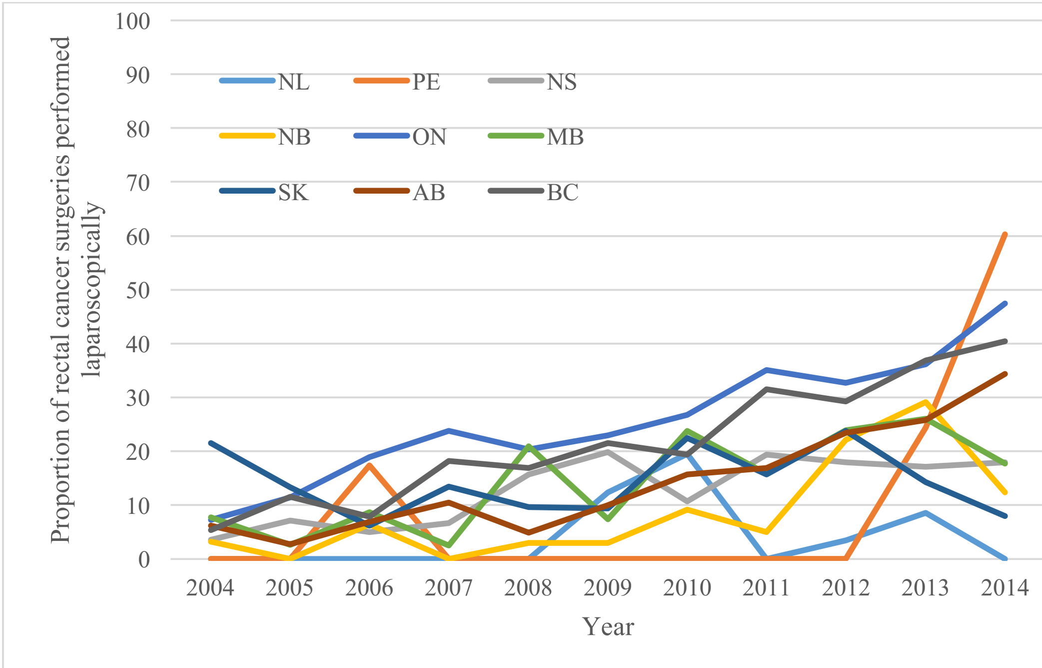

Figure 18. Age-adjusted proportions of rectal cancer surgeries performed laparoscopically among females in Canada from 2004-2014

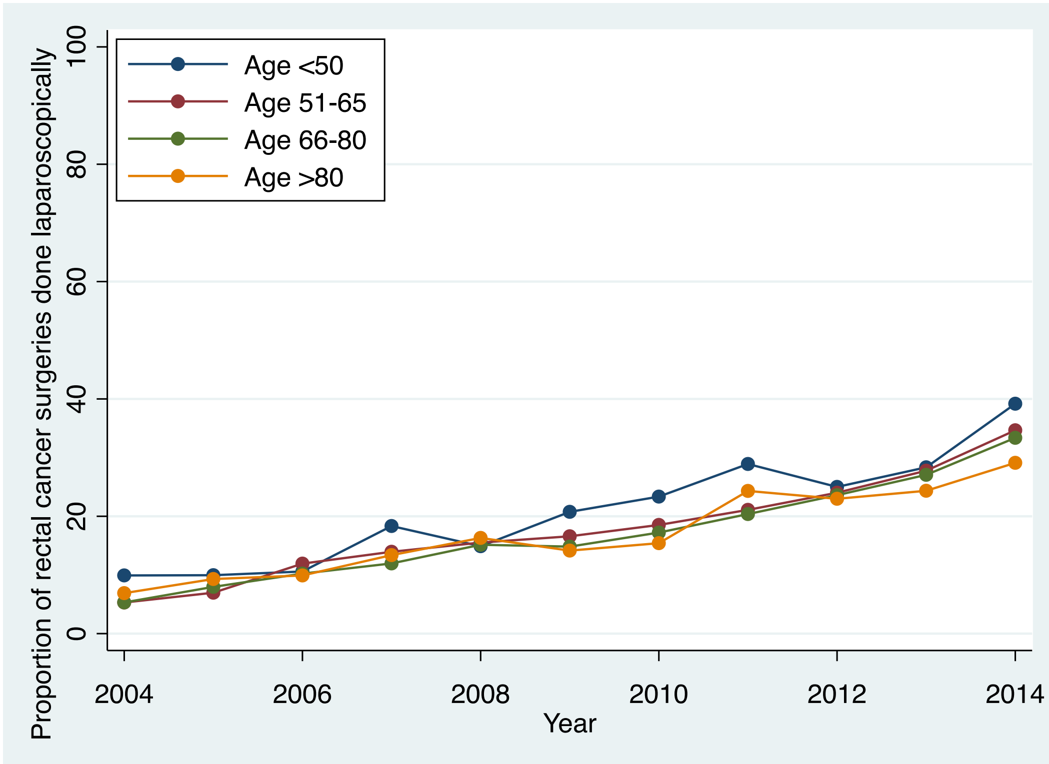

Figure 19. The uptake of LS for rectal cancer by age-category in Canada from 2004-2014

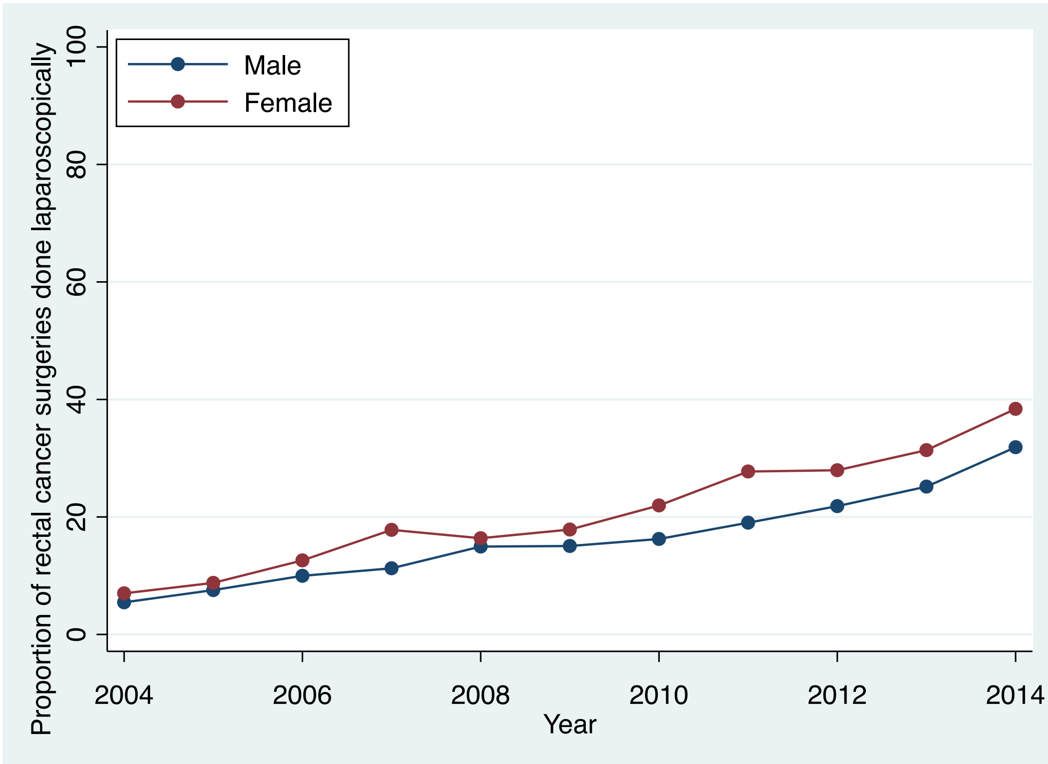

Figure 20. The uptake of LS for rectal cancer by sex in Canada from 2004-2014

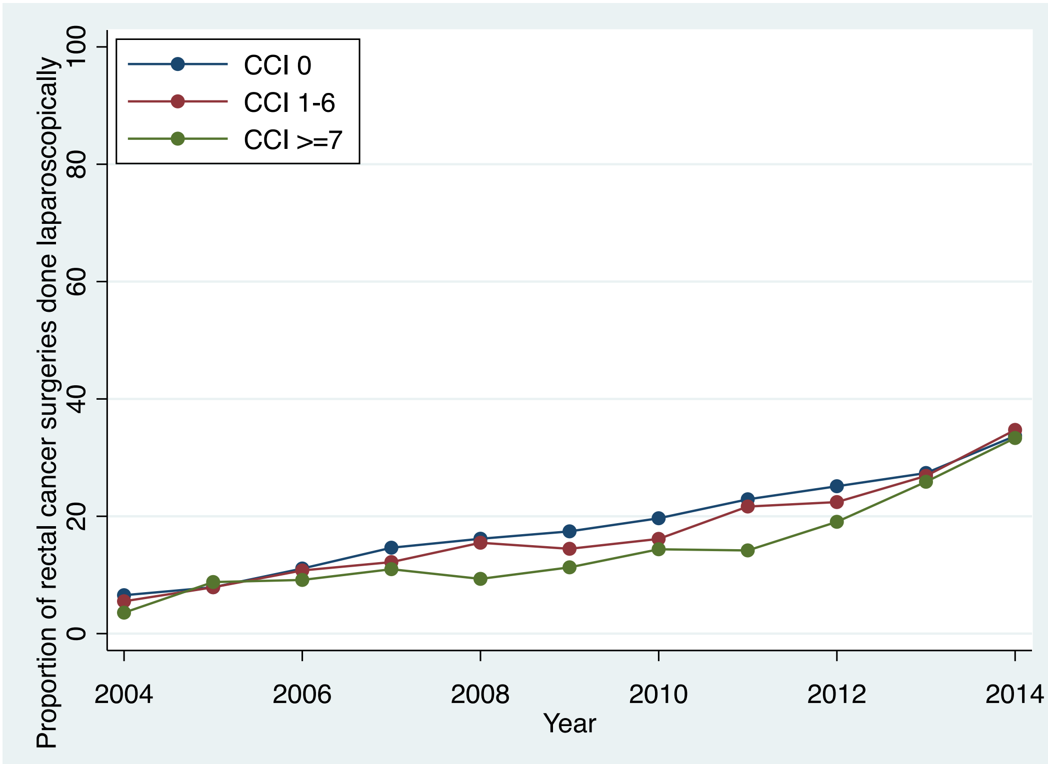

Figure 21. The uptake of LS for rectal cancer by CCI score in Canada from 2004-2014

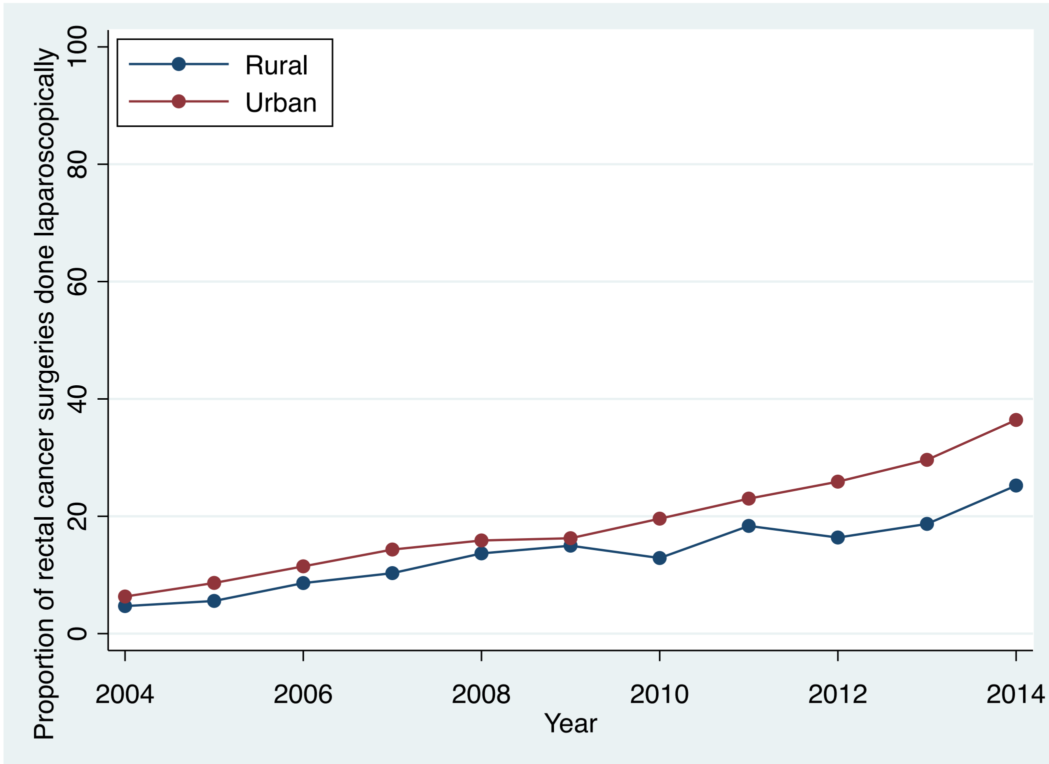

Figure 22. The uptake of LS for rectal cancer by residence in Canada from 2004-2014

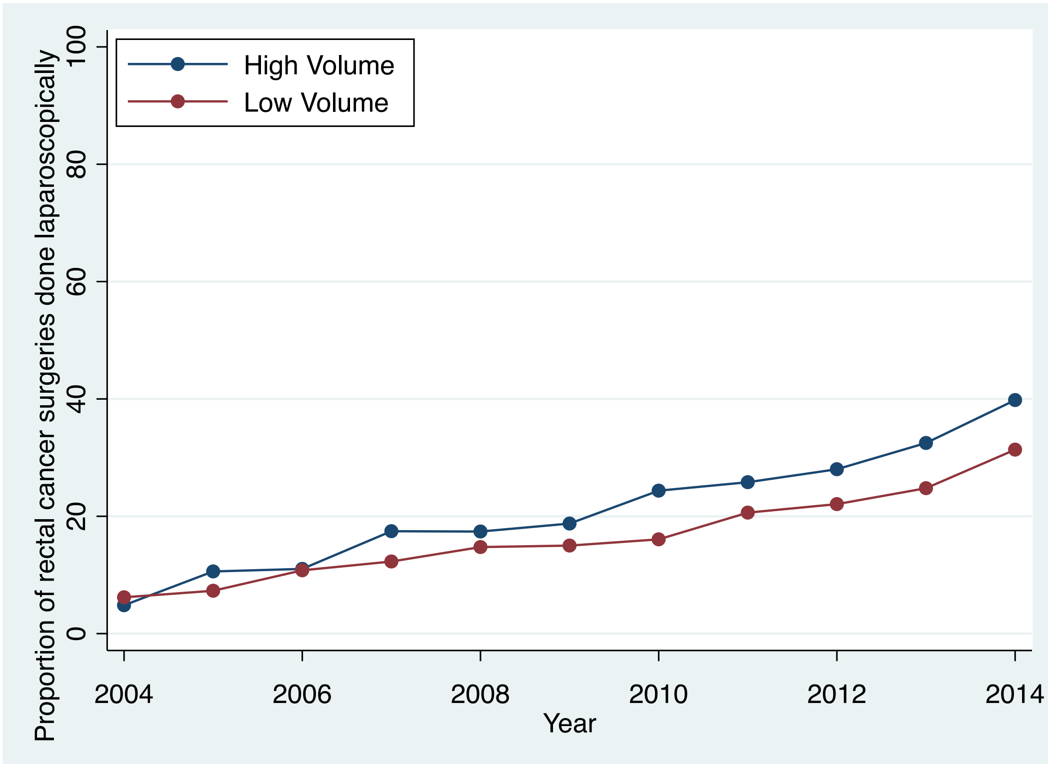

Figure 23. The uptake of LS for rectal cancer by surgeon-volume in Canada from 2004-2014

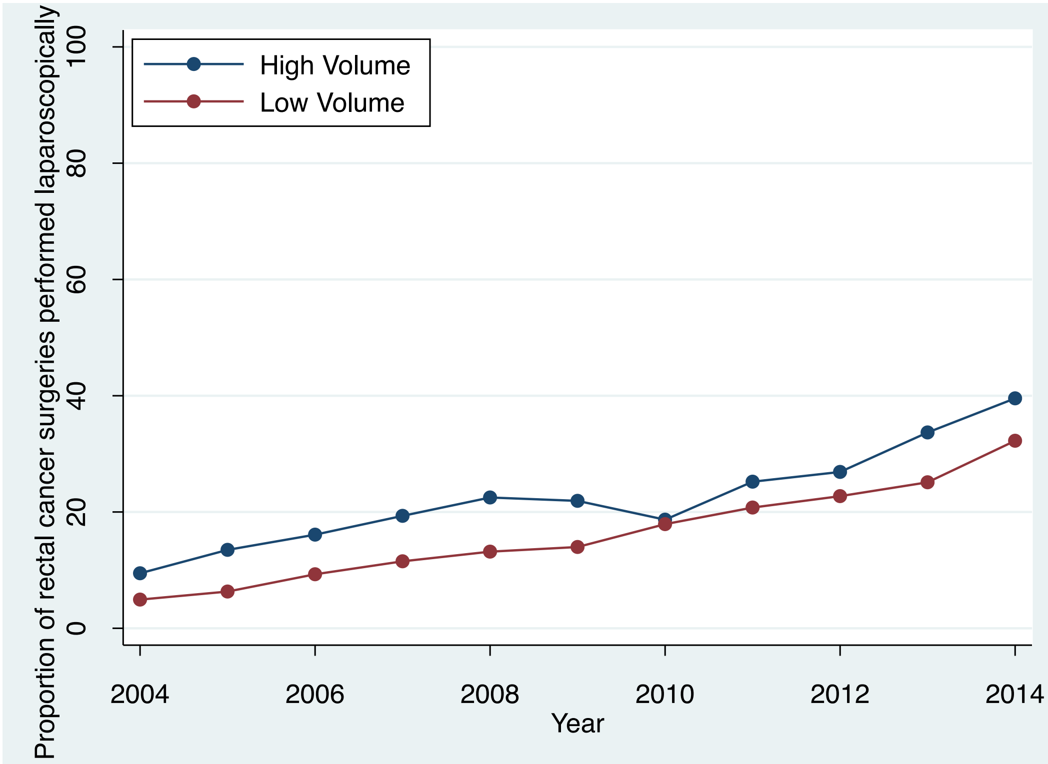

Figure 24. The uptake of LS for rectal cancer by hospital-volume in Canada from 2004-2014

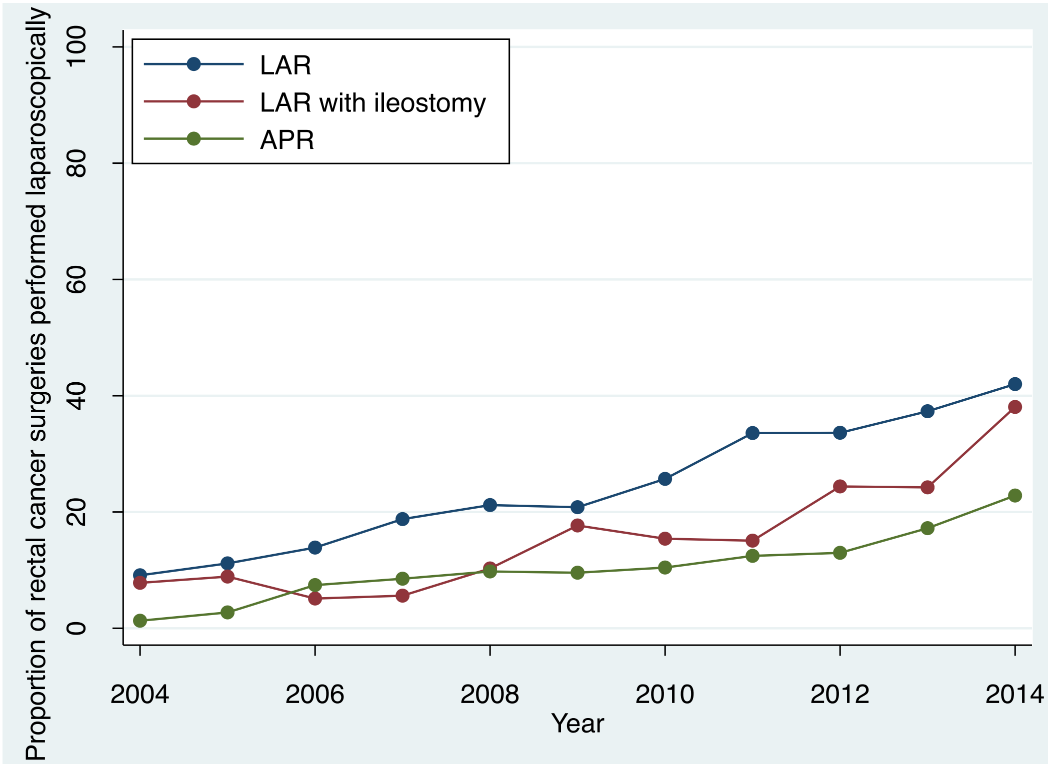

Figure 25. The uptake of laparoscopic rectal surgery by type of surgical resection in Canada from 2004-2014

Table 7. Univariate and multivariable analysis of factors associated with the uptake of LS for rectal cancer in Canada from 2004-2014

	N=28,455	**Unadjusted**		**Adjusted***	
	N (%)	OR	p-value	OR	p-value
Age category (years)					
≤50	2,750 (9.7)	1.00			
51-65	10,369 (36.4)	0.81	<0.001	0.86	0.010
66-80	11,885 (41.8)	0.74	<0.001	0.82	0.001
>80	3,451 (12.1)	0.74	<0.001	0.82	0.004
Gender					
Male	19,192 (67.5)	1.00			
Female	9,263 (32.6)	1.36	<0.001	1.25	<0.001
Charlson Comorbidity Index					
0	16,360 (57.5)	1.00			
1-6	10,373 (36.5)	0.88	<0.001	0.96	0.307
≥7	1,722 (6.0)	0.69	<0.001	0.84	0.020
Residence					
Urban	22,195 (78.0)	1.00			
Rural	6,260 (22.0)	0.67	<0.001	0.82	<0.001
Surgeon volume					
Low (<10/year)	21,358 (75.1)	1.00			
High (10-28/year)	7,097 (24.9)	1.52	<0.001	1.42	<0.001
Hospital volume					
Low (<32/year)	21,495 (75.5)	1.00			
High (32-65/year)	6,960 (24.5)	1.53	<0.001	1.41	<0.001
Surgery type					
LAR	13,854 (48.7)	1.00			
LAR + ileostomy	3,391 (11.9)	0.75	<0.001	0.50	<0.001
APR	11,210 (39.4)	0.39	<0.001	0.34	<0.001
Year of surgery					
2004	2,539 (8.9)	1.00			
2005	2,730 (9.6)	1.37	0.097	1.34	0.008
2006	2,593 (9.1)	1.92	<0.001	1.96	<0.001
2007	2,559 (9.0)	2.46	<0.001	2.62	<0.001
2008	2,591 (9.1)	2.88	<0.001	3.11	<0.001
2009	2,749 (9.7)	3.01	<0.001	3.30	<0.001
2010	2,558 (9.0)	3.50	<0.001	3.90	<0.001
2011	2,525 (8.9)	4.47	<0.001	5.04	<0.001
2012	2,611 (9.2)	4.95	<0.001	5.69	<0.001
2013	2,482 (8.7)	5.88	<0.001	7.10	<0.001
2014	2,518 (8.9)	8.16	<0.001	9.63	<0.001
Province					
NL	886 (3.1)	0.12	<0.001	0.12	<0.001
PE	175 (0.6)	0.42	0.001	0.44	0.002
NS	1,358 (4.8)	0.45	<0.001	0.40	<0.001

	N=28,455 N (%)	Unadjusted OR	 p-value	Adjusted* OR	 p-value
NB	1,035 (3.7)	0.21	<0.001	0.18	<0.001
ON	12,943 (45.5)	1.00			
MB	1,497 (5.3)	0.61	<0.001	0.59	<0.001
SK	1,250 (4.4)	0.45	<0.001	0.51	<0.001
AB	3,519 (12.4)	0.56	<0.001	0.43	<0.001
BC	5,792 (20.4)	0.92	0.026	0.79	<0.001

Table 8. Univariate and multivariable analysis of factors associated with the uptake of LS for rectal cancer in Canada among patients operated on by a surgeon who has performed at-least one laparoscopic rectal cancer surgery from 2004-2014

	N=21,173 N (%)	Unadjusted OR OR	 p-value	Adjusted OR* OR	 p-value
Age category (years)					
≤50	2,111 (9.7)	1.00			
51-65	7,714 (36.4)	0.84	0.002	0.86	0.009
66-80	8,782 (41.5)	0.76	<0.001	0.82	0.001
>80	2,566 (12.1)	0.76	<0.001	0.82	0.008
Gender					
Male	14,212 (67.1)	1.00			
Female	6,961 (32.9)	1.36	<0.001	1.25	<0.001
Charlson Comorbidity Index					
0	12,289 (58.0)	1.00			
1-6	7,615 (36.0)	0.90	0.002	0.98	0.552
≥7	1,269 (6.0)	0.69	<0.001	0.84	0.0.27
Residence					
Urban	16,686 (78.8)	1.00			
Rural	4,487 (21.2)	0.69	<0.001	0.81	<0.001
Surgeon volume					
Low (<16/year)	14,580 (76.4)	1.00			
High (16-28/year)	4,493 (24.8)	1.10	0.014	1.12	0.010
Hospital volume					
Low (<45/year)	15,893 (75.1)	1.00			
High (45-62/year)	5,280 (24.9)	1.27	<0.001	1.26	<0.001
Surgery type					
LAR	10,120 (47.8)	1.00			
LAR + ileostomy	2,798 (13.2)	0.62	<0.001	0.45	<0.001
APR	8,255 (39.0)	0.36	<0.001	0.32	<0.001
Year of surgery					
2004	1,687 (8.0)	1.00			
2005	1,843 (8.7)	1.36	0.006	1.33	0.011
2006	1,809 (8.5)	1.87	<0.001	1.90	<0.001
2007	1,839 (8.7)	2.34	<0.001	2.56	<0.001
2008	1,915 (9.0)	2.68	<0.001	2.96	<0.001

	N=19,073 N (%)	Unadjusted OR	 p-value	Adjusted* OR	 p-value
2009	2,056 (9.7)	2.76	<0.001	3.14	<0.001
2010	1,951 (9.2)	3.17	<0.001	3.66	<0.001
2011	1,975 (9.3)	3.99	<0.001	4.66	<0.001
2012	2,062 (9.7)	4.39	<0.001	5.30	<0.001
2013	1,964 (9.3)	5.30	<0.001	6.72	<0.001
2014	2,072 (9.8)	7.17	<0.001	8.98	<0.001
Province					
NL	335 (1.6)	0.23	<0.001	0.26	<0.001
PE	130 (0.6)	0.43	0.001	0.37	<0.001
NS	797 (3.8)	0.61	<0.001	0.58	<0.001
NB	261 (1,2)	0.71	0.028	0.59	0.001
ON	10,187 (48.1)	1.00			
MB	1,184 (5.6)	0.59	<0.001	0.59	<0.001
SK	882 (4.2)	0.49	<0.001	0.53	<0.001
AB	2,597 (12.3)	0.59	<0.001	0.51	<0.001
BC	4,800 (22.7)	0.85	<0.001	0.72	<0.001

Table 9. Univariate and multivariable analysis of factors associated with the uptake of LS for rectal cancer in Canada after exclusion of patients who had a Hartmann's procedure

	N=24,222 N (%)	**Unadjusted** OR	 p-value	**Adjusted*** OR	 p-value
Age category (years)					
≤50	2,368 (9.8)	1.00			
51-65	8,936 (36.9)	0.82	0.001	0.87	0.019
66-80	10,132 (41.8)	0.75	<0.001	0.82	0.001
>80	2,786 (11.5)	0.75	<0.001	0.82	0.009
Gender					
Male	16,237 (67.0)	1.00			
Female	7,985 (33.0)	1.34	<0.001	1.23	<0.001
Charlson Comorbidity Index					
0	14,035 (57.9)	1.00			
1-6	8,772 (36.2)	0.89	0.001	0.97	0.499
≥7	1,415 (5.8)	0.69	<0.001	0.83	0.028
Residence					
Urban	18,940 (78.2)	1.00			
Rural	5,282 (22.8)	0.69	<0.001	0.85	0.001
Surgeon volume					
Low	18,184 (75.0)	1.00			
High	6,038 (24.9)	1.57	<0.001	1.45	<0.001
Hospital volume					
Low	18,213 (75.2)	1.00			
High	6,009 (24.8)	1.57	<0.001	1.49	<0.001
Surgery type					

	N=23,281 N (%)	**Unadjusted** OR	 p-value	**Adjusted*** OR	 p-value
LAR	13,854 (57.2)	1.00			
LAR + ileostomy	3,391 (14.0)	0.75	<0.001	0.49	<0.001
APR	6,977 (28.8)	0.30	<0.001	0.27	<0.001
Year of surgery					
2004	2,213 (9.1)	1.00			
2005	2,391 (9.9)	1.31	0.019	1.28	0.033
2006	2,242 (9.3)	1.92	<0.001	1.94	<0.001
2007	2,178 (9.0)	2.51	<0.001	2.65	<0.001
2008	2,196 (9.1)	2.88	<0.001	3.07	<0.001
2009	2,352 (9.7)	2.95	<0.001	3.21	<0.001
2010	2,186 (9.0)	3.46	<0.001	3.83	<0.001
2011	2,099 (8.7)	4.54	<0.001	5.01	<0.001
2012	2,173 (9.0)	5.08	<0.001	5.70	<0.001
2013	2,062 (8.5)	5.88	<0.001	6.95	<0.001
2014	2,130 (8.8)	8.29	<0.001	9.65	<0.001
Province					
NL	734 (3.0)	0.10	<0.001	0.11	<0.001
PE	161 (0.7)	0.42	0.001	0.47	0.005
NS	1,167 (4.8)	0.47	<0.001	0.42	<0.001
NB	876 (3.6)	0.22	<0.001	0.20	<0.001
ON	10,934 (45.1)	1.00			
MB	1,263 (5.2)	0.58	<0.001	0.56	<0.001
SK	1,107 (4.6)	0.42	<0.001	0.51	<0.001
AB	2,876 (11.9)	0.62	<0.001	0.46	<0.001
BC	5,104 (21.1)	0.93	0.092	0.81	<0.001

Table 10. Change in remuneration and timing and provincial policies for financial remuneration for LS in Canada

	***FI**	**Content of policy**	**Date of implementation**
NL	No	-	-
PE	No	-	-
NS	Yes	↑5% Laparoscopic LAR	March 2012
NB	No	-	-
ON	Yes	↑25% Laparoscopic LAR ↑25% Laparoscopic APR	Oct 2009 25% April 2012 ↓ 10% April 2013 ↑ 25%
MB	No	-	-
SK	No	-	-
AB	No	-	-
BC	Yes	↑25% Laparoscopic LAR ↑$11% Laparoscopic APR	April 2011

*FI: financial incentive

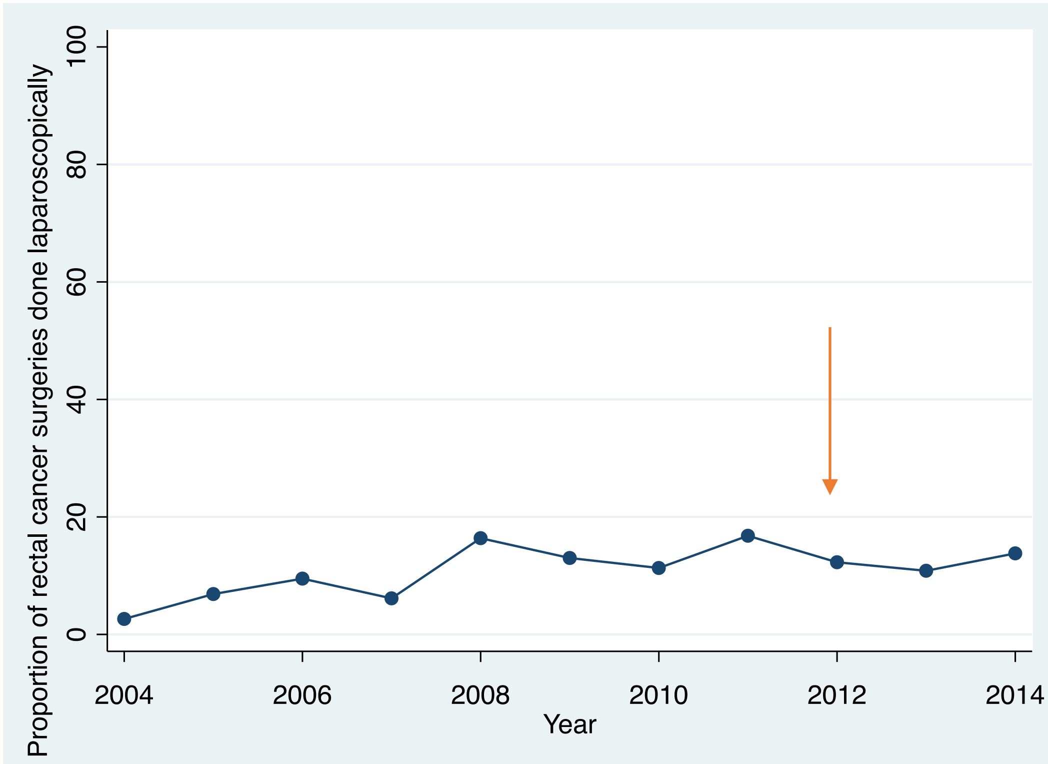

Figure 26. Timing of financial incentive implementation and the uptake of LS for rectal cancer in Nova Scotia

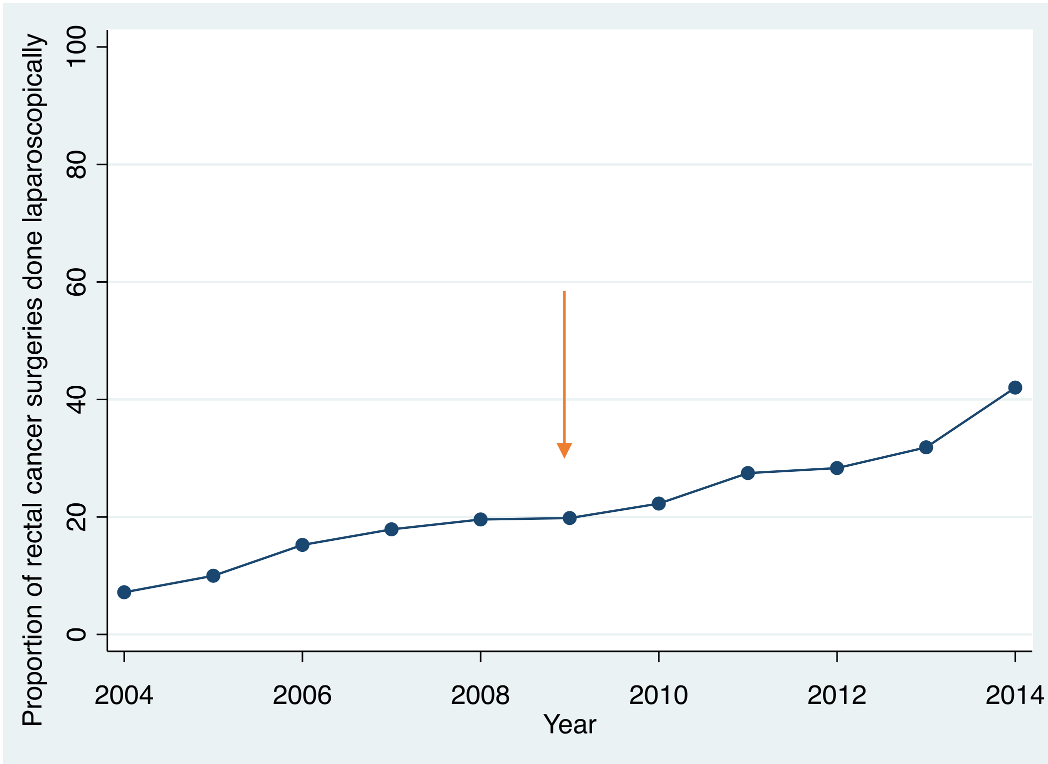

Figure 27. Timing of financial incentive implementation and the uptake of LS for rectal cancer in Ontario

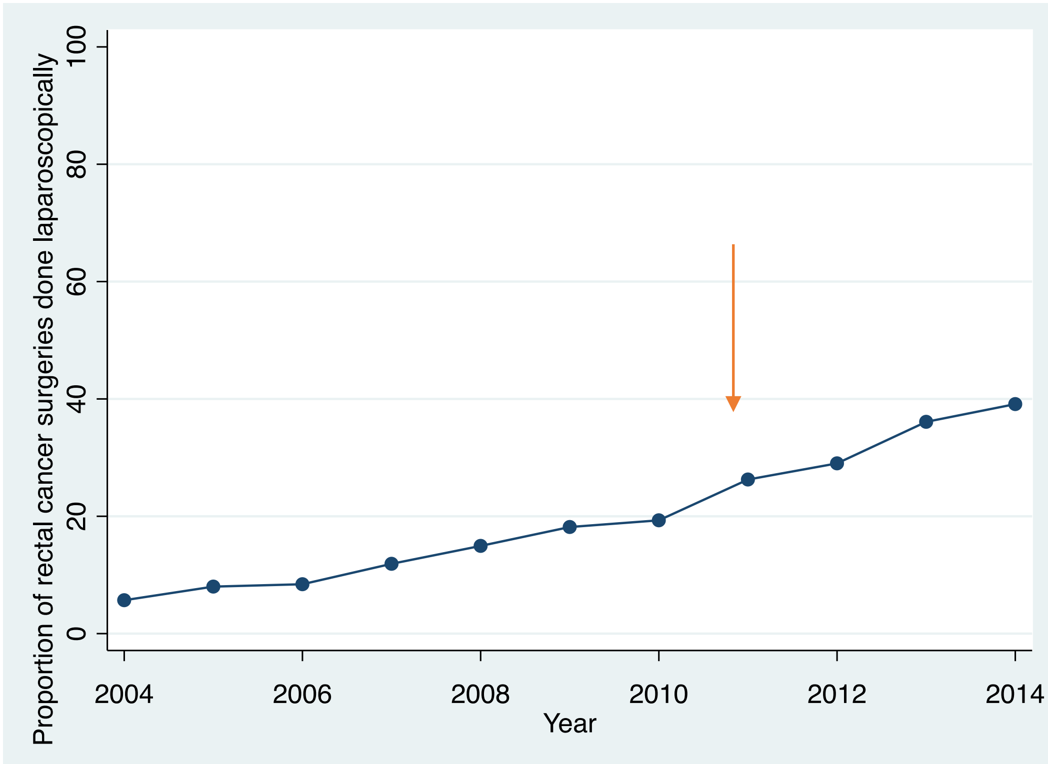

Figure 28. Timing of financial incentive implementation and the uptake of LS for rectal cancer in British Columbia

Chapter 4: Discussion

This population-based retrospective analysis of 28,455 patients with rectal cancer provides the first pan-Canadian description of the uptake of LS for rectal cancer over time. Overall, 17.6% of patients underwent LS and 82.4% OS, and the proportional use of LS increased substantially from 5.9% in 2004 to 34.0% in 2014. The uptake of LS increased significantly among all provinces, except NL, but there was marked interprovincial variation in the magnitude and timing of uptake. Additionally, we have identified geographic, patient, surgeon and hospital factors independently associated with the use of LS. Understanding the use of LS can aid healthcare providers in increasing laparoscopic approaches and surgical quality for rectal cancer patients in Canada.

Our results indicate that the uptake of LS for rectal cancer in Canada is comparable to some countries, including Australia, but lags behind others. In 2014, almost half of rectal cancer resections were performed laparoscopically in the United States (46.4%)[48] and Italy (52.5%),[50] while Australia reported an increase in LS from 0.6% in 2000 and to 15.5% in 2008. [52] The results of our pan-Canadian analysis are consistent with the only Canadian single province study. Simunovic *et al.* reported an increase in the utilization of LS for rectal cancer in Ontario from approximately 5% in 2004 to 22% in 2010.[53] Results of our study parallel these findings, with an increase from 7.1% to 22.3% over the same period.

The uptake of LS was relatively constant over time between 2004-2014. Based on our results, it does not appear that the uptake of LS for rectal cancer in Canada has reached a plateau, and could be hypothesized to continue to rise. However, our data precedes the publication ACOSOG Z601 and ALaCaRT and the subsequent safety concerns with LS regarding pathologic endpoints,[35,36] which may have dampened enthusiasm for LS. Given the complexity of the literature, an ideal target for the proportional use of LS for rectal cancer in Canada cannot be determined at this time.

Our study is the first to describe marked interprovincial variation in the uptake of LS for rectal cancer. In 2014, the proportion of patients undergoing LS ranged from 1.3% (NL) to 52.4% (PE) and the highest proportional use was in PE, ON, and BC. Regional variation in the care of patients with rectal cancer in Canada has been previously described.[91,109,110,112-117] Specifically, there are geographic differences in the use of neoadjuvant/adjuvant chemoradiotherapy,[112,114-116] rates of inappropriate colostomy use,[109,114] approach to pre-operative workup,[112,113] and adherence to follow-up guidelines.[117] Our study adds to this growing body of literature and helps better understand the treatment of patients with rectal cancer in Canada, and the differences among provinces.

Recent evidence from other countries has demonstrated an association between the centralization of rectal cancer treatment and improved survival, decreased postoperative morbidity and superior quality of care.[118-121] However, Canada does not currently employ a nationally coordinated effort to centralize the treatment of rectal cancer, and the majority of patients in this study were treated in centers that performed an average of less than 25 rectal cancer surgeries per year. Therefore, there are likely other factors besides an intentional centralization of care which are driving the interprovincial variation in use of LS.

Our results suggest that surgeon factors may explain some of this variation**.** Individual surgeon-practice, defined as the procedures a particular surgeon performs given their skill and experience, is likely driving some the differences in uptakes among provinces. LS for rectal cancer is an advanced minimally invasive procedure with a protracted learning-curve estimated between 50-200 cases,[78-80,82,122,123] likely hindering its adoption by older surgeons who were not trained in the era of laparoscopy and those who do not routinely use LS. It is likely that younger surgeons, or those with advanced training in minimally invasive surgery or colorectal surgery use LS more often than surgeons with more traditional general-surgery training. Therefore, provinces with lower uptake may not have many (or any) surgeon who posses the skills and experience to use LS. The effect of individual surgeon-practice on the provincial uptake of LS is illustrated by PE, where the hiring of a recent general surgery graduate coincided with an increase in the proportional use of LS from 0% in 2012 to 52% in 2014.

Surgeon volume may also influence the uptake of LS. In our study, only half of surgeons had performed at least one LS for rectal cancer, and over 75% of patients were treated by a surgeon who performed less than ten rectal surgeries a year, suggesting it may be difficult for most surgeons in Canada to reach the volume necessary for mastery of LS. Our multivariable analysis further supports the association between surgeon-volume and uptake of LS, whereby high surgeon volume was independently associated with LS (OR 1.42, $p<0.001$). This relationship persisted in our sensitivity analysis, indicating that high surgeon volume is a predictor of LS, even among those surgeons who perform both LS and OS. Similarly, high hospital volume was significantly associated with LS in both model 1 and model 2. Therefore, among patients treated by surgeons who perform both LS and OS, the odds of undergoing LS is higher in the group treated by surgeons who perform at least 16 rectal cancer surgeries a year (high volume) and are cared for in high volume hospitals (□45 a year).

Unfortunately, our data could not capture surgeon training. Given the difficulty of laparoscopic rectal surgery, it is likely that surgeons with additional fellowship training after general surgery residency in colorectal or minimally invasive surgery use LS more often than surgeons without sub-specialty training. Future research on the impact of surgical training on use of LS in Canada may further explain the relationship between surgeon factors and interprovincial variation.

In addition to surgeon and hospital factors, we have identified several other geographic and patient factors predictive of use of LS for rectal cancer in Canada. Year of surgery had the strongest association with LS. Patients who underwent rectal cancer surgery in 2014 were 9.63 times more likely to have LS compared to those who had surgery in 2004. Before 2004, there was limited prospective randomized data supporting the use of LS for rectal cancer. After 2004, evidence supporting its use began to accumulate, with randomized data demonstrating decreased postoperative morbidity and improved short-term outcomes after LS.[37-40,124] By 2014, long-term results of multiple randomized trials had established equivalent oncologic outcomes between LS and OS for rectal cancer.[27-29,39]

Decreased utilization of LS in the elderly, as was found in our study, has been previously described,[61] perhaps stemming from concerns of physiologic derangements and cardiopulmonary stress after carbon dioxide insufflation and pneumoperitoneum. However, these historical concerns have been challenged with recent evidence demonstrating that age is not an independent risk factor for post-operative morbidity after LS for rectal cancer.[22,65,125] Similar to age, there were initial concerns regarding the safety of LS in patients with medical comorbidities. However, LS may benefit medically comorbid patients in terms of decreased morbidity, intra-operative blood loss, post-operative pain and length of stay.[70-72] In our study, high comorbidity score was a negatively associated with LS. Collectively, these results suggest that surgeons are hesitant to apply LS in the geriatric or comorbid patient populations, or that these patient groups do not prioritize the benefits of LS and choose to undergo OS.

In this study, patients living in rural areas had a lower probability of undergoing LS compared to urban areas. Geographic differences, including urban/rural status, have been associated with important clinical outcomes in rectal cancer; patients living in rural areas have decreased survival when compared to patients living in urban areas.[126 127]Differences in survival may be associated with barriers to appropriate care, including the burden of increased travel distance for treatment[127] Decreased use of LS in patients from rural areas may be related to increased travel distance and decreased access to LS. With the increasing complexity and rapid evolution in the management of rectal cancer, the centralization of rectal cancer treatment to urban centers is inevitable. However, programs and services should be in place to optimize access to rectal cancer surgery and treatment for patients living in rural areas such that they can still receive necessary care in urban centers. Our results suggest that patients living in rural areas may not have equal access to LS compared to urban areas; further research of these findings is warranted.

Type of surgical resection was strongly associated with the use of LS, with LS more common among patients undergoing LAR. This has previously been described in the US[128] and Ontario.[54] This finding could be explained by a potential selection bias by surgeons, whereby patients with high rectal tumors are being selected for LS, while those with low tumors are not. This is further supported by the overall low proportion of laparoscopic LAR patients receiving an ileostomy (8.5%). High rectal tumors pose less technical demand for the surgeon and potentially avoid the need for neoadjuvant chemoradiotherapy. A second possible explanation is that patients requiring APR and permanent colostomy may be less likely to prioritize the short-term morbidity benefits of LS and choose to undergo OS. Thirdly, RCT data demonstrated high CRM positivity among patients undergoing APR,[27,28,129] perhaps reducing the confidence of some surgeons in the safety of LS for this procedure.

The results of sensitivity analyses model 3 (HP) and model 4 (rectosigmoid tumor) found that patients who undergo HP have the same predictors of LS than those who undergo other types of rectal resections (including APR, LAR, LAR with ileostomy) and patients with tumors of the rectosigmoid junction also have the same predictors of LS as those with tumors of the rectum. The categorization of HP and APR in the same group, as done in this study, has been previously used in other studies of rectal cancer outcomes[54], and our results further support this approach. Overall, our sensitivity analyses justified the inclusion of HP and rectosigmoid in our primary analysis, as these groups did not appear to be systematically different than the rest of the cohort in terms of patient charactertistics and predictors of LS.

Based on our data, the uptake of LS for rectal cancer is lagging behind LS for colon cancer. A recent population-based analysis by Hoogerboord *et al.*[26] using a similar methodology as our study found the uptake of LS for colon cancer in Canada increased from 9% in 2004 to 52% in 2014. It is not surprising that the uptake of LS for colon cancer exceeds that of rectal cancer; colon cancer resection is technically easier than rectal cancer resection. Moreover, evidence demonstrating oncologic equivalence between LS and OS for colon cancer was published earlier than rectal cancer. For these reasons and others, international studies describe earlier and more rapid uptake of LS for colon cancer than rectal cancer.[48,52-54,83,130-133] Predictors of LS for colon cancer in Canada are similar to rectal cancer; year of surgery, female sex, younger age, higher comorbidity score, specific province, urban residence, surgeon/hospital volume, and resection type are all associated with the use of LS. [26]

To our knowledge, this study was the first to explore the association between financial incentives and uptake of LS for rectal cancer. Currently, three provinces (NS, BC and ON) have provincial policies containing specific remuneration fees for LS. In NS, where there is a 5% premium for laparoscopic LAR, the uptake of LS did not appear to be affected by financial incentive. However, the proportional use of LS increased in both BC and ON after introduction of 25% (ON) and 11% (BC) increases to remuneration for LS. Our results suggest that financial incentive may be associated with increased use of LS, but only if this incentive exceeds a specific value. For example, surgeons in NS may not perceive the additional 5% in remuneration as enough to justify the increased technical difficulty and operative time with LS compared to OS.

In summary, we have demonstrated that the uptake of LS in Canada is increasing and there is significant variation in use of LS among provinces. Knowledge translation and implications of these findings will be influenced by the impending publication of the long term oncologic outcomes of the ALaCaRT[35] and ACOSOG[36] trials. However, regardless of these results, LS for rectal cancer will likely continue to be utilized by many surgeons. Collectively, RCT data has demonstrated the importance of patient selection and surgeon experience, and our results further support this concept such that patients with certain characteristics are more likely to undergo LS and high volume surgeons are more likely to use LS.

Our study has also identified low uptake in sub-populations that is likely not a reflection of appropriate patient/surgeon selection- for example, patients living in rural areas have lower uptake of LS compared to those living in urban areas and patients undergoing LAR were significantly more likely to have LS compared to those undergoing APR. Further research and hypothesis generation of these findings could aid in fostering the growth of LS in appropriate settings and influence policy interventions on provincial levels to promote equity and access to patients who are currently not being offered LS.

4.2 Potential limitations

This is a cohort study that uses a discharge abstract database, which lacks several important clinical variables. For example, obesity can increase the technical difficulty of LS for rectal cancer and may influence the uptake of LS but is not captured in the DAD.[56,58,134] The distribution of BMI varies among Canadian provinces and may confound our measures of association between factors and the uptake of LS.[135] Similarly, the DAD does not contain information on other cancer-specific variables such as stage, size, level of the rectum and pathologic type. Tumor size may influence the uptake of LS; large, bulky tumors increase the difficulty of laparoscopic TME.[57,58] Similarly, tumor in the distal rectum are likely more difficulty to remove than tumors located at the rectosigmoid junction, and tumor location likely influences the uptake of LS.

We have attempted to include only those patients eligible for either LS or OS, but unmeasured clinical characteristics may have led to the inclusion of patients where this is not the case. For example, patients who have undergone previous extensive abdominal surgery may have been included in our cohort and would be unlikely to be offered LS given the high likelihood of intraabdominal adhesions and increased technical difficulty.

With our methodology and data source, the designation of laparoscopic included not only surgical procedures performed in a complete laparoscopic fashion but also likely included laparoscopic-assisted or hand-assisted (an additional incision is made to allow for the insertion of the surgeon’s hand) cases and cases that began laparoscopically but were converted to OS.

Conversion may occur for several reasons including bleeding, poor visualization, unclear anatomy, obesity, intra-abdominal adhesions, or failure to progress.[136,137] Conversion rates in RCTs vary from 1.2% in the COREAN trial[28], 17% in COLOR II[29] and 29% in MRC-CLASICC[37]. More recent trials, ALaCaRT[35] and ACOSOG[138], had lower conversion rates of 9% and 11%, respectively. This likely reflects the high level of operative experience and volume among the surgeons participating in these trials. A systematic review and meta-analysis of 13 observational studies and case-series of laparoscopically attempted rectal cancer surgeries found an overall conversion rate of 11.75%, likely providing a more accurate representation of the "real-world" experience.[139]

The surgical management of rectal cancer is evolving, and this study did not address some of the newer surgical techniques for rectal cancer. The laparoscopic trans-anal TME (TaTME) has been introduced as a novel surgical approach for mid and low rectal cancer. This technique is similar to LS for rectal cancer, but the distal aspect of the rectum is mobilized via a trans-anal approach. Hypothesized benefits of TaTME over LS include improved visualization, better specimen quality, less morbidity and increased rates of sphincter-preservation.[140,141] This technique was first described in 2010[142], and large case-series have shown promising results.[143-145] However, multi-center RCT data are lacking, and the role of TaTME remains unclear. Our dataset precedes the publication of the majority of experiences with TaTME, and will not be used to describe the use of this surgical technique in Canada. It is likely that the surgical treatment of rectal cancer will continue to evolve and the role of TaTME will be more clear after the publication of the COLOR III trial.[140]

The DAD does not include any data from Quebec; thus patients from this second most populous province in Canada were not included in our study. Over 8 million Canadians live in this province such that we are unable to describe the true population growth of LS for rectal cancer in Canada.

Our study is also limited by its design. Given the retrospective data, we were able to identify factors associated with the use of LS for rectal cancer, but could not determine causality. To further evaluate patient, surgeon and system variables that cause patients to undergo LS, large prospective cohort studies with clinical data collection would be required.

Lastly, our data are now three years old and we are unable to determine the current uptake of LS in 2018. Rectal cancer treatment is evolving rapidly and the use of retrospective data creates time lags between data analysis and knowledge translation, hindering our ability to develop strategies for quality improvement and innovation implementation. Real-time monitoring of surgical cancer care at a national level is needed to provide accurate and up to date information, and facilitate timely development of interventions, policies and system level changes aimed at improving the surgical management of patients with rectal cancer.

4.3 Conclusions

This study provides the first pan-Canadian description of the use of LS for rectal cancer and describes factors associated with its use. Although there has been a substantial increase in LS between 2004 and 2014, the minority (34.0%) of Canadians with rectal cancer underwent LS in 2014. We have identified significant interprovincial variation in the uptake of LS, and our results suggest that this is mainly driven by differences in patient, surgeon and geographic variables associated with the utilization of LS in Canada.

As the surgical management of rectal cancer continues to evolve, it is becoming clear that LS will continue to be used in Canada and is an important addition to the rectal cancer surgeons' "toolbox". However, the technical difficulty of LS and concern regarding potentially inferior pathologic outcomes may have slowed the widespread adoption of LS in all patients, and by all surgeons. The influence of surgeon volume and practice patterns demonstrated in our study emphasizes the importance of training and recruitment to increase utilization of LS; this information may be used to foster the growth of LS in appropriate settings and improve the surgical management of patients with rectal cancer.

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