The Population Uptake of Laparoscopic Colon Cancer Surgery in Canada: 2004-2014

by

C. Marius Hoogerboord

Submitted in partial fulfilment of the requirements
for the degree of Master of Science

at

Dalhousie University
Halifax, Nova Scotia
May 2017

DEDICATION

To my family

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

BACKGROUND

Although the safety and efficacy of laparoscopic surgery in colon cancer (LAC) have been established, the proportion of colectomies for cancer being performed laparoscopically (use) and uptake (change in use) of the procedure in Canada is not known.

OBJECTIVES

The primary objective of this study was to describe the use and uptake of LAC in Canada on national and provincial levels. The secondary objective was to examine the impact of demographic (province, rural/urban residence, year of surgery), patient (age, sex, comorbidities, segment of colon resected), and system (average annual surgeon and hospital volume) factors on the use of LAC.

METHODS

This study was a time series analysis. The Discharge Abstract Database (DAD), held by the Canadian Institute for Health Information (CIHI), was used to identify all colectomies for colon cancer performed in all Canadian provinces, except Quebec, from April 1, 2004 to March 31, 2015. The overall and annual numbers of colectomies as well as proportions performed open and laparoscopically were described at national and provincial level. The impact of predictor variables on LAC by year of surgery was described. Multiple logistic regression was used to estimate the associations between demographic, patient and system covariates and the outcome of undergoing LAC.

RESULTS

Among 63,504 patients undergoing colon cancer resection, LAC was used in 19,691 (31%) while an open approach was used in 43,813 (69%). Across the nine provinces, the overall proportion of patients undergoing LAC increased from 9% in 2004 to 52% in 2014 in a relatively constant fashion. There were marked differences in rates of LAC by province; at the end of the study period it ranged from 11% in Newfoundland (NL) to 60% in British Columbia ($p<0.001$).

On multivariate analysis, year of surgery (OR 9.31; 95% CI=8.60-10.09 for 2014 compared to 2004), urban residence (OR 1.24; 95% CI=1.18-1.30), high hospital volume (OR 2.04; 95% CI=1.96-2.13) and high surgeon volume (OR 1.29; 95% CI=1.24-1.35) were associated with increased use of LAC, whereas male sex (OR 0.94; 95% CI=0.90-0.98), low provincial uptake [OR 0.14; 95% CI=0.12-0.16 for NL compared to Ontario (ON)], higher level of comorbidities (OR 0.79; 95% CI=0.63-0.98 compared to no comorbidities) and left sided resections (OR 0.91; 95% CI=0.87-0.95 for left hemicolectomy, OR 0.58; 95% CI=0.55-0.62 for anterior resection compared to right hemicolectomy) were associated with decreased use.

CONCLUSION

Although there has been considerable uptake of LAC in Canada over the past decade, wide interprovincial variation remains. The use of laparoscopy at the individual patient level is related to patient factors, urban versus rural residence, and the local practice pattern as measured by average colectomy volumes at the surgeon level and hospital level.

LIST OF ABBREVIATIONS USED

AB	Alberta
ASCRS	American Society of Colon and Rectal Surgeons
BC	British Columbia
CCI	Canadian Classification of Health Intervention
CI	Confidence Interval
CIHI	Canadian Institute for Health Information
COLOR	Colon Cancer Laparoscopic or Open Resection
COST	Clinical Outcomes of Surgical Therapy
DAD	Discharge Abstract Database
FSA	Forward Sortation Area
ICD-10-CA	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
LAC	Laparoscopic Colectomy for Cancer
LOS	Postoperative Length of Hospital Stay
MB	Manitoba
MIS	Minimally Invasive Surgery
NB	New Brunswick
NHS	National Health Service
NIS	National Inpatient Sample Database
NL	Newfoundland
NS	Nova Scotia

NSQIP	National Surgical Quality Improvement Program
ON	Ontario
OR	Odds Ratio
PE	Prince Edward Island
SK	Saskatchewan
US	United States

ACKNOWLEDGEMENTS

My thesis committee, Drs. Geoff Porter, Adrian Levy and Gordon Flowerdew, each contributed in a unique way to the successful completion of this thesis. I am much indebted to Dr. Porter for his patient guidance and assistance throughout this project. You are a mentor and role model who continues to inspire me. Thank you very much Dr. Flowerdew. You not only provided invaluable support on the statistics but also contributed to this work on many other levels. Thank you for the emotional support and encouragement. I would like to extend my gratitude to Dr. Adrian Levy for the time invested. I benefitted from your extensive experience and knowledge. A big thank you to Min Hu, a STATA® master with whom I spent many hours and who became a friend. This project would not have been possible without the support of my wonderful wife Irene and our children Conrad and Claudia. Thank you for sacrificing so much and for allowing me to achieve this goal.

CHAPTER 1 INTRODUCTION

Colorectal cancer is the third most commonly diagnosed cancer in Canada, excluding non-melanoma skin cancers (1). In addition, it is the second most common cause for cancer related deaths in men and the third most common in women (2). On average, 69 Canadians are diagnosed with colorectal cancer every day, and 25 die from it (3). Risk factors include genetic predisposition, smoking, obesity, sedentary lifestyle, and ingestion of large amounts of red and processed meats (4). However, aging remains the single most important predictor of the disease. Overall, 90% of new cases and 93% of deaths occur in patients older than 50 years (5, 6). With the current trends in population demographics, it is estimated that the number of Canadians over the age of 65 will exceed 10.9 million by 2036. It is expected that the aging population will lead to a significant increase in the number of new cases of colorectal cancer (1).

The overall age-standardized population-based incidence rates of colon cancer are similar for Canada and the US at 60 per 100 000 males and 40 per 100 000 females in 2014. It declined from the mid 1980's to mid 1990's, with the decline most prominent for females. It again rose through the 2000's, followed by a slight decline around 2010 (1, 7). However, the latest decline was confined to the age group older than 50 years and is mostly attributed to increased use of screening programs (8). Conversely, incidence rates increased for those under the age of 50 years, likely due to poor diet and increased prevalence of obesity and diabetes mellitus (9).

Colorectal cancer is highly suited to screening; it is a common, lethal disease with a long pre-clinical phase, early detection improves survival and it usually develops from a treatable precursor lesion that can be identified by screening (10, 11). Fecal immunochemical testing (FIT) provides for a cost-effective, low-risk, noninvasive screening test (12). In addition, colonoscopy is a highly sensitive primary diagnostic procedure, which, in addition to diagnosis, also allows for resection of precancerous polyps and very early cancers thereby providing secondary and tertiary cancer prevention (13). Every province in Canada has an established screening program which starts at age 50 for the average risk population (3). With an aging population the use of screening programs will increase and therefore also the diagnosis of early stage colorectal cancer.

The primary treatment modality for colon cancer is surgical resection (colectomy) (14). The resection margins are determined by the location of the tumor and include the segment of involved bowel along with its blood supply and lymphatic drainage (en bloc resection). Regional metastases typically involve the lymphatic chain and resecting it is essential to accurately stage the cancer and reduce the risk for logoregional recurrence. Traditionally, colectomy is achieved by entering the abdomen via a midline incision (laparotomy) and by using manual retraction and manipulation for exposure and mobilization of the surgical planes. However, during the early 1990s surgeons started using a minimally invasive technique, known as laparoscopic surgery (14, 15). Compared to open colectomy, LAC reduces the physiologic stress of surgery and allows for an enhanced postoperative recovery with less pain, earlier return of bowel function, reduced postoperative length of hospital stay (LOS) and earlier return to preoperative level of activity (16, 17).

For laparoscopic surgery to be an acceptable alternative to open surgery, it is essential that the principles of en bloc resection are adhered to and outcomes such as disease free and overall survival be equivalent (if not improved). Since 2002, oncological equipoise has been established by several randomized controlled trials and meta-analyses (18-22). In 2004, the Clinical Outcomes of Surgical Therapy (COST) trial that was conducted in the United States (US) reported equivalent 3-year disease free and overall survival rates (19). This represented a pivotal point in the adoption of LAC by the surgical community. However, despite significant progress, disparities still exist in the use of this procedure (23, 24).

The benefits of enhanced postoperative recovery with LAC are not limited to patients. Fewer postoperative complications and shorter LOS imply cost savings to the healthcare system, which is of significant importance in an era of rising health care expenditures across all of Canada (25).

CHAPTER 2 BACKGROUND

Colon (large bowel) cancer is the third most common cancer, excluding non-melanoma skin cancers, and is also the second most common cause of cancer death in the Western world (2). In 2016 it is estimated that 25,100 Canadians will be diagnosed with colon cancer and that 9,300 will die of the disease (26). This represents 13% of all new cancer cases and 12% of all cancer deaths (26). With an aging population and increasing use of screening programs, the incidence is expected to rise.

Surgery is the only curative treatment option for colon cancer and also provides the best palliation for patients with advanced systemic metastases who become symptomatic from the primary tumor (27). The minimally invasive approach achieved by LAC limits surgical trauma and pain and allows for faster postoperative recovery and reduced LOS (28). However, it is a technically challenging procedure that requires advanced laparoscopic skills as well as specialized operating room equipment and is not universally available. In the US, LAC exceeded open colectomy since 2009, however, there still exists significant variation in adoption of the technique (24, 29). This study is the first to describe the use of LAC in Canada, and to estimate the impact of demographic, patient and system factors on its use.

2.1 LAC- A Primer

2.1.1 Theory and Principles

With improved understanding of the physiology of surgically induced stress it has become clear that the extent of the surgical incision and intra-abdominal manipulation, as well as the severity of surgical pain, are directly correlated with the magnitude of a systemic inflammatory response (30). The systemic inflammatory response is a neuro-endocrine reaction that leads to an increased production and reduced peripheral utilization of glucose with resultant hyperglycemia (increased blood glucose level), increased protein breakdown with muscle loss (protein catabolism), water retention with tissue edema, paralysis of the bowel (ileus), increased production of stress hormones with an increased metabolic rate, increased oxygen free radical production and reduced cellular immunity (30, 31). The postoperative physiological status of the patient who undergoes major abdominal surgery such as a colon resection is therefore similar to that of a poorly controlled type II diabetic in a hypermetabolic state, which poses a significant impediment to postoperative recovery (32).

Laparoscopic surgery reduces surgical pain and attenuates the stress response by limiting the extent of abdominal wall incisions, intra-abdominal manipulation and blood loss (33). Consequently, serum levels of pro-inflammatory cytokines, e.g. interleukin-6, and biomarkers of tissue damage are significantly reduced (34, 35). The technique involves access to the abdominal cavity via placement of metal or plastic sleeves (ports) 5-12 mm in diameter. Carbon dioxide is then insufflated into the abdominal cavity to create a working domain (pneumoperitoneum). A laparoscopic camera is introduced through a port to enable visualization and various instruments are used to manipulate, dissect and divide tissue, to maintain hemostasis and to anastomose (surgically reconnect) the ends of the remaining bowel after segmental resection.

LAC expedites postoperative recovery and reduces LOS compared to open colectomy (36). The duration of postoperative ileus is reduced, which facilitates earlier resumption of oral intake. Early refeeding supports the immunologic function of the bowel and decreases the rate of postoperative infectious complications (37, 38). LAC limits stress-induced insulin resistance and proteolysis and expedites return to anabolic metabolism (39). Minimizing the extent of the surgical incision leads to less postoperative pain with reduced need for opioid analgesia, avoiding common side-effects that slows down recovery e.g. nausea, vomiting, constipation, lethargy and dizziness (40). Patients are also able to mobilize earlier, which supports pulmonary function, stimulates return of bowel function and increases psychological well-being and independence (41).

Compared to open colectomy, LAC reduces the risk for postoperative complications, including wound infection, urinary tract infection, pneumonia and cardiovascular sequelae, as well as the risk of in-hospital mortality, defined as death during the index admission (42-44). Older patients, who have limited physiological reserve and higher frequency of medical comorbidities, stand to benefit more from LAC (45). The physiological stress of surgery and anesthesia can cause functional decline in this cohort, which may imperil their pre-operative level of independence (46). This can lead to a need for an increased level of specialized care and/or temporary or permanent institutionalization post discharge, with significant implications for quality of life and health care costs (47, 48). The extent to which LAC can facilitate return to preoperative level of independence at the time of discharge has not been well studied.

2.1.2 Early Experience with LAC

In the early 1990s, the benefits of laparoscopic surgery were well established and the technique widely adopted for procedures such as cholecystectomy and appendectomy (49, 50). Further technological advancements and improvement in surgeons' skill led to an interest in also applying laparoscopy to colon resection. Moises Jacobs performed the first laparoscopic colon resection in June 1990, and published the first series of laparoscopic colectomy in twenty patients, eleven of whom underwent resection for cancer (15). Subsequently, Dennis Fowler published his technique for laparoscopic-assisted sigmoid colon resection (51). In both these studies the mean LOS was significantly shorter compared to the open approach. Several other studies confirmed reduced duration of postoperative ileus, less postoperative pain and shorter LOS (52-55).

For LAC to be a feasible alternative to open surgery, it was essential that the principles of oncologic resection be adhered to and long-term cancer outcomes not be jeopardized. During the early 1990s, several reports of an increased incidence of tumor recurrence in the abdominal wall in locations where laparoscopic ports were placed (port site metastases) raised concerns regarding the oncologic safety and effectiveness of LAC for malignant disease (56-58). These concerns led to a recommendation by the American Society of Colon and Rectal Surgeons (ASCRS) that LAC be conducted only in the setting of an approved research protocol with prospective retrieval of data (59).

2.1.3 Randomized Trials of LAC

Subsequently, four large multicenter randomized controlled trials comparing LAC to open colectomy have demonstrated oncologic equipoise of the two approaches (18-21). The seminal trial in the US was the COST (19). This multicenter trial included 872 patients who underwent resection of colon cancer from 1994 to 1999 and was reported in 2004. There were no statistical differences in time to cancer recurrence, 3-year recurrence or overall survival for patients who underwent laparoscopic resection compared to open colectomy. LAC was associated with shorter LOS, decreased use of analgesia and improved quality of life compared to open colectomy.

The results from these initial trials encouraged further research and the literature expanded rapidly. A Cochrane review including 33 randomized trials was published in 2008 (22). It confirmed equivalence in long-term (> 5 years) oncologic outcomes for LAC compared to open colectomy.

2.2 Predictors of uptake of LAC

2.2.1 Geographic Factors

In spite of clear advantages in terms of patient recovery and quality of life, the adoption of LAC has been slow and fragmented (60). There exists a wide geographic variation in the utilization of LAC in the US (61). Regional variation in medical practice is likely multifactorial, including hospital infrastructure, billing incentive and patient factors including age, sex and medical comorbidities (62). However, for technically advanced subspecialty procedures like LAC, uptake is predominantly dependent on provider expertise and preference (62).

Studies in the US found significant disparities in access to LAC due to socio-economic status (63-66). Patients of lower income are often served by smaller, rural hospitals that may not have the necessary infrastructure to support advanced laparoscopic procedures. Health care providers at these centers are also more likely to perform lower volumes of laparoscopic surgery and have less experience in the technique (63). However, discrepancies in access to LAC also exist in high-volume urban institutions. Robinson et al. found that patients with higher household incomes were 70% more likely to undergo LAC compared to those with lower incomes (64). Patients of lower socio-economic status do not have the same access to primary and preventive care, which results in more advanced tumor stage at presentation as well as more extensive, poorly controlled medical comorbidities (65, 66). The socio-economic impact on access to LAC is clearly multifactorial and dependent upon diverse patient- and provider-level determinants.

2.2.2 Patient Factors

Patient factors predicting application of a laparoscopic approach to colon cancer surgery include age, comorbid status and location of the tumor (67-69). It is estimated that 23% of the population in the western world will be older than 65 years by 2050 (70). The incidence of colon cancer increases with age and it is therefore important to determine whether LAC can be safely applied to this patient population. Older patients have a lower physiological reserve. Most importantly from a surgical perspective are limitations in pulmonary, cardiovascular, neurological and musculoskeletal function (71). During laparoscopic surgery, the increased intra-abdominal pressure from the pneumoperitoneum is transduced to the chest and may lead to decreased lung compliance and lower lung volumes. The pneumoperitoneum also causes an extrinsic compression on large intra-abdominal veins that can potentially impair venous return to the heart, resulting in decreased cardiac filling and reduced output. These changes can be amplified by the extreme head-down positioning that is often required during laparoscopic colon surgery. This is of no consequence in patients with normal cardiopulmonary function but could lead to ventilatory and/or hemodynamic compromise in those with limited reserve (72). However, more recent studies confirmed that LAC is well tolerated by patients over the age of 65 and that age per se should not be a contraindication to a laparoscopic approach (68, 73-75). To the contrary, older patients stand to benefit more from LAC in terms of improved postoperative recovery (due to earlier mobilization and less surgical pain) and consequently a decrease in LOS (68, 74). They often have impaired mobility and muscle strength at baseline and limiting surgical trauma and pain provide for earlier mobilization, which reduces the risks for complications from extended bed rest including muscle catabolism, pneumonia, deep venous thrombosis and pulmonary embolism (blood clots in the lungs) and prolonged ileus (76). Also, less surgical pain obviates the need for opioid analgesics like morphine and hydromorphone and side effects such as psychosis, hallucinations, insomnia, dizziness, imbalance and constipation, which are more significant in the elderly, are avoided (77).

Patients with major medical comorbidities are better served by a laparoscopic approach (78). A major comorbidity is defined as a condition that is present at the time of admission, is not related to the primary diagnosis and is likely to adversely affect in-hospital resource use, LOS and/or mortality (79). Paradoxically, surgeons often deem LAC as "too risky" to be employed in comorbid patients. However, several studies have reported that a minimally invasive approach is not only safe and feasible in this patient group, but that such patients benefit from a decreased incidence of postoperative complications, earlier return of bowel function, decreased LOS and potentially decreased in-hospital mortality when compared to an open approach (78, 80-82). However, the incidence of in-hospital mortality for elective colon cancer resection is less than 2%, and more dependent on patient age and degree and severity of medical comorbidities than on surgical approach (83, 84).

Compared to the left side of the colon (left hemicolectomy), laparoscopic resection of the right side (right hemicolectomy) is technically easier due to its relative mobility and accessibility (69). For the same reasons, visualization and exposure is most complex for resection of the lower (distal) sigmoid colon and rectum (anterior resection). Left hemicolectomy and anterior resection are therefore more time consuming and require a higher number of procedures to master (85). The uptake for LAC can therefore be expected to be higher for tumors located in the right side of the colon, compared to tumors in the left side, especially if situated in the lower sigmoid or rectosigmoid junction (86).

2.2.3 The Impact of Surgeon and Hospital Volumes

A surgeons' annual overall caseload (volume) of colectomies is related to the uptake of the minimally invasive approach (87). The number of procedures required to complete the learning curve, defined as reaching a plateau comparable to peers in terms of 1) operative time, 2) conversion rate from laparoscopic to open surgery, 3) postoperative surgery-related complications and 4) oncologic outcomes, ranges from 30-70 and depends among others on the extent of formal training in laparoscopic surgery, exposure to other advanced laparoscopic techniques, dexterity, and ability to perform delicate maneuvers with 2-dimensional vision (88-93). A study using the American Board of Surgery database found that general surgeons performed an average of 11.6 colectomies per year, with 17 being the 75th percentile (94). The average surgeon will therefore require several years to attain competency in LAC and may not perform the procedure often enough to maintain their skills. The paucity of experienced laparoscopic mentors also hampers implementation by established surgeons, whereas newly qualified surgeons often feel that they require more formal training in advanced laparoscopy in order to be comfortable with the technique (93).

In 2012, the ASCRS set 20 laparoscopic colectomies for benign disease as minimum standard of competency for utilizing the technique for resection of curable cancer (95). However, advances in laparoscopic equipment led to improved optics, ergonomics and instrumentation, addressing many of the obstacles originally faced by surgeons. There is also evidence for video games developing cognitive skills applicable to laparoscopic surgery (96). A younger generation who grew up in an era of video games and who were more exposed to advanced laparoscopy during their training may therefore require a lower number of cases to become proficient at LAC (97). In Canada, surgeons who perform LAC are more likely to have recently entered practice, have completed a minimally invasive surgery fellowship, and/or be affiliated with a university (98).

Hospital volume is an important determinant of short-term outcome after LAC. In an ad-hoc analysis of 546 patients who underwent laparoscopic colectomy within the Colon Cancer Laparoscopic or Open Resection (COLOR) trial, Kuhry et al. defined hospital case volumes as high (> 10 cases per year), medium (5-10 cases per year) and low (< 5 cases per year) (99). High-volume hospitals had better outcomes in terms of intraoperative complications, operative times, conversion rate to open surgery, number of lymph nodes harvested, postoperative recovery of bowel function, postoperative complications and hospital stay.

The enhanced experience of higher surgeon volume improves technical ability, clinical judgement and patient selection with subsequent superior outcomes in terms of overall and 5-year disease-free survival and reduced postoperative complications and LOS (87, 100). However, hospital volume may be a more important determinant of early postoperative outcome than individual surgeon volume (101). Higher volume hospitals provide more sophisticated clinical services and experienced providers (100). Among others, this level of care facilitates earlier recognition and expeditious management of complications, minimizing its impact on postoperative recovery, LOS and mortality (102).

2.3 Population Uptake of LAC

2.3.1 International

Despite the evidence on the advantages of LAC, initial uptake was slow. Kemp and Finlayson reported that 3% and 4% of colectomies for cancer were performed laparoscopically in 2000 and 2004 respectively (103). There was a steady increase since the publication of the COST trial in 2004. Rea et al. found that the proportion of LAC increased to 9% for 2005-2007, while 12% of colectomies for benign disease were performed laparoscopically (104). For both of these studies the National Inpatient Sample Database (NIS) was used. An important limitation to these and other trials using this database was the absence of a dedicated code for LAC within the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Investigators had to rely on procedure modifier codes, which were believed to have been inconsistently applied. Kiran and colleagues took another approach and used the National Surgical Quality Improvement Program (NSQIP) database, in which specific codes for LAC were available, to examine use of laparoscopy for colon resection from 2006-2007 (105). In this study the proportion of laparoscopic colon resections was 45%. They did not differentiate between benign and malignant pathology but the clear discrepancy in utilization underscored concerns regarding the effect of coding error on the accuracy of studies in which the NIS were used. A retrospective cohort study on medical record-based data evaluated the use of laparoscopy in 9,705 patients who underwent elective colorectal resections between 2005 and 2010 (106). Use of laparoscopy increased from 23% to 42%. This study also did not differentiate between benign and malignant disease but again highlighted the underreporting of studies using NIS data. Sticca et al. reviewed the surgical approach in 3,393 patients with stage III colon cancer who were enrolled in a clinical trial for adjuvant therapy (North Central Cancer Treatment Group trial N0147) from 2004-2009 (29). Overall, 38% of colectomies were performed laparoscopically. More importantly they observed increasing uptake of LAC over time with more than 50% of procedures being completed by minimally invasive technique in 2009. Surgical efficacy, measured as number of lymph nodes retrieved, was similar between the open and laparoscopic groups. Using the NIS, Moghadamyeghaneh et al reported a 45% to 54% increase in the utilization of LAC from 2009-2012 (24).

Taylor et al. (67) studied the use of LAC in the National Health Service (NHS) of England from 2006-2008. Data were extracted from the National Cancer Data Repository, a national database that contains information on every patient diagnosed with cancer in England. Use of LAC increased from 10% to 28% over the 2-year study period. Patients who presented with advanced cancer, had a higher level of medical comorbidities and who required emergency surgery were less likely to undergo laparoscopic surgery. Data from the National Bowel Cancer Audit showed that the proportion of LAC further increased to 48% by 2014 (107). A study on the use of LAC in the Netherlands used the Durch Surgical Colorectal Audit, a prospective national database (108). Of 4,986 patients who underwent colectomy for cancer in 2010, 44% was done laparoscopically. Patients in the LAC group had lower risk for postoperative complications and in-hospital mortality as well as for hospital stay of longer than 14 days.

Using population-level data that encompassed both private and public hospitals in New South Wales, Australia, Dobbins et al. (109) found that the use of LAC increased from 2% in 2000 to 21% in 2008. Use of LAC led to reduced LOS and 30-day readmission rate and was also associated with reduced overall and cancer-specific mortality, although the survival benefits were limited to high-volume institutions. A retrospective study on national level in Australia obtained data from the National Hospital Morbidity Database to assess elective use of LAC from 2000 to 2008 (110). Overall, proportional use increased from 2% to 28% with highest use in 2008 in high-volume public (32%) and private (34%) hospitals.

2.3.2 Canada

Currently there are few epidemiological data on the use and uptake of LAC in Canada. Moloo et al. examined the adoption of laparoscopic colorectal surgery by a national survey of all general surgery fellows of the Royal College of Physicians and

Surgeons of Canada in 2009 (98). The response rate was 55%, and 67% of respondents indicated that they perform laparoscopic colorectal surgery. The study had several limitations: the sample selection is prone to volunteer bias and, although a response rate of 55% is acceptable for the study population and research design, it limits statistical power. Chan and colleagues found that, in ON, the proportion of LAC increased from 13% in 2002 to 37% in 2009 (111). Although this study used a robust administrative database it was limited to only one province. It also did not examine the association of geography, surgeon and hospital volumes and patient factors on uptake of LAC. Simunovic et al. also studied the patterns of uptake as well as short-term outcomes of LAC in ON from 2002 to 2009, using administrative databases (112). They reported a rise in the use of LAC from 9% to 39%, with the greatest increase from October 1, 2005 to April 1, 2006. They hypothesized that this was mainly due to the institution of a 25% fee premium for LAC in ON on October 1, 2005. Thirty-day mortality and cancer-specific and overall survival were not affected by increased use of LAC, while LOS was only minimally reduced. A study on the management of colon cancer in the emergency setting in ON found that use of LAC increased from 6% in 2002 to 12% in 2009 (113). This study is not relevant to our research question, as we will only include colectomies done on an elective basis. These four studies, of which 3 are limited to the province of ON, comprise the extent of the literature on use of LAC in Canada.

2.4 OBJECTIVES

2.4.1 Purpose

To describe the use of LAC in Canada from April 01, 2004 to March 31, 2015 at both national and provincial levels.

2.4.2 Specific Objectives

1. To describe, both nationally and by province, the number of patients undergoing laparoscopic and open colectomy for colon cancer, as well as the overall proportion and annual uptake of LAC in Canada.
2. To describe the contrast in province-specific uptake
3. To estimate the impact of demographic (province, rural/urban residence, year of surgery), patient (age, sex, comorbidities, location of tumor), and system (surgeon and hospital volume) predictors on use of LAC.

CHAPTER 3 MATERIALS AND METHODS

3.1 Cohort Selection

This population-based time series analysis utilized information from a discharge abstract database. All colectomies for colon cancer performed in all Canadian provinces, except Quebec, from April 1, 2004 to March 31, 2015 were identified by use of the DAD held by CIHI. CIHI is an independent, pan-Canadian not-for-profit organization (114). Its mandate is to coordinate the development and maintenance of a comprehensive and integrated approach to health information in Canada, and to provide and coordinate the provision of accurate and timely data and information required for 1) establishing sound health policy; 2) effectively managing the Canadian health system; and 3) generating public awareness about factors affecting good health. The DAD is a national database that was originally developed in 1963 (115). It captures administrative, clinical and demographic information on hospital separations (discharges, deaths, sign-outs and transfers). Data are received directly from acute care facilities or from their respective health/regional authority or ministry/department of health. Facilities in all provinces, except Quebec, are required to report these data. Since fiscal year 2004-2005 all diagnostic and therapeutic data were recorded in the DAD according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada (ICD-10-CA) and Canadian Classification of Health Intervention (CCI) (116).

The intent was to select a cohort of patients that could potentially have been treated by either the open or laparoscopic approach. We included all patients who underwent planned (non-emergent) colon resection and had a valid Canadian postal address, and excluded complex cases that were likely to require an open approach such as locally advanced colon cancers requiring multivisceral resections (concomitant resections of adjacent organs invaded by tumor such as bladder, small bowel, stomach), concomitant liver resection for hepatic metastases, colectomy in pregnancy, and emergency presentation with peritonitis and/or bowel obstruction.

We identified potential cases by primary diagnosis of colon cancer, as captured by ICD-10-CA codes (specific codes listed in table 3.1). All potential cases who underwent a colectomy during the same admission, as captured by CCI codes (specific codes listed in table 3.2), were assessed for eligibility for inclusion in our study. Participants were assigned to the year in which they were admitted to hospital for colectomy. Open and laparoscopic resections were differentiated by CCI codes.

3.2 Use and Longitudinal Uptake of LAC, 2004-2014

The total, open and laparoscopic number of colectomies as well as proportional use of LAC were reported at national and provincial levels, from April 2004 to March 2015. The annual proportion of LAC was described by sex, age groups, rural/urban residence, level of medical comorbidities, segment of colon resected, surgeon and hospital volume of colectomies and province.

3.3 Demographic, Patient and System Factors Predicting Use of LAC

3.3.1 Province, Rural/Urban Residence and Year of Surgery

The association between use of LAC and province, patient residence (rural vs. urban) and year of surgery were analyzed. Rural/urban status was defined by use of the forward sortation area (FSA) (117). The FSA constitutes the first three characters (alpha-numeric-alpha) of the 6-digit postal code and is provided by CIHI. The second character of the FSA identifies a major geographic area in an urban or rural location: 0 indicates a rural postal code and 1-9 urban. Year of surgery was analyzed as continuous variable.

3.3.2 Age, Sex, Comorbidities and Segment of Colon Resected

Age in years at admission to hospital was analyzed in 4 categories; 18-50, 51-65, 66-80 and > 80. Sex (male/female) was analyzed as binary variable.

A major medical comorbidity was defined according to the Elixhauser comorbidity index as a condition that was present at the time of admission, not related to the primary diagnosis and likely to adversely affect in-hospital resource use, LOS and/or mortality (79). The index was developed specifically to be applied to administrative databases, to quantify the burden of major medical comorbidities and to predict hospital charges (used as proxy for postoperative complications, LOS and in-hospital mortality) (79). It has been validated in both homogenous and heterogeneous study populations and outperforms other methods of comorbidity measurement in administrative data (118-120). It is therefore the ideal measurement tool to quantify major medical comorbidity in our study.

The index is made up of 30 categories originally based on the ICD-9-CM. It has since been modified and updated to comply with ICD-10 codes (table 3.3) (121). Each category is dichotomous; it is either present or not. The primary cancer diagnosis is not included as comorbidity. The index is meant to be flexible; categories may be added or omitted relevant to the research question and /or disease process under investigation. For the purpose of our study, we omitted the following categories: other neurological disorders, metastatic cancer, solid tumor without metastases, weight loss, fluid and electrolyte disorders and obesity. Elixhauser score was analyzed in 3 levels; 0, 1-3 and 4-8.

Segmental resections were defined by use of ICD-10-CA diagnostic codes and classified as right hemicolectomy, left hemicolectomy, anterior resection and other (including resection of multiple or adjacent segments) (table 3.4).

3.3.3 System Factors

In order to examine the impact of surgeon and hospital experience on use of LAC, volume of both open and laparoscopic colectomies for cancer were included. Mean annual volume of colectomies, for years in which at least 1 colectomy for cancer was performed, was calculated for each surgeon and hospital. Average annual volumes were categorized into quartiles and dichotomized into high and low, defined as above and below the 75th percentile.

3.4 Data Analysis

Demographic, patient and system characteristics were compared between the laparoscopic and open colectomy groups by Student's t-test for continuous and chi square test for categorical variables. For multivariate analysis, a model that best fit the data was developed using a stepwise procedure. The order in which variables were considered for inclusion was driven by logical consideration. Inclusion of variables was based on p-values of the likelihood ratio and Hosmer-Lemeshow tests.

Multiple logistic regression was used to estimate the impact of predictor variables on the use of LAC over the entire study period. The model was repeated limited to the final year of the study to estimate most current differences in provincial LAC odds. Associations were reported as adjusted odds ratios (OR) with 95% confidence intervals (CI) and p-values less than 0.05 declared as statistically significant. Since year of surgery was being analyzed as continuous variable, the odds ratio (and 95% CI) was raised to the power 10, being the odds ratio estimate for the last fiscal year relative to the first fiscal year. Reference categories were included for residence (rural), province (ON), age (66-80 years), sex (female), Elixhauser comorbidity score (0), segmental resection (right hemicolectomy) and surgeon and hospital volume (low).

All analyses were conducted with STATA 14® StataCorp. 2015. *Stata Statistical Software: Release 14.* College Station, TX: StataCorp LP.

Table 3.1 ICD-10-CA diagnostic codes for colon cancer

C18 Malignant neoplasm of colon	
C18.0	Malignant neoplasm of caecum (includes ileocecal valve)
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon (excludes rectosigmoid junction)
C18.8	Overlapping malignant lesion of colon*
C18.9	Malignant neoplasm of colon, unspecified (Includes large intestine not otherwise specified)
C19	Malignant neoplasm of rectosigmoid junction

* overlapping 2 or more contiguous sites within the 3-character category

Table 3.2 CCI procedure codes for colectomy

1.NM.87. Excision partial, large intestine		
Colocolostomy anastomosis* technique.	1.NM.87.DF	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.87.LA	Open approach
	1.NM.87.RN	Open approach
Colorectal anastomosis technique	1.NM.87.DE	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.87.RD	Open approach
Enterocolostomy anastomosis technique	1.NM.87.DN	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.87.RE	Open approach
Stoma formation and distal closure	1.NM.87.DX	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.87.TF	Open approach
Stoma formation with creation of mucus fistula	1.NM.87.DY	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.87.TG	Open approach
1.NM.89. Excision total, large intestine		
Ileorectal anastomosis	1.NM.89.DF	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.89.RN	Open approach
Stoma formation with distal closure	1.NM.89.DX	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.89.TF	Open approach

Table 3.2 cont'd

1.NM.91. Excision radical, large intestine		
Colocolostomy anastomosis technique.	1.NM.91.DF	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.91.RN	Open approach
Colorectal anastomosis technique	1.NM.91.DE	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.91.RD	Open approach
Enterocolostomy anastomosis technique	1.NM.91.DN	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.91.RE	Open approach
Stoma formation with distal closure	1.NM.91.DX	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.91.TF	Open approach
Stoma formation with creation of mucus fistula	1.NM.91.DY	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NM.91.TG	Open approach
1.NQ.87. Excision partial, rectum		
Colorectal anastomosis	1.NQ.87.DE	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NQ.87.RD	Open approach
Closure of rectum with colostomy (Hartmann's technique)	1.NQ.87.DX	Laparoscopic, laparoscopic assisted, hand-assisted approach
	1.NQ.87.TF	Open approach

*Surgical reconnection of 2 remaining ends of bowel after segmental resection.

Table 3.3 Elixhauser comorbidity index

Category
Congestive heart failure
Cardiac arrhythmias
Valvular disease
Pulmonary circulation disorders
Peripheral vascular disorders
Hypertension, uncomplicated
Hypertension, complicated
Paralysis
Other neurological disorders*
Chronic pulmonary disease
Diabetes, uncomplicated
Diabetes, complicated
Hypothyroidism
Renal failure
Liver disease
Peptic ulcer disease excluding bleeding
AIDS/HIV
Lymphoma
Metastatic cancer*
Solid tumor without metastasis*
Rheumatoid arthritis/ collagen vascular diseases
Coagulopathy
Obesity
Weight loss*
Fluid and electrolyte disorders*
Blood loss anemia
Deficiency anemia

Table 3.3 cont'd

Category
Alcohol abuse
Drug abuse
Psychoses
Depression or Bipolar affective disorder

*Omitted

Table 3.4 Definitions of segmental resections according to ICD-10-CA diagnostic codes

Segmental resection	**ICD-10-CA diagnostic codes**
Right hemicolectomy*	C18.0 Malignant neoplasm of cecum C18.2 Malignant neoplasm of ascending colon C18.3 Malignant neoplasm of hepatic flexure C18.4 Malignant neoplasm of transverse colon
Left hemicolectomy*	C18.5 Malignant neoplasm of splenic flexure C18.6 Malignant neoplasm of descending colon C18.7 Malignant neoplasm of sigmoid colon
Anterior resection	C19 Malignant neoplasm of rectosigmoid junction
Other	C18.8 Overlapping malignant lesions of colon[ł]

*Has to meet 1 of the specified diagnostic codes
[ł]Overlapping 2 or more contiguous sites within the 3-character category

CHAPTER 4 RESULTS

The CIHI search identified 105,302 adult patients who underwent colectomy for colon cancer during the study period (figure 4.1.1). 377 (0.4%) patients did not meet the inclusion criteria of a valid postal code at the time of admission and were therefore excluded. Of the remaining 104,925 patients, 41,798 (40%) met the following exclusion criteria: Pregnant at the time of admission (N=22), pre-admit diagnosis of peritonitis (N=2,412), admitted via emergency department (N=20,684) and underwent complex resections (N=18,303). Therefore, our final study population included 63,504 cases.

The patient, system and demographic characteristics of laparoscopic and open colectomy groups are presented in table 4.1. Although statistically significant, the magnitude of differences in age ($p<0.001$), sex ($p<0.001$) and degree of medical comorbidities ($p=0.04$) were minor and likely not clinically significant. The groups differed significantly in terms of the type of resection ($p<0.001$); compared to open colectomy the proportion of patients was higher for right hemicolectomy (6%), but lower for left hemicolectomy (2%), anterior resection (5%) and other (2%) in the laparoscopic group. In terms of system factors, the annual weighted mean surgeon ($p<0.001$) and hospital ($p<0.001$) volume of colectomies were significantly higher for patients who underwent laparoscopic colectomy (12 vs. 10 and 49 vs. 41 respectively). As for residency, the proportion of patients who lived in an urban environment was significantly higher in the laparoscopic group (84% vs. 76%, $p<0.001$). There was also a significant variation in the number of open and laparoscopic colectomies between provinces ($p<0.001$) as well as for year of surgery ($p<0.001$).

4.1 PAN-CANADIAN USE AND UPTAKE OF LAC

Of the 63,504 cases overall, 19,691 (31%) underwent laparoscopic and 43,813 (69%) open colectomy. The national total, open and laparoscopic numbers of colectomies are presented in figure 4.1.2. The annual number of colectomies increased slightly over the course of the study, consistent with the known increase in colon cancer incidence, from 5,601 (2004) to 5,976 (2014). The number of LAC increased from 513 in 2004 to 3,080 in 2014 while the number of open colectomies declined from 5,088 in 2004 to 2,896 in 2014. 2014 represented the crossover point where the majority of colectomies were performed laparoscopically. Overall, the proportional use of LAC increased from 9% in 2004 to 52% in 2014 in a relatively constant fashion (figure 4.1.3).

4.2 Provincial use and uptake of LAC

Consistent with wide variation in provincial populations, the overall number of colectomies ranged from 503 (0.8%) in Prince Edward Island (PE) to 31,594 (50%) in ON (figure 4.2.1). 78% of all cases occurred within three provinces [ON, British Columbia (BC) and Alberta (AB)]. The annual proportional use of LAC varied between provinces (figure 4.2.2). Use of LAC in 2014 was higher than overall use in all provinces; this was most evident for PE and least marked in NL (figure 4.2.3). In general, more populous provinces tended to perform a higher proportion of colectomies laparoscopically.

The use and uptake of LAC by province are represented by figures 4.2.4 to 4.2.21. The following represents a synopsis of each province's experience with LAC over the study period.

In ON, 11,506 (36%) of colectomies were performed laparoscopically over the study period and, as of 2013, LAC was applied in the majority of cases (figure 4.2.4). The most rapid year over year increase in use of LAC happened between 2005-2006 (9%) (figure 4.2.5). Thereafter use of LAC continued to increase at an average annual rate of 4% and again spiked in 2013 and 2014 at 6% and 5% respectively.

In BC a total of 11,500 colectomies were performed, 4,011 (35%) of which were done laparoscopically. The annual number of laparoscopic colectomies increased from 69 in 2004 to 741 in 2014 in a fairly linear fashion (figure 4.2.6). In 2012, LAC became the preferred approach. The proportion LAC increased at an average rate of 5% per year from 7% in 2004 to 60% in 2014, the highest of all provinces (figure 4.2.7). However, uptake decreased from 7% in 2013 to 2% in 2014.

In AB, 1,949 (30%) of a total of 6,680 colectomies were performed laparoscopically over the study period. In 2014, the majority of colectomies were performed laparoscopically (figure 4.2.8). The proportional use increased at an average rate of 4% per year, with the sharpest increase happening from 2013-2014 (12%) (figure 4.2.9).

In all other provinces open remained the most common approach. NL had the lowest use of LAC, with 172 of 2,231 (8%) colectomies being performed laparoscopically (figure 4.2.10). The annual proportion of LAC remained under 12% and the average annual increase of 0,6% was the lowest of all provinces (figure 4.2.11).

New Brunswick (NB) had the second lowest use, with 196 of 2,154 (9%) colectomies done laparoscopically (figure 4.2.12). The proportion LAC remained more or less stable from 2004 (3%) to 2009 (5%) followed by a fairly steep increase to 21% from 2010 to 2014 (figure 4.2.13). Average annual increase in proportional use was 2% per year.

The lowest number of colectomies was performed in PE, which is also the province with the smallest population in Canada. Overall, laparoscopic colectomy was utilized in 10% (49 of 503) cases (figure 4.2.14). Uptake was almost non existent from 2004 to 2012, with no laparoscopic colectomies done in 2004, 06, 09 and 2010 (figure 4.2.15). The proportion of LAC then rapidly increased from 2% in 2012 to 27% in 2013 and 43% in 2014, resulting in an average increase in proportional use of 4% per year.

Nova Scotia (NS) had the highest overall use of LAC of all the maritime provinces. Of 2,984 colectomies, 636 (21%) was done by laparoscopic approach (figure 4.2.16). The average uptake was 2% per year and the proportional use increased from 4% in 2004 to a maximum of 33% in 2011, after which it decreased somewhat to 28% in 2014 (figure 4.2.17).

In Manitoba (MB), 623 of 3,363 (19%) patients underwent LAC, the lowest rate in the prairie provinces (figure 4.2.18). Proportional use of LAC increased from 6% in 2004 to a maximum of 36% in 2012 at an average rate of 3% per year, after which it decreased to 28% at the end of the study (figure 4.2.19). In Saskatchewan (SK), the laparoscopic approach was used in 549 of 2,495 (22%) cases (figure 4.2.20). The proportion of LAC went from 14% in 2004 to 38% in 2014 at an average rate of 2% per year (figure 4.2.21).

Figure 4.2.22 shows, with the exception of ON and NS, an increase in use of LAC moving from east to west in Canada.

4.3 Annual proportion of LAC by demographic, patient and system variables

The proportion of LAC increased from 7% to 39% and 10% to 55% for rural and urban patients respectively. Throughout the study period urban patients were more likely to undergo LAC and the variance increased during the later years (figure 4.3.1). Increasing age was associated with a lower probability of undergoing LAC (figure 4.3.2). However, the use of LAC increased in all 4 age groups. The proportion of patients who underwent LAC increased from 13% to 58% for age group 18-50 years, 9% to 55% for age group 51-65, and 9% to 47% for age groups 66-80 and older than 80 years. As of 2005, female patients were somewhat more likely to undergo laparoscopic surgery, compared to males (figure 4.3.3). Comparing the crude and age-adjusted rate of LAC showed that age was not biasing the sex effect (figure 4.3.4a and 4.3.4b). Use of LAC increased for all 3 categories of Elixhauser comorbidity index but was highest in the group with no comorbidities, where it went from 9% to 53% in a fairly constant fashion, compared to 8% to 49% and 16% to 44% in those with 1-3 and 4-8 comorbidities respectively (Figure 4.3.5). In terms of segmental resection, right hemicolectomy was most likely to be performed by laparoscopy with a proportional increase of 46% (8% in 2004 to 54% in 2014), followed by 42% for left hemicolectomy (12% in 2004 to 54% in 2014), 36% for other resections (7% in 2004 to 43% in 2014) and 35% for anterior resection (8% in 2004 to 43% in 2014) (figure 4.3.6). The LAC rate increased from 11% to 56% in high-volume surgeons, who performed and average of 7 - 37 colectomies per year, compared to a more moderate increase of 7% to 44% for low-volume surgeons (figure 4.3.7). Similarly, the rate of LAC increased in high-volume hospitals - in which an average of 37 – 103 colectomies were performed annually - from 7% to 36%, compared to 2% to 16% for low-volume hospitals (figure 4.3.8). The proportion of colectomies being performed laparoscopically by high- and low-volume surgeons in high-volume hospitals increased from 14% to 62% and 9% to 54% respectively, whereas in low-volume hospitals it increased from 5% to 40% and 4% to 38% respectively (figure 4.3.9).

4.4 Regression analysis

A regression model that best fit the observed rate of LAC was estimated by stepwise selection (appendix A). All predictor variables were included in the final model. Model fit was improved by addition of squared and cubic terms for year of surgery, as well as by interaction terms with year for sex, province, hospital and surgeon volume and segmental resection. However, although statistically significant, the magnitude of the interaction effects was too small to be visually significant. Furthermore, a sophisticated model describing the annual distribution of LAC is of value in providing a historical perspective on uptake but does not contribute to the purpose of this study, which is to understand how LAC was incorporated into standard practice and how this process can be accelerated. Therefore, in order to prevent the model from becoming overly complex, the squared and cubic terms for year of surgery as well as the interaction terms were not included in the final model.

Results of the multiple regression analysis are presented in table 4.2.1. The odds of undergoing LAC in 2014 were 9 times higher, compared to 2004. The LAC odds for a male patient was 1.24 of what it was for a female patient. Compared to the age group 66-80 years, the odds for LAC was highest in the youngest age group (1.15) followed by those aged 51-65 years (1.14), whereas the odds of undergoing a laparoscopic procedure was approximately one eighth in patients older than 80 years. For a patient with 1-3 or 4-8 medical comorbidities the LAC odds were respectively one tenth and one fifth of what it was if they had no comorbidity. There was a considerable difference in odds of LAC between provinces. The LAC odds in NL was approximately one seventh of what it was in ON. The odds for urban patients for undergoing LAC was 1.24 of what it was for rural patients. As for segmental resection, LAC odds for a left hemicolectomy was slightly lower (0.91) and for anterior resection, approximately one half of what it was for a right hemicolectomy. In terms of system factors, LAC odds in a high-volume hospital was approximately twice that for a low-volume hospital. Also, LAC odds for a high-volume surgeon was almost 1.3 times that for a low-volume surgeon.

In order to further describe the contrast in province-specific uptake the model was repeated for the final year of the study (2014) (table 4.2.2). Compared to the overall study period, LAC odds for PE, AB and BC have moved closer to ON, were smaller for MB and NS and similar for NL, NB and SK.

Table 4.1 Demographic, patient and system characteristics of laparoscopic and open colectomy groups

Variable	Laparoscopic (N = 19,691)	Open (N = 43,813)	p-value
Age (years): mean (SD)	69 (12)	70 (12)	*
Gender: N (%)			*
Male	10,416 (53)	24,158 (55)	
Female	9,275 (47)	19,655 (45)	
Elixhauser comorbidity score: N (%)			0.04
0	12,854 (65)	28,176 (64)	
1-3	6,714 (34)	15,297 (35)	
4-8	123 (1)	340 (1)	
Residence: N (%)			*
Rural	3,253 (17)	10,560 (24)	
Urban	16,438 (84)	33,253 (76)	
Annual weighted mean surgeon volume of colectomies: mean (SD)	12 (7)	10 (7)	*
Surgeon mean annual volume quartiles: N (%)			
1: 1 – 2	274 (1)	1,311 (3)	
2: 2.1 – 3.88	1221 (6)	4,183 (10)	
3: 3.9 – 7.0	4,276 (22)	12,187 (28)	
4: 7.09 – 37.27	13,920 (71)	26,132 (60)	
Annual weighted mean hospital volume of colectomies: mean (SD)	49 (21)	41 (24)	*
Hospital mean annual volume quartiles: N (%)			
1: 1 - 3.89	128 (1)	691 (2)	
2: 3.90 – 16.18	1,252 (6)	5,231 (12)	
3: 16.27 – 36.63	3,912 (20)	14,196 (32)	
4: 37.36 – 102.81	14,390 (73)	23,713 (54)	

*$p < 0.001$

Table 4.1 cont'd

Variable	**Laparoscopic (N = 19 691)**	**Open (N = 43813)**	**p-value**
Resection type: N (%)			*
Right hemicolectomy	10,004 (51)	19,902 (45)	
Left hemicolectomy	5,809 (30)	12,200 (28)	
Anterior resection	2,706 (14)	8,403 (19)	
Other	1,172 (6)	3,308 (8)	
Year of surgery: N (%)			*
2004	513 (3)	5,088 (12)	
2005	789 (4)	4,932 (11)	
2006	1,149 (6)	4,577 (11)	
2007	1,410 (7)	4,428 (10)	
2008	1,658 (8)	4,467 (10)	
2009	1,842 (9)	4,048 (9)	
2010	1,982 (10)	3,633 (8)	
2011	2,250 (11)	3,510 (8)	
2012	2,384 (12)	3,199 (7)	
2013	2,634 (13)	3,035 (7)	
2014	3,080 (16)	2,896 (7)	
Province: N (%)			*
NL	172 (1)	2,059 (5)	
PE	49 (0.3)	454 (1)	
NS	636 (3)	2,348 (5)	
NB	196 (1)	1,958 (5)	
ON	11,506 (58)	20,088 (46)	
MB	623 (3)	2,740 (6)	
SK	549 (3)	1,946 (4)	
AB	1,949 (10)	4,731 (11)	
BC	4,011 (20)	7,489 (17)	

*$p < 0.001$

Table 4.2.1 Logistic regression of factors associated with LAC

Variable	**Multivariate Adjusted OR (95% CI)**	**Multivariate p-value**
Odds ratio estimate, 2014 relative to 2004	9.31 (8.60-10.09)	*
Male sex	0.94 (0.90-0.98)	0.001
Female sex (reference)	1.00	
Age		
18-50 years	1.15 (1.07-1.24)	*
51-65	1.14 (1.09-1.19)	*
66-80 (reference)	1.00	
>80	0.87 (0.83-0.92)	*
Province		
NL	0.14 (0.12-0.16)	*
NB	0.16 (0.14-0.19)	*
PE	0.23 (0.17-0.32)	*
MB	0.39 (0.36-0.43)	*
SK	0.54 (0.49-0.60)	*
NS	0.53 (0.48-0.59)	*
AB	0.57 (0.53-0.60)	*
BC	0.89 (0.85-0.93)	*
ON (reference)	1.00	
Residence		
Rural (reference)	1.00	
Urban	1.24 (1.18-1.30)	*
Elixhauser score		
0 (reference)	1.00	
1-3	0.90 (0.87-0.94)	*
4-8	0.79 (0.63-0.98)	0.035
Hospital volume		
Low (reference)	1.00	
High	2.04 (1.96-2.13)	*
Surgeon volume		
Low (reference)	1.00	
High	1.29 (1.24-1.35)	*
Resection type		
Right (reference)	1.00	
Left	0.91 (0.87-0.95)	*
Anterior	0.58 (0.55-0.62)	*
Other	0.71 (0.66-0.76)	*

*p<0.001

Table 4.2.2 Logistic regression of association of provinces with LAC, 2014

Province	Multivariate Adjusted OR† (95% CI)	Multivariate p-value
NL	0.09 (0.06-0.14)	*
NB	0.18 (0.13-0.26)	*
PE	0.80 (0.48-1.34)	0.40
MB	0.30 (0.22-0.38)	*
SK	0.51 (0.39-0.68)	*
NS	0.33 (0.25-0.44)	*
AB	0.68 (0.57-0.81)	*
BC	1.10 (0.92-1.22)	0.46
ON (reference)	1.00	

† adjusted for sex, age, residence, Elixhauser score, hospital volume, surgeon volume and resection type

*p<0.001

Figure 4.1.1 Flow diagram of cohort selection

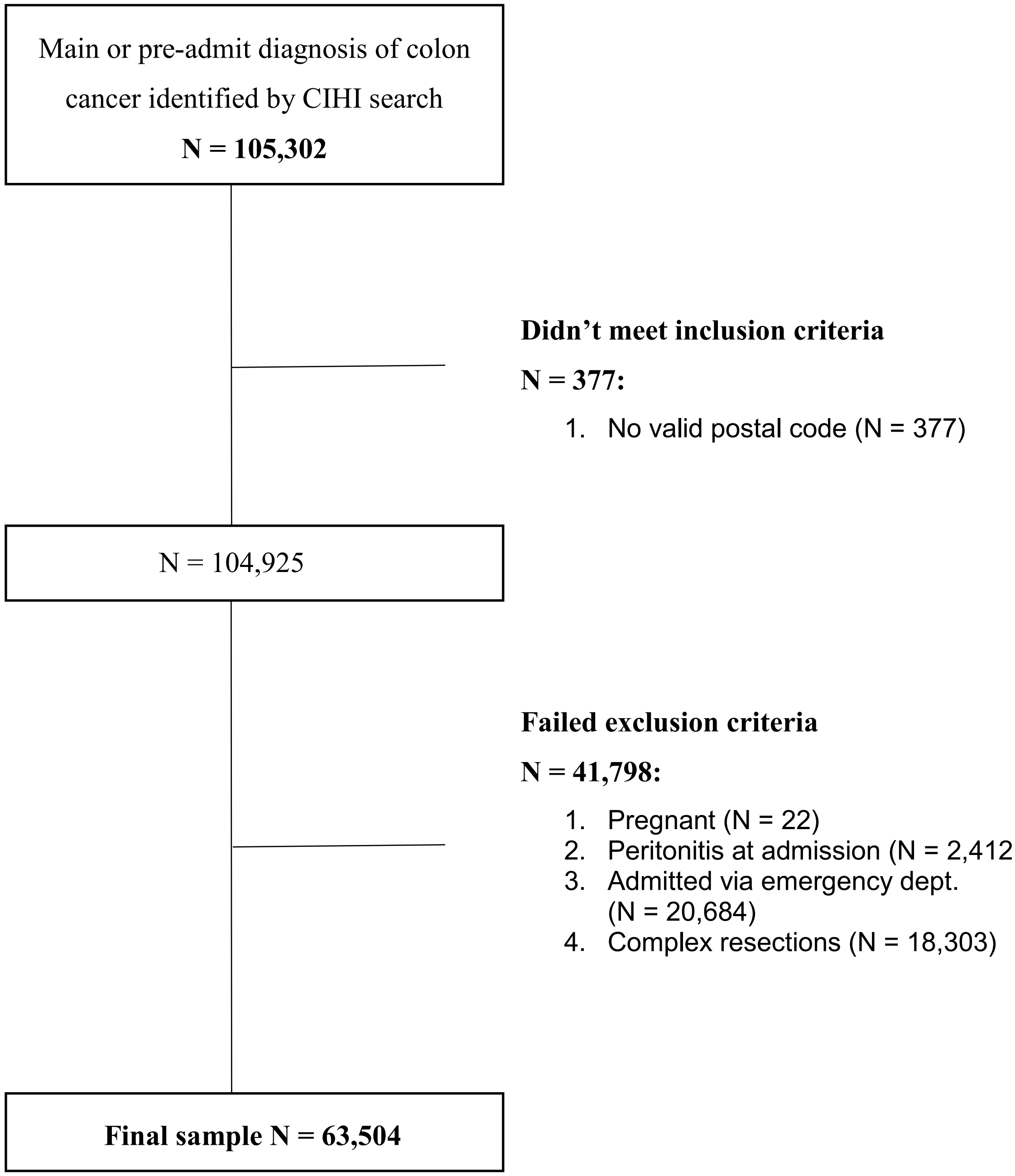


Figure 4.1.2 Overall, open and laparoscopic number of colectomies for cancer in Canada, 2004-2014

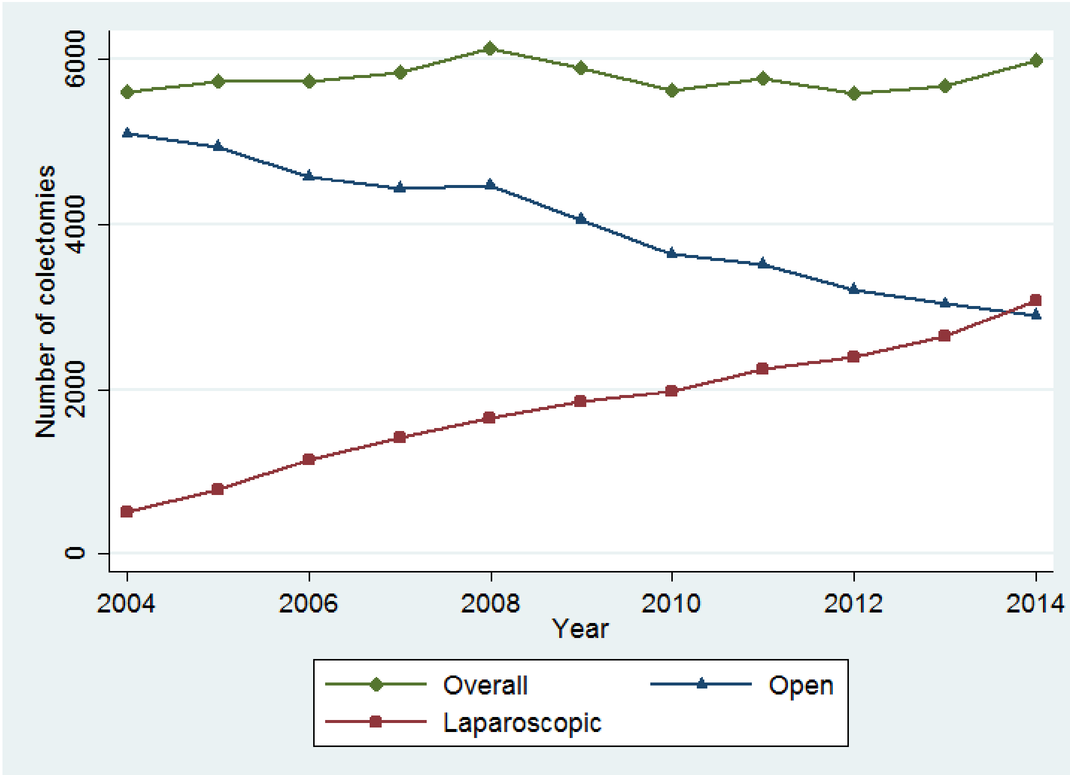


Figure 4.1.3 Annual proportional use of LAC: Canada

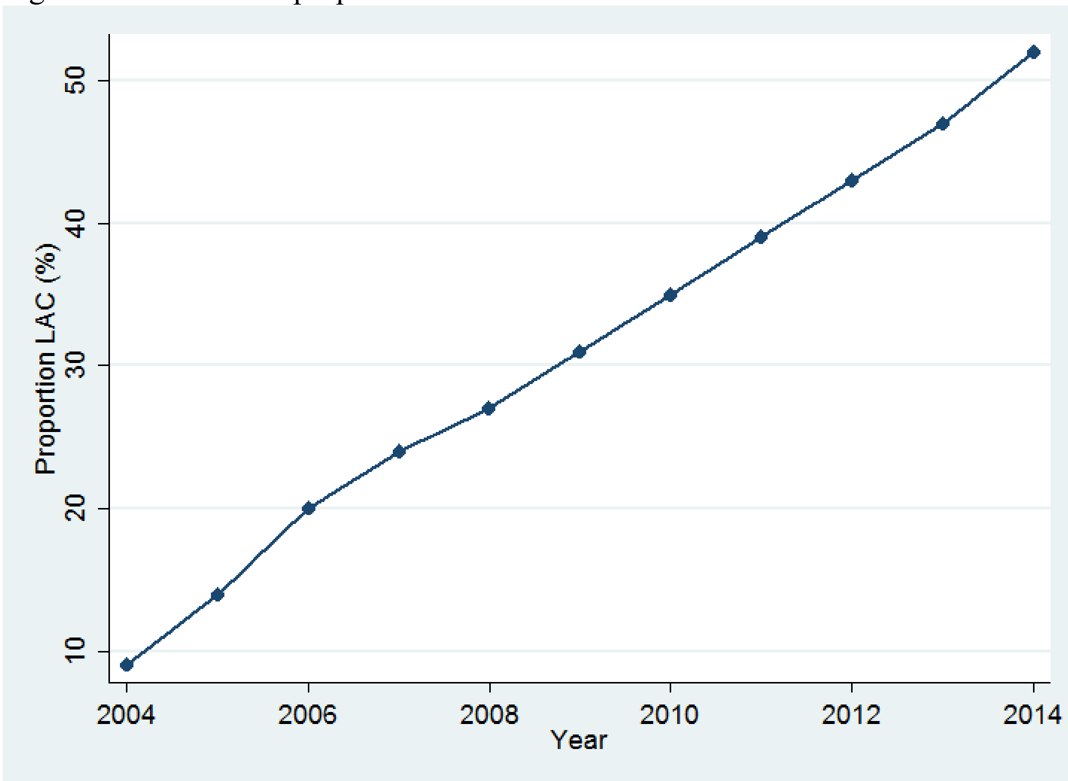


Figure 4.2.1 Overall number of colectomies by province

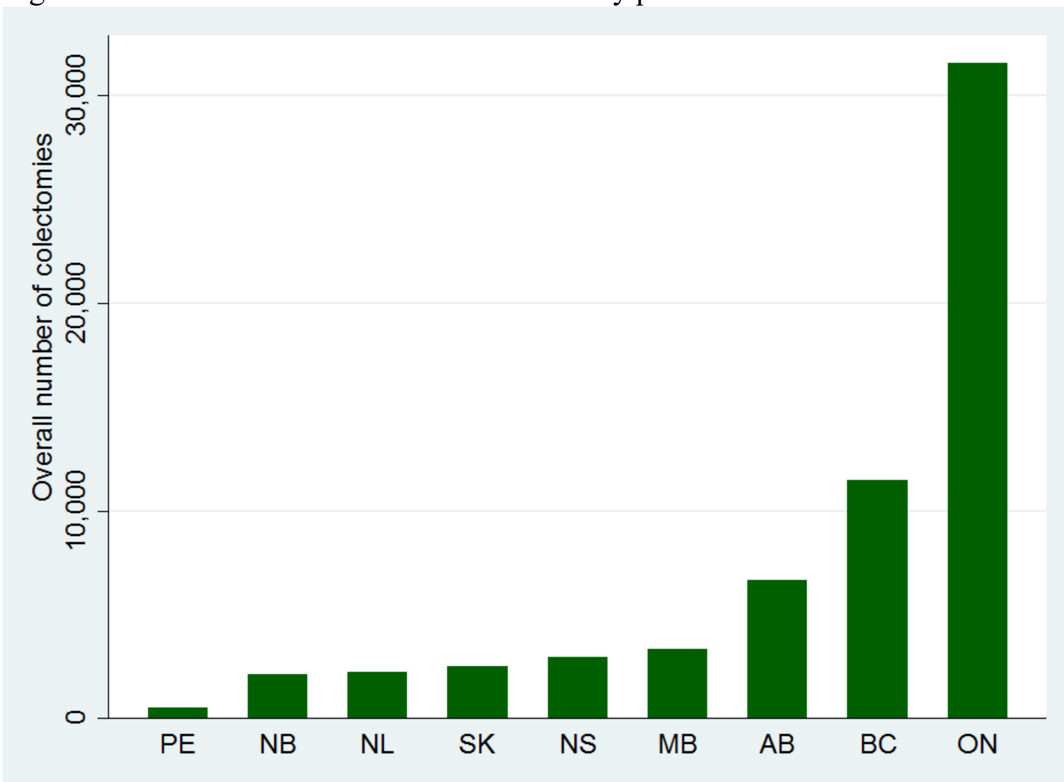


Figure 4.2.2 Annual proportion of LAC by province

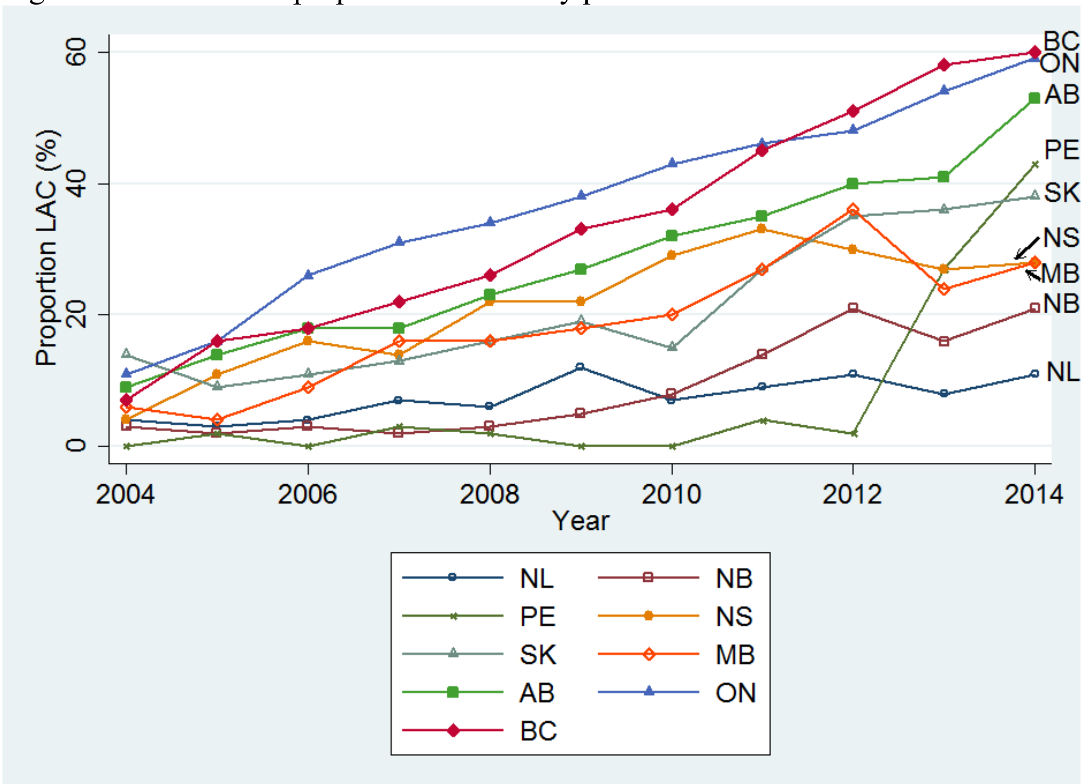


Figure 4.2.3 Proportional use of LAC by province, overall and 2014

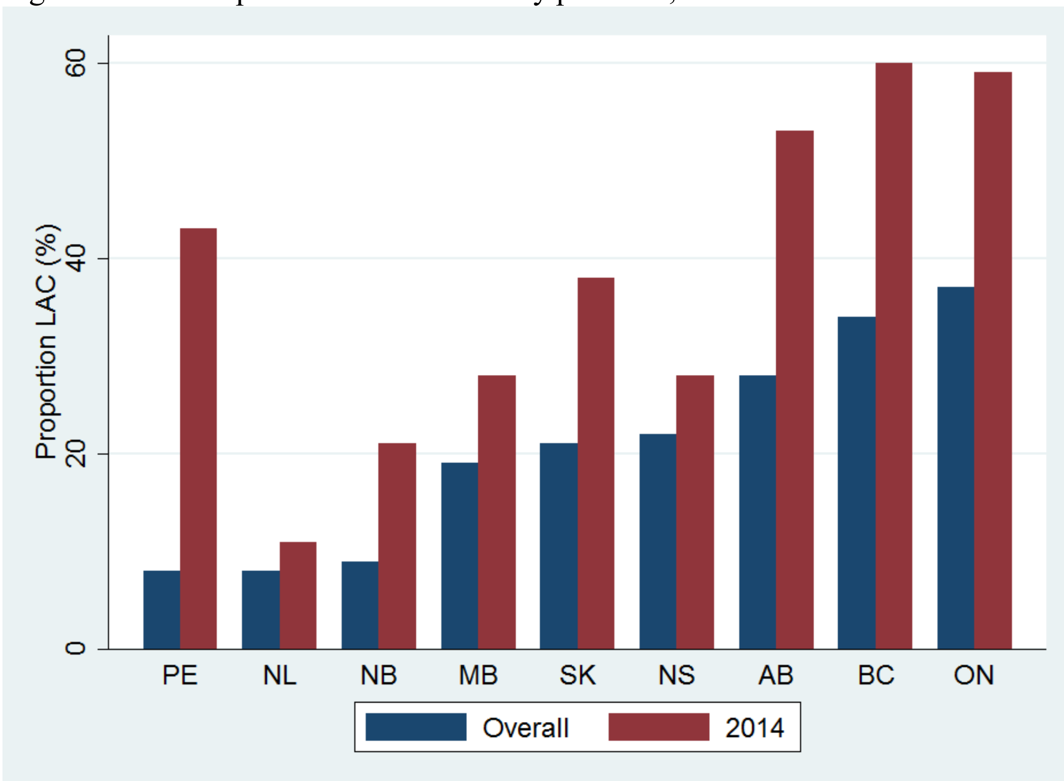


Figure 4.2.4 Annual number of open and laparoscopic colectomies: ON

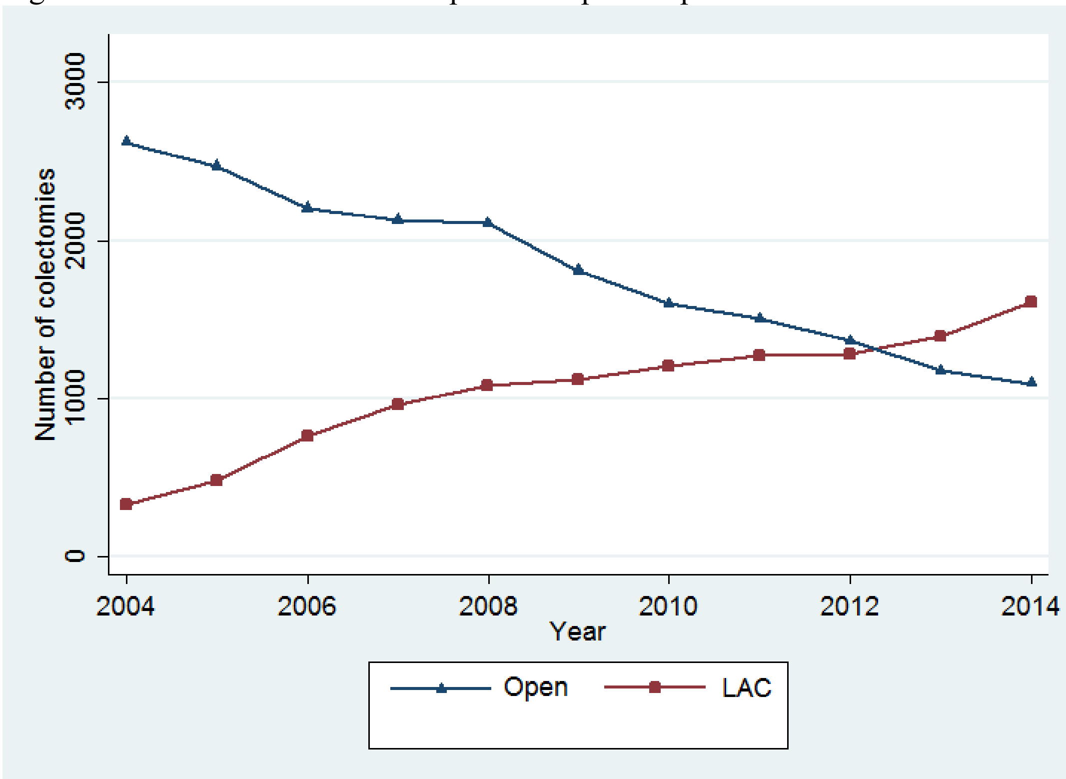


Figure 4.2.5 Annual proportional use of LAC: ON

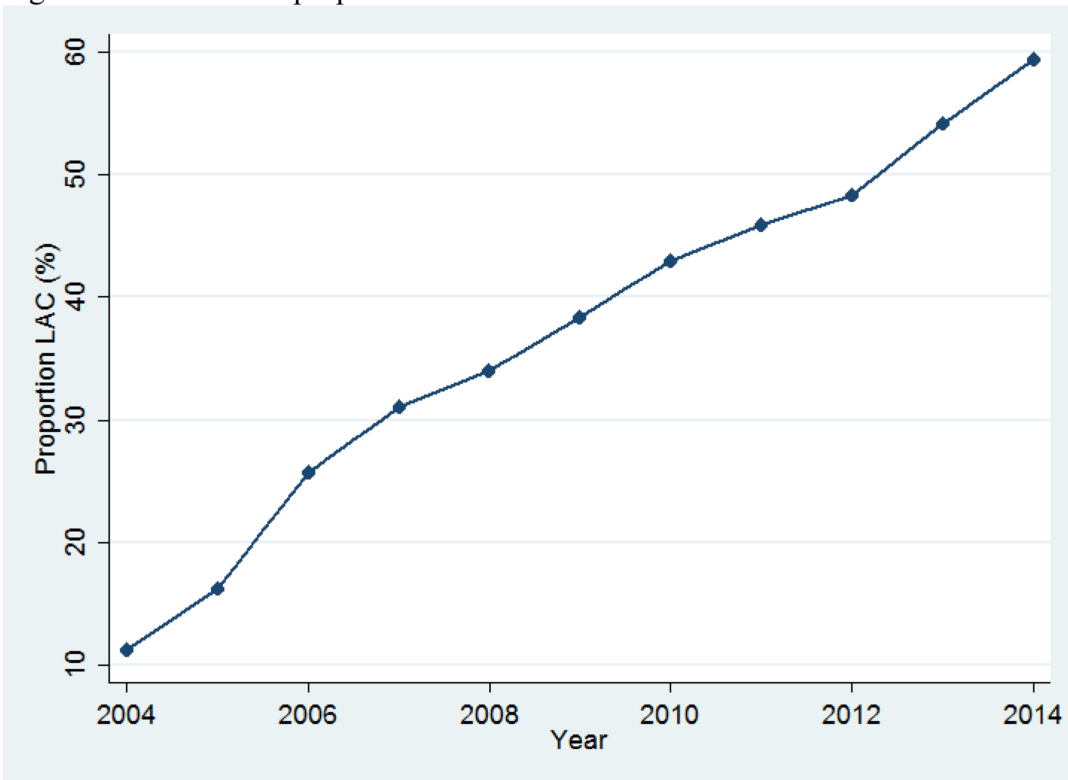


Figure 4.2.6 Annual number of open and laparoscopic colectomies: BC

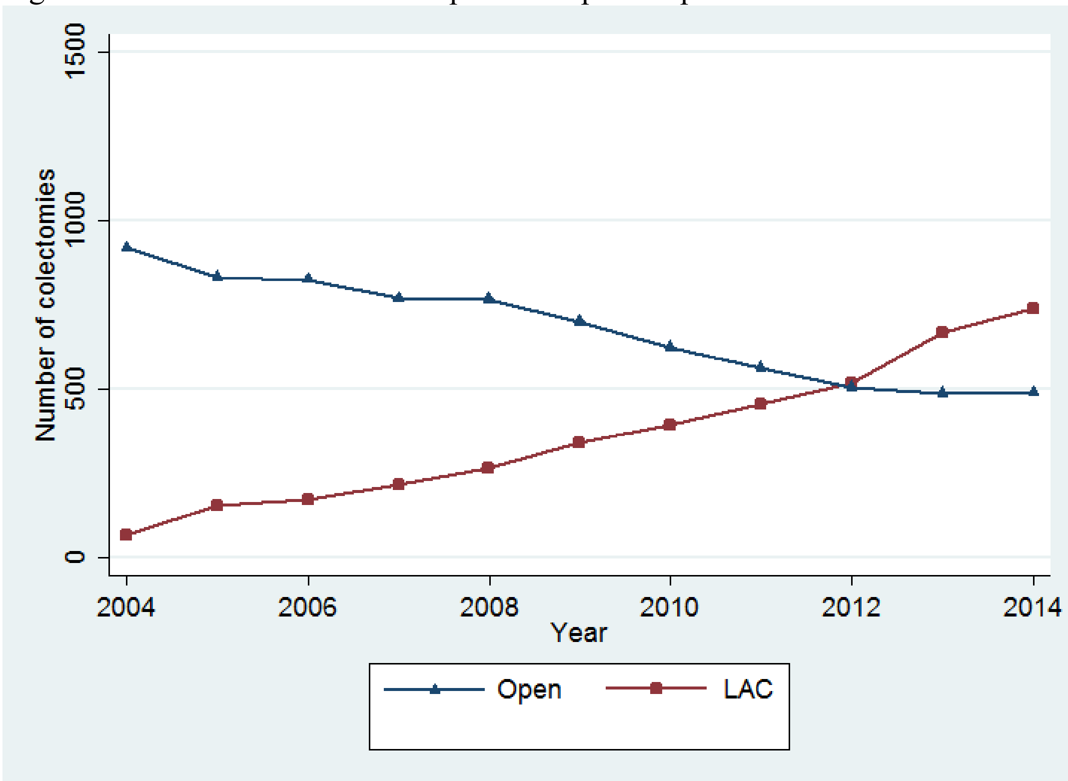


Figure 4.2.7 Annual proportional use of LAC: BC

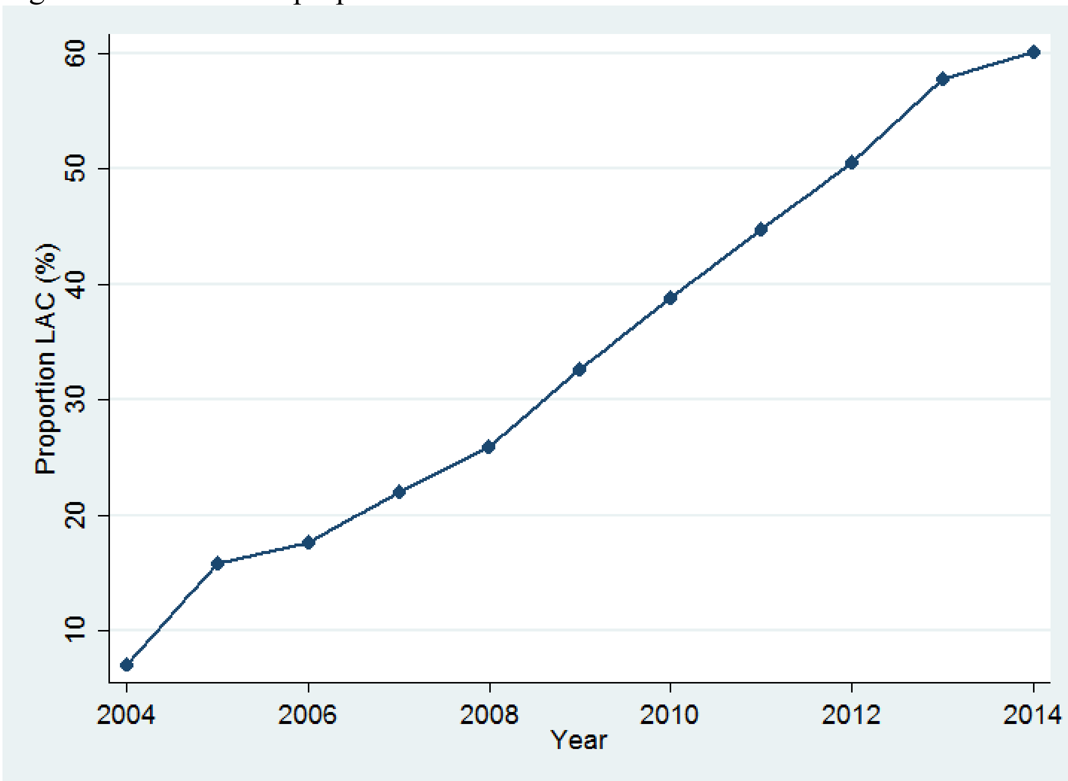


Figure 4.2.8 Annual number of open and laparoscopic colectomies: AB

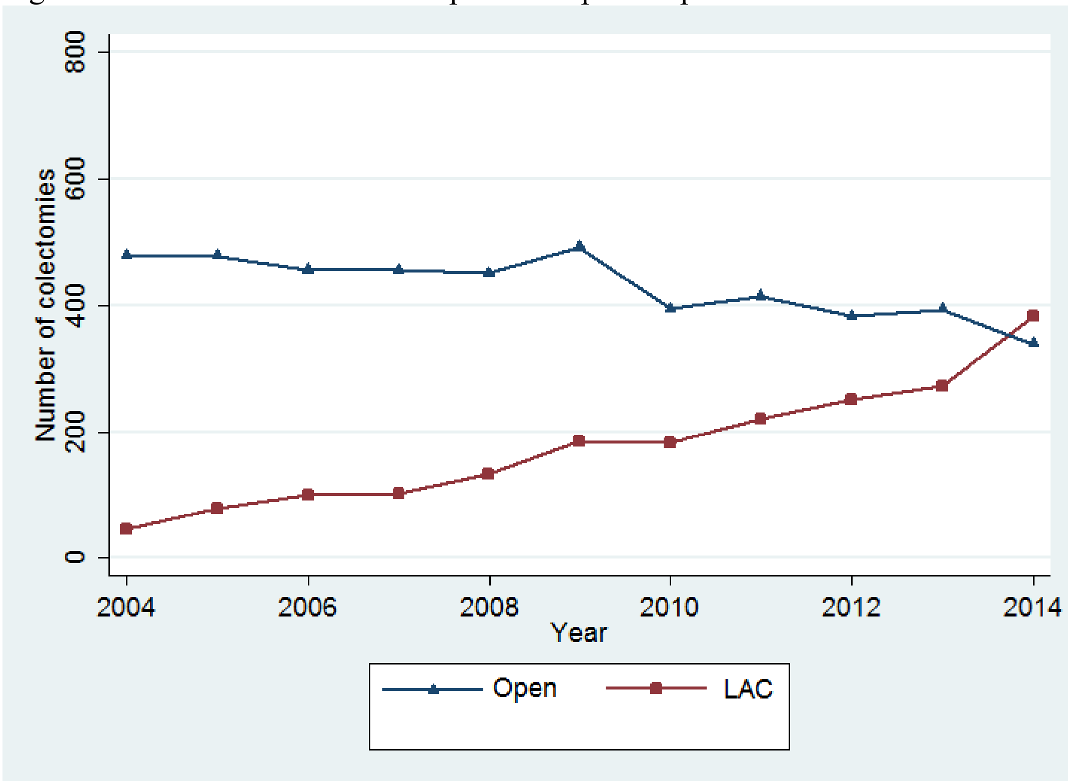


Figure 4.2.9 Annual proportional use of LAC: AB

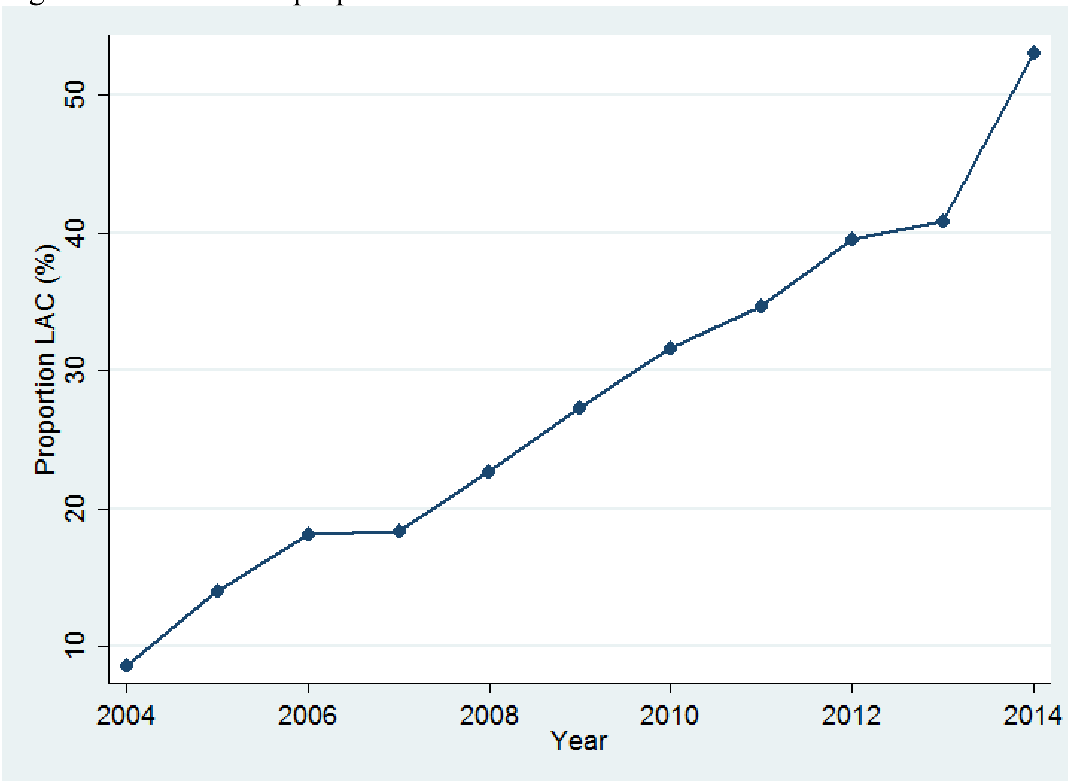


Figure 4.2.10   Annual number of open and laparoscopic colectomies: NL

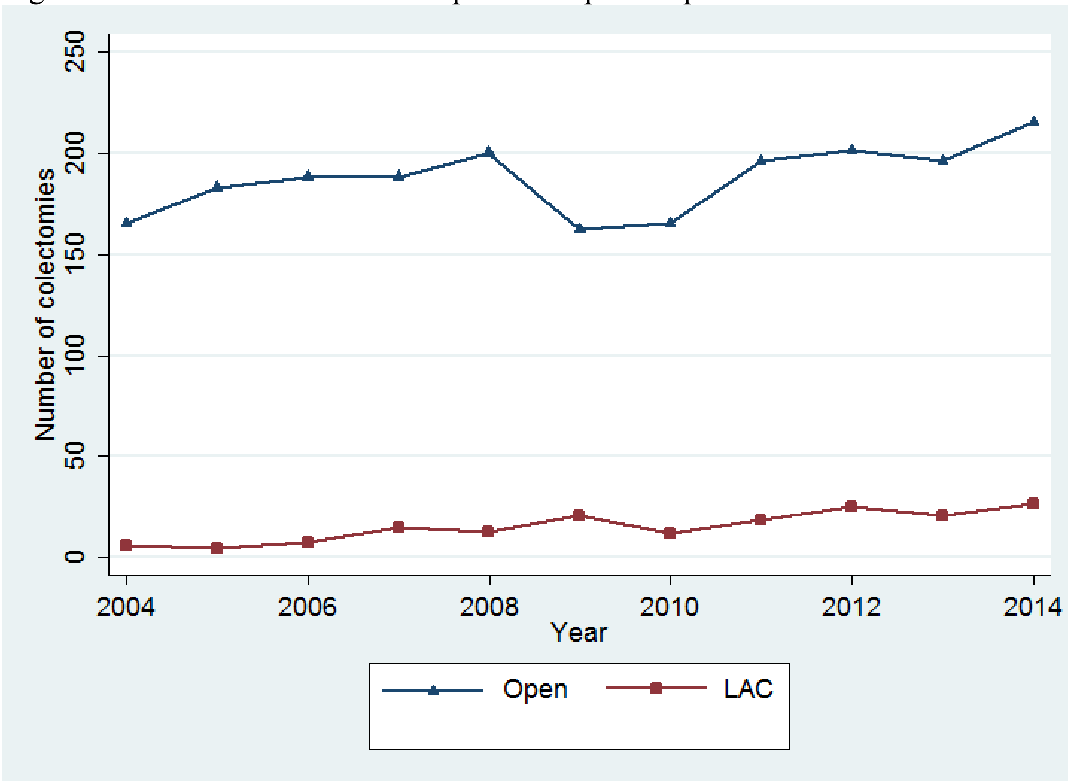


Figure 4.2.11   Annual proportional use of LAC: NL

Figure 4.2.12 Annual number of open and laparoscopic colectomies: NB

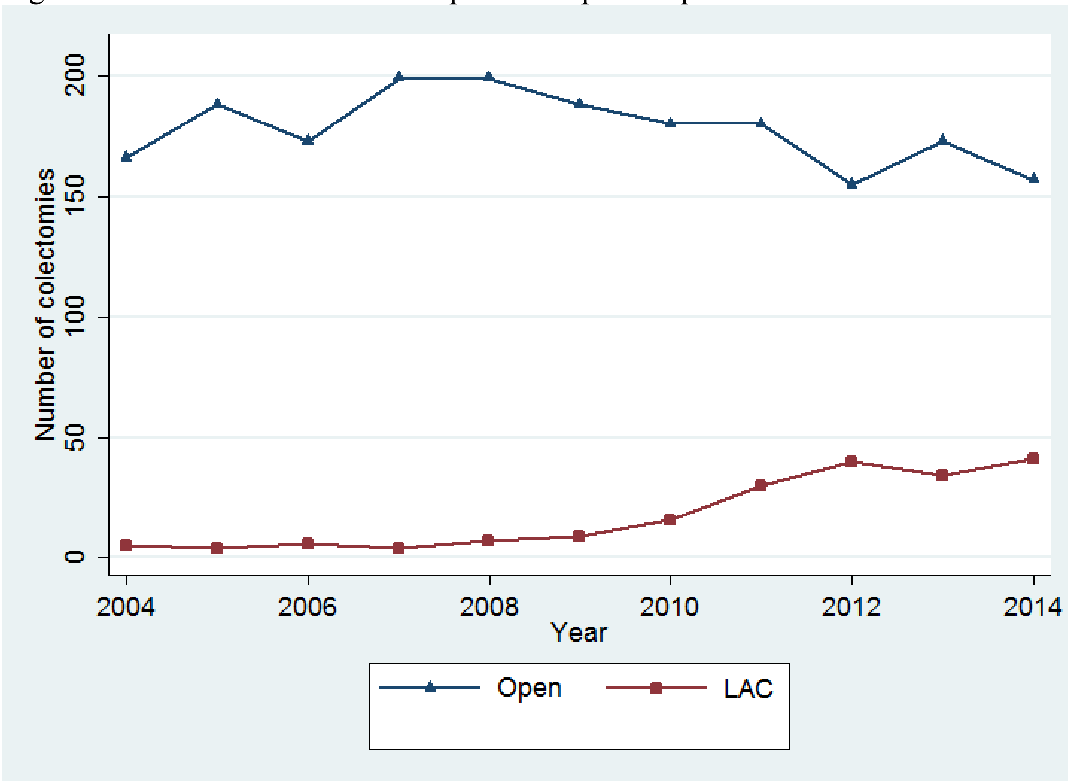


Figure 4.2.13 Annual proportional use of LAC: NB

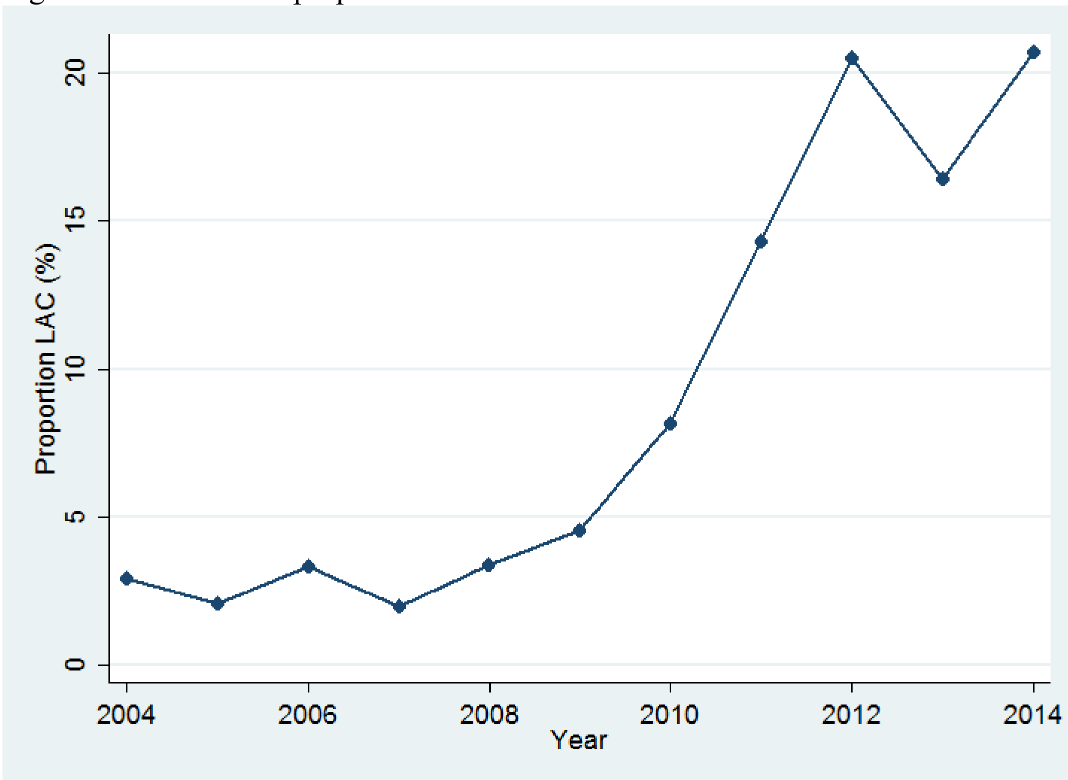


Figure 4.2.14 Annual number of open and laparoscopic colectomies: PE

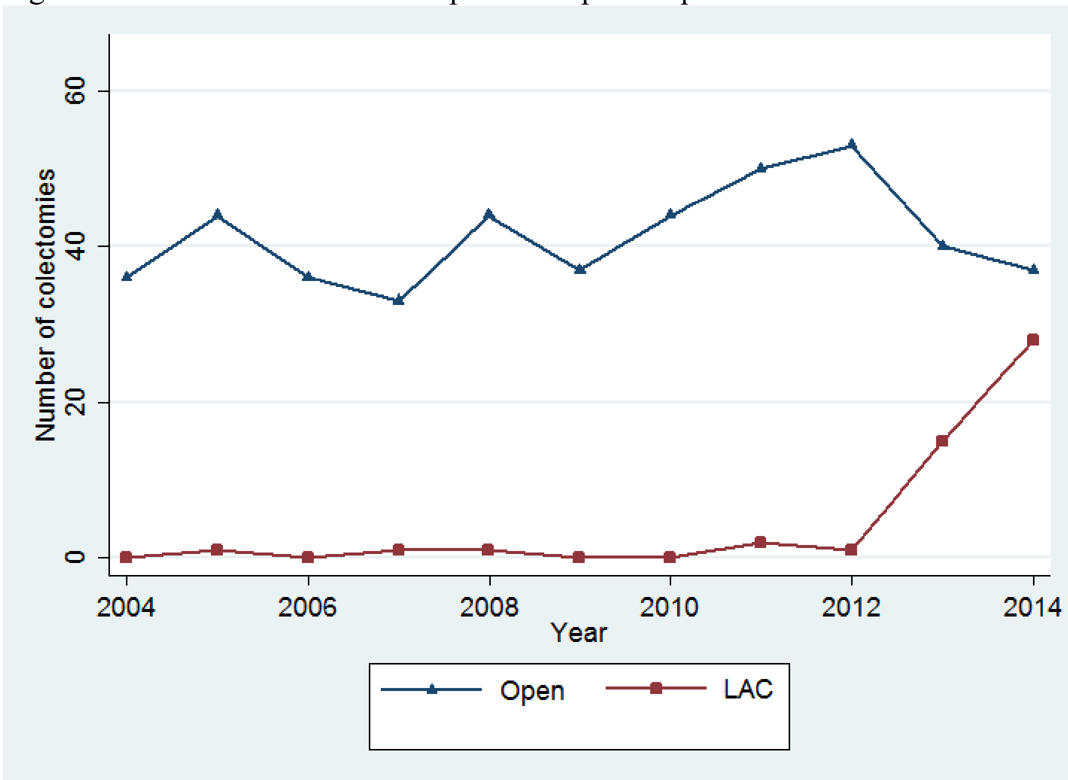


Figure 4.2.15 Annual proportional use of LAC: PE

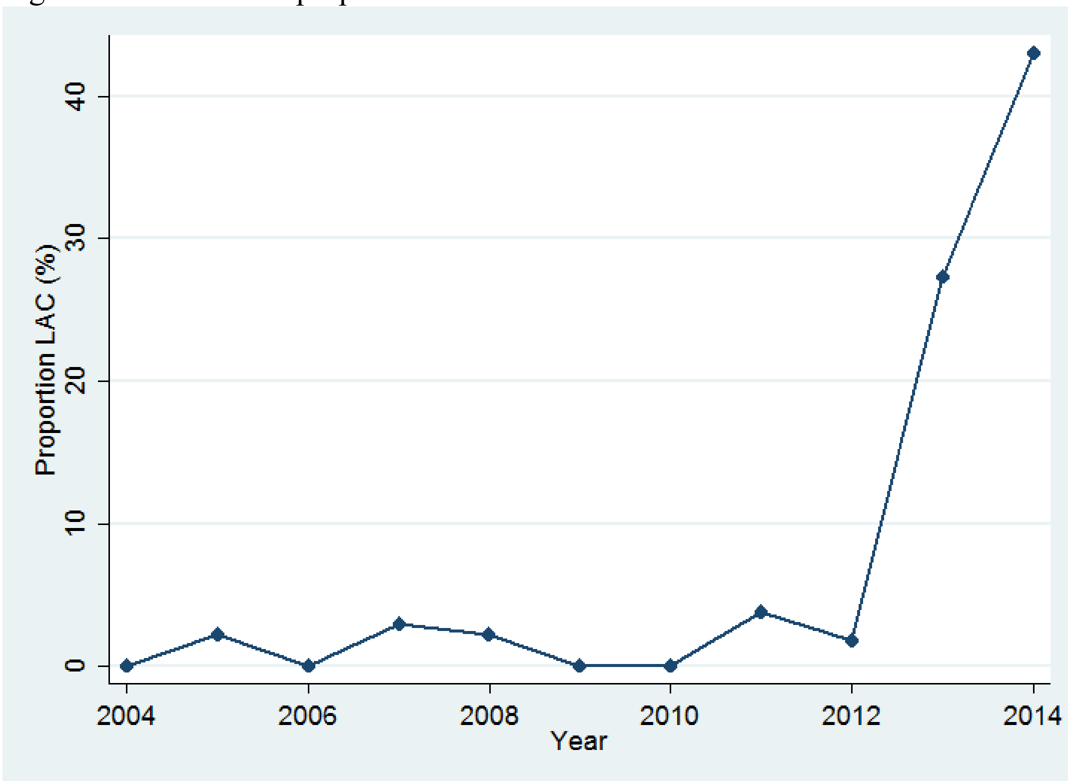


Figure 4.2.16 Annual number of open and laparoscopic colectomies: NS

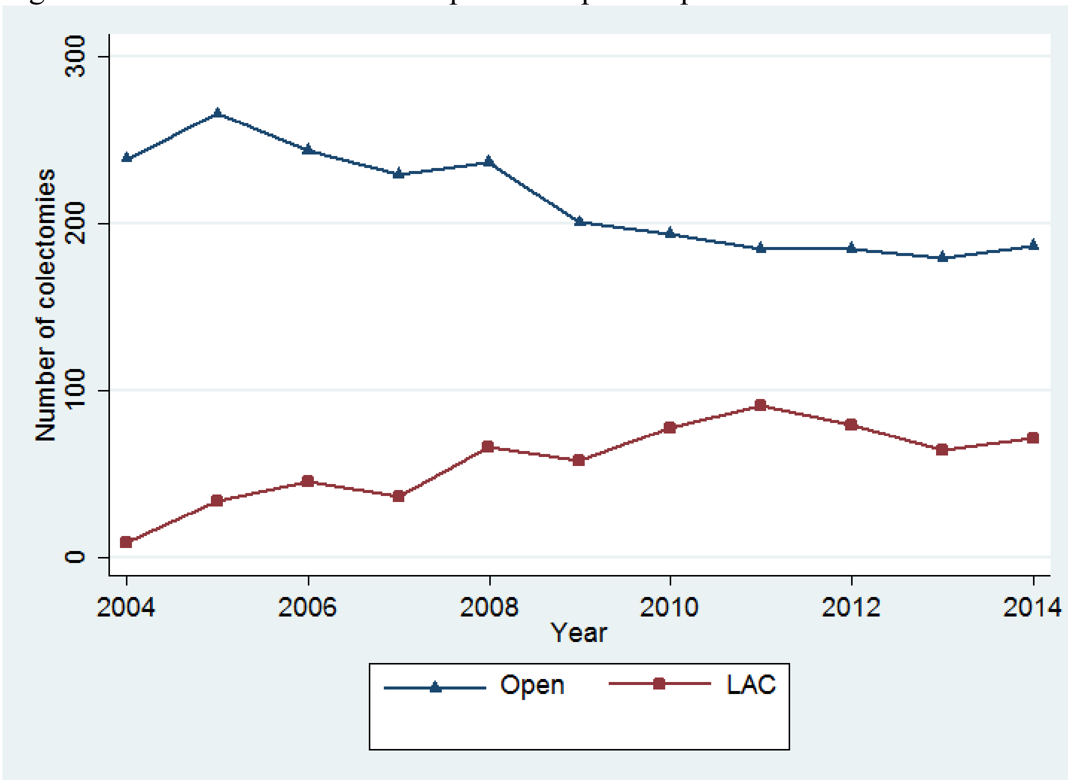


Figure 4.2.17 Annual proportional use of LAC: NS

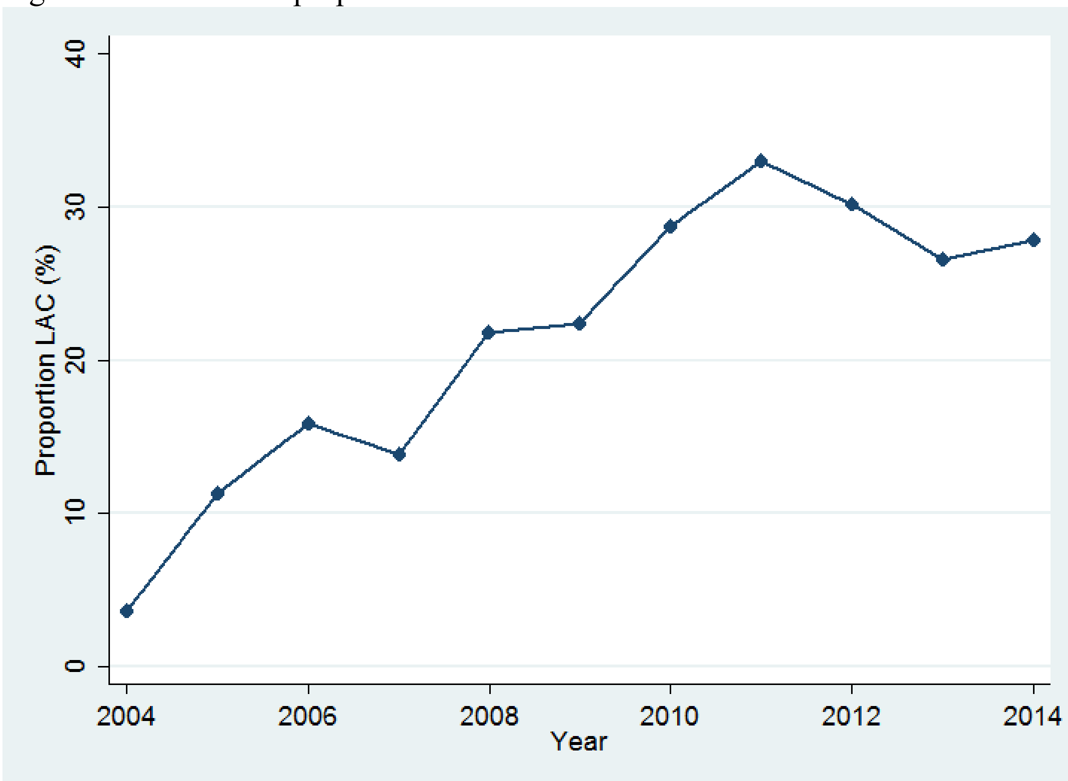


Figure 4.2.18 Annual number of open and laparoscopic colectomies: MB

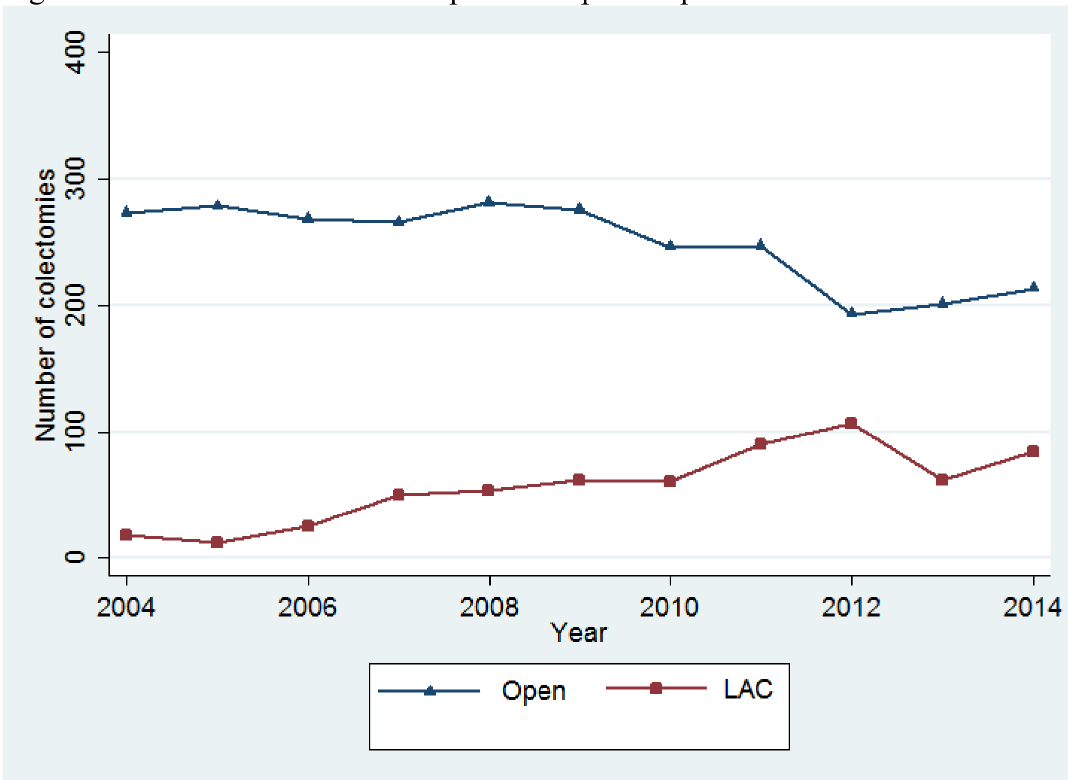


Figure 4.2.19 Annual proportional use of LAC: MB

Figure 4.2.20 Annual number of open and laparoscopic colectomies: SK

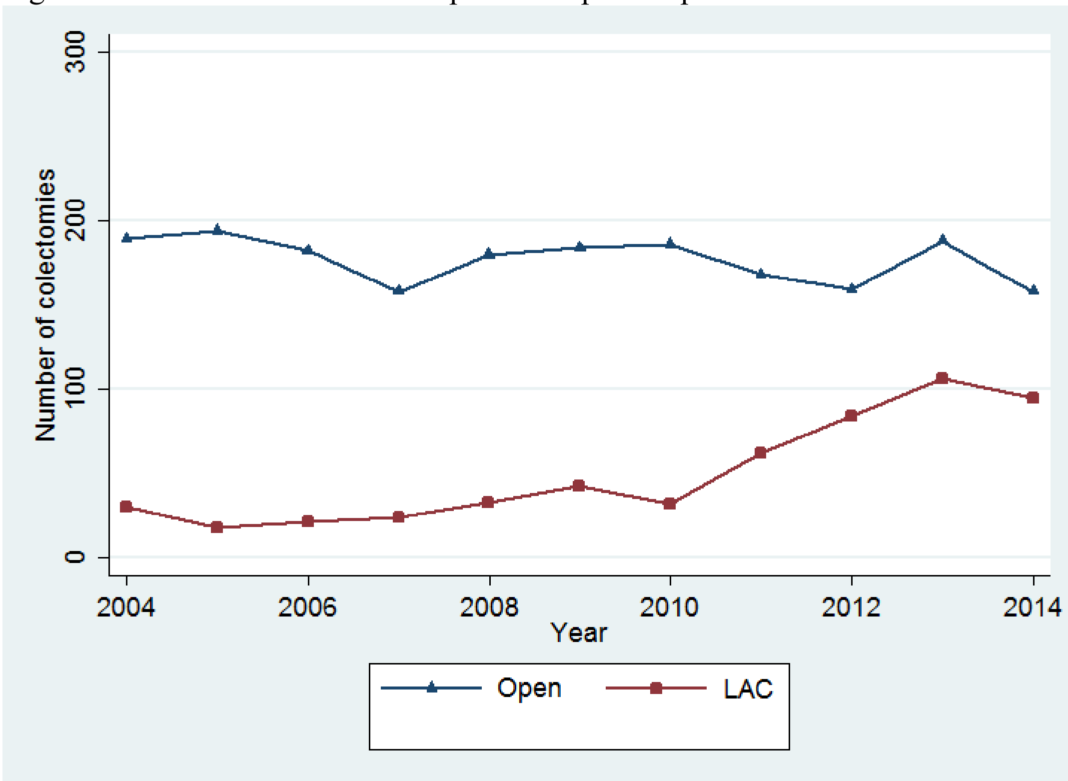


Figure 4.2.21   Annual proportional use of LAC: SK

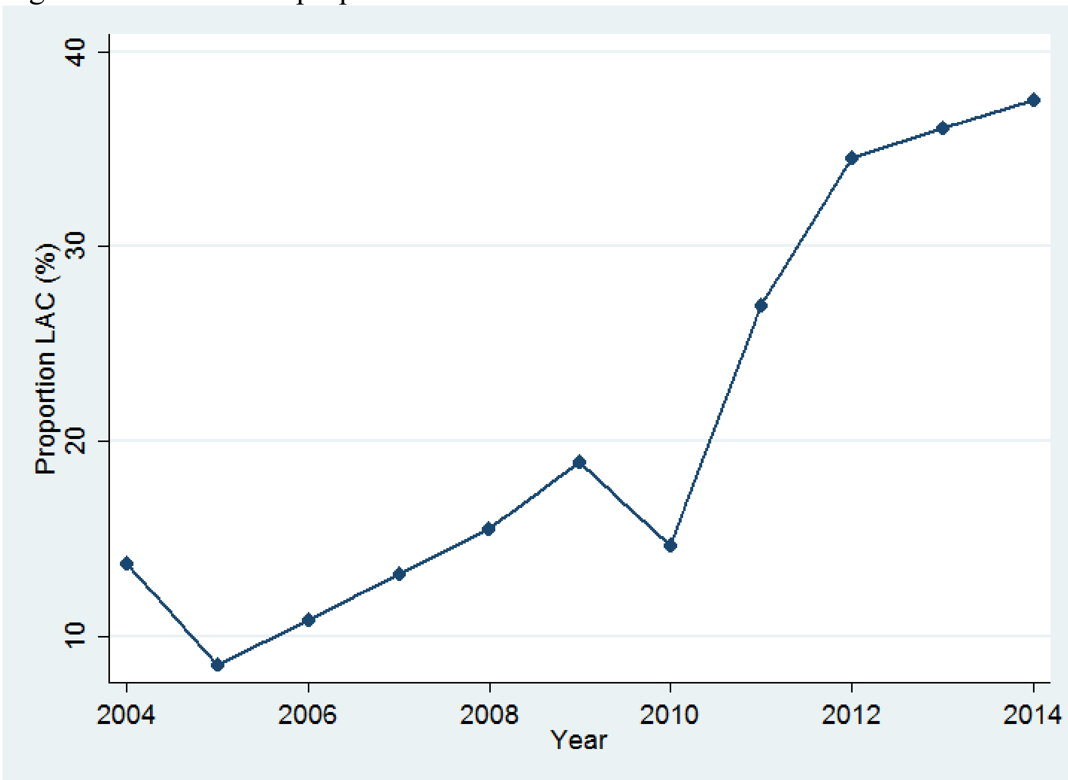


Figure 4.2.22 Average provincial proportion of LAC, east to west

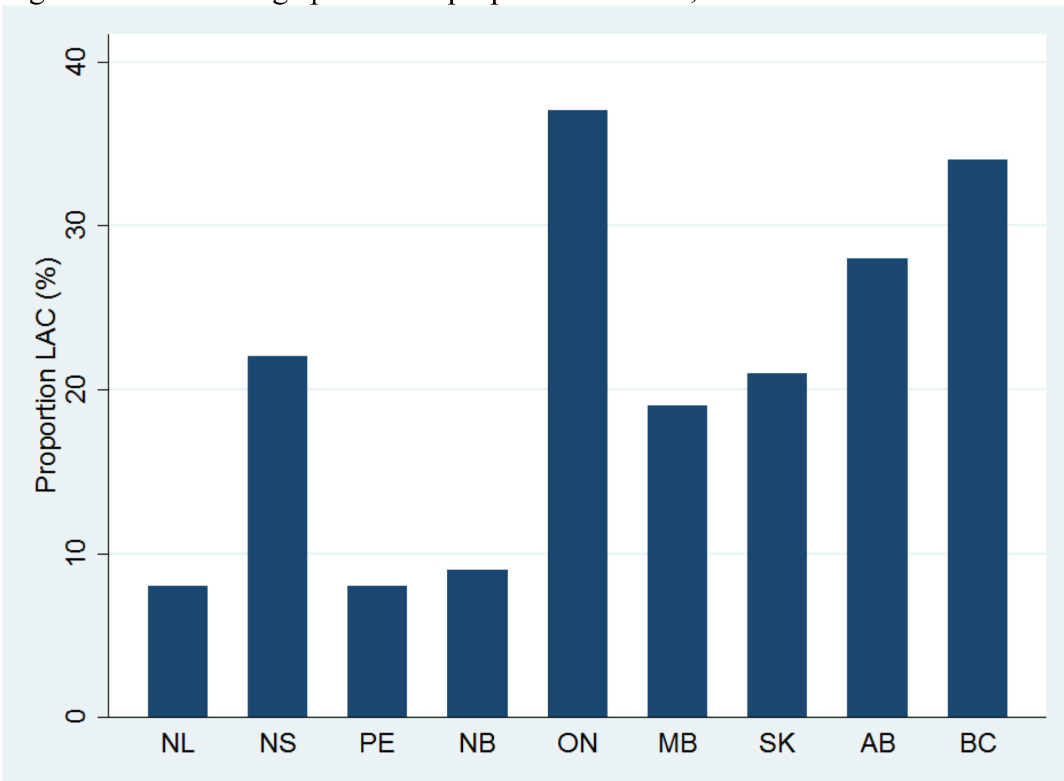


Figure 4.3.1 Annual proportion of LAC by residence

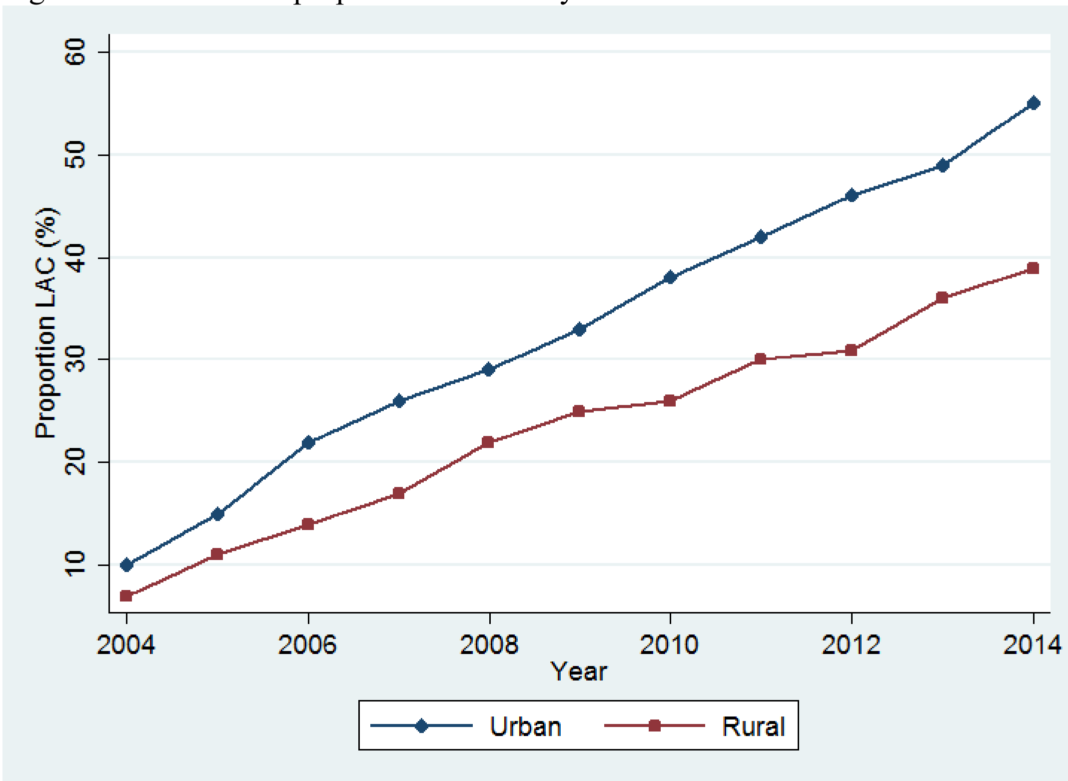


Figure 4.3.2 Annual proportion of LAC by age groups

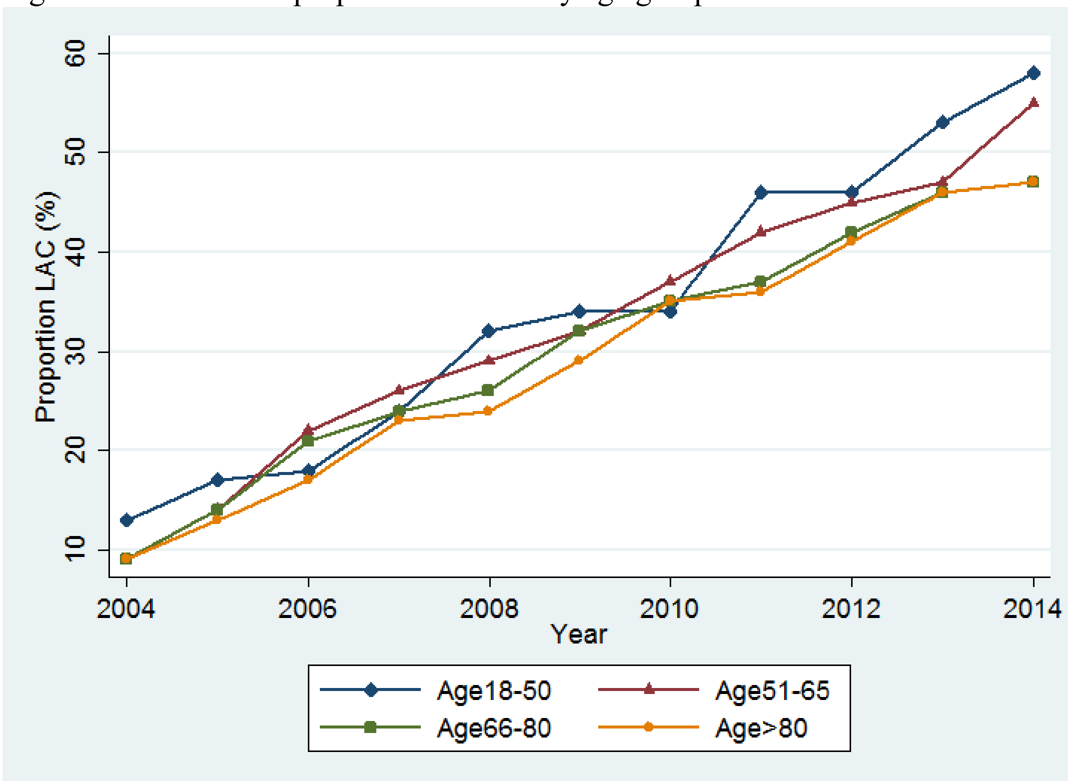


Figure 4.3.3   Annual proportion of LAC by sex

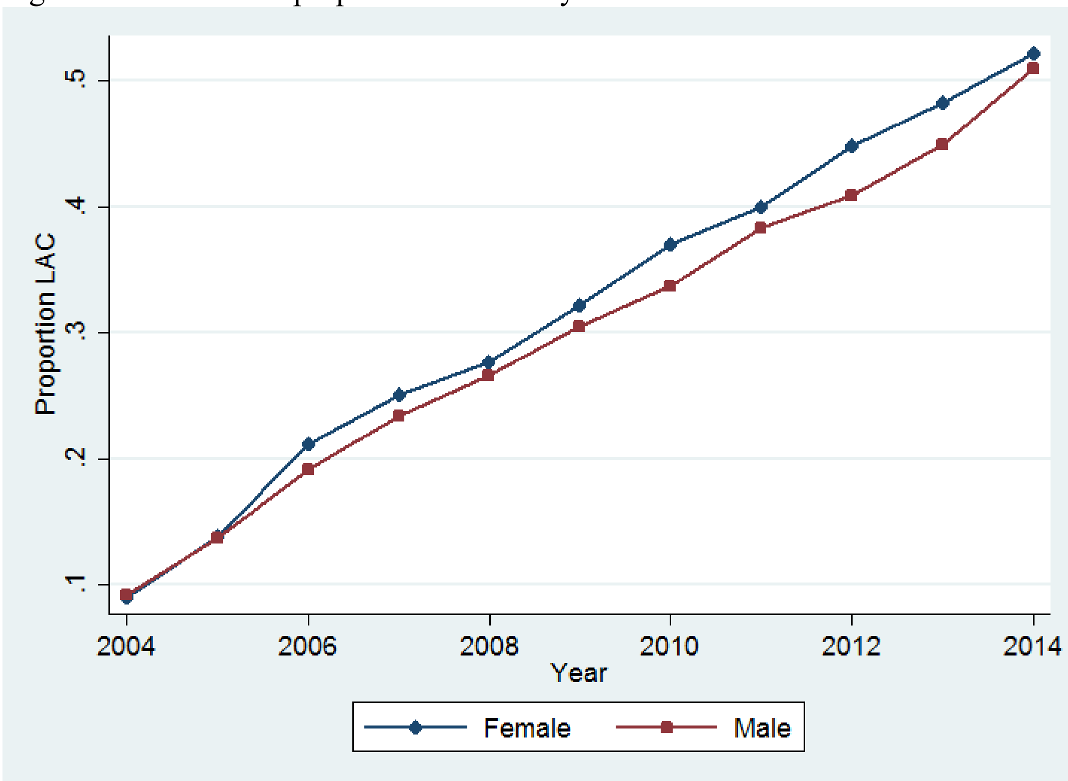


Figure 4.3.4a Crude and age-adjusted rate of LAC: Females

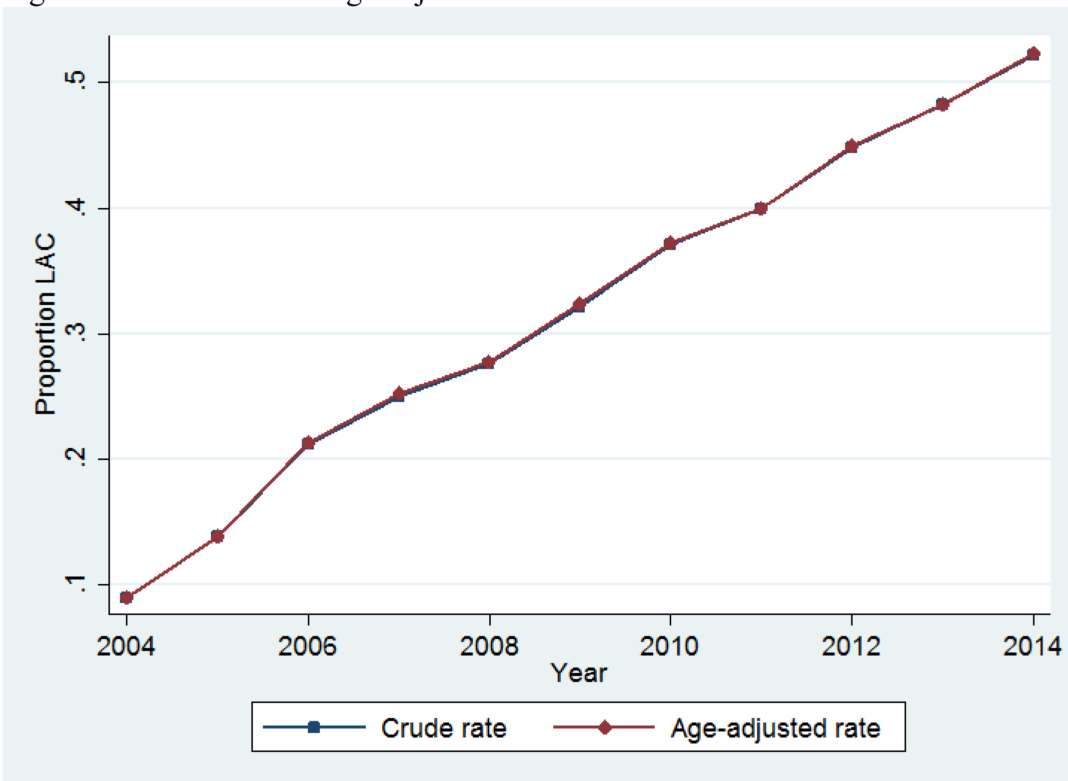


Figure 4.3.4b Crude and age-adjusted rate of LAC: Males

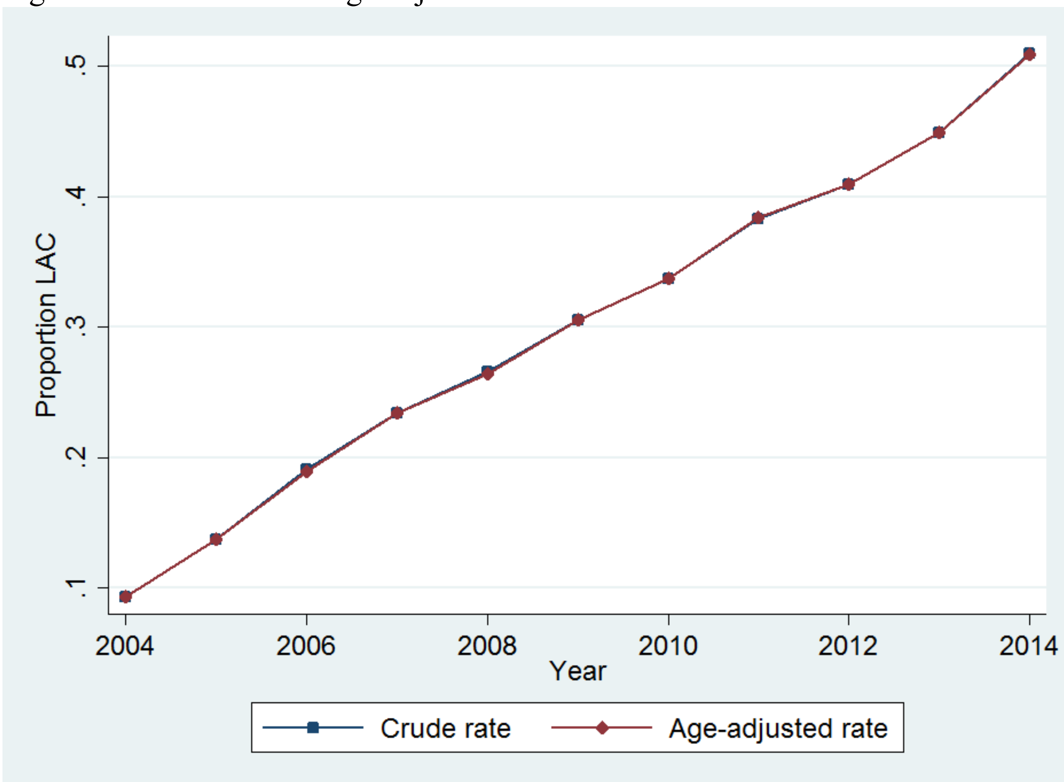


Figure 4.3.5 Annual proportion of LAC by Elixhauser comorbidity score

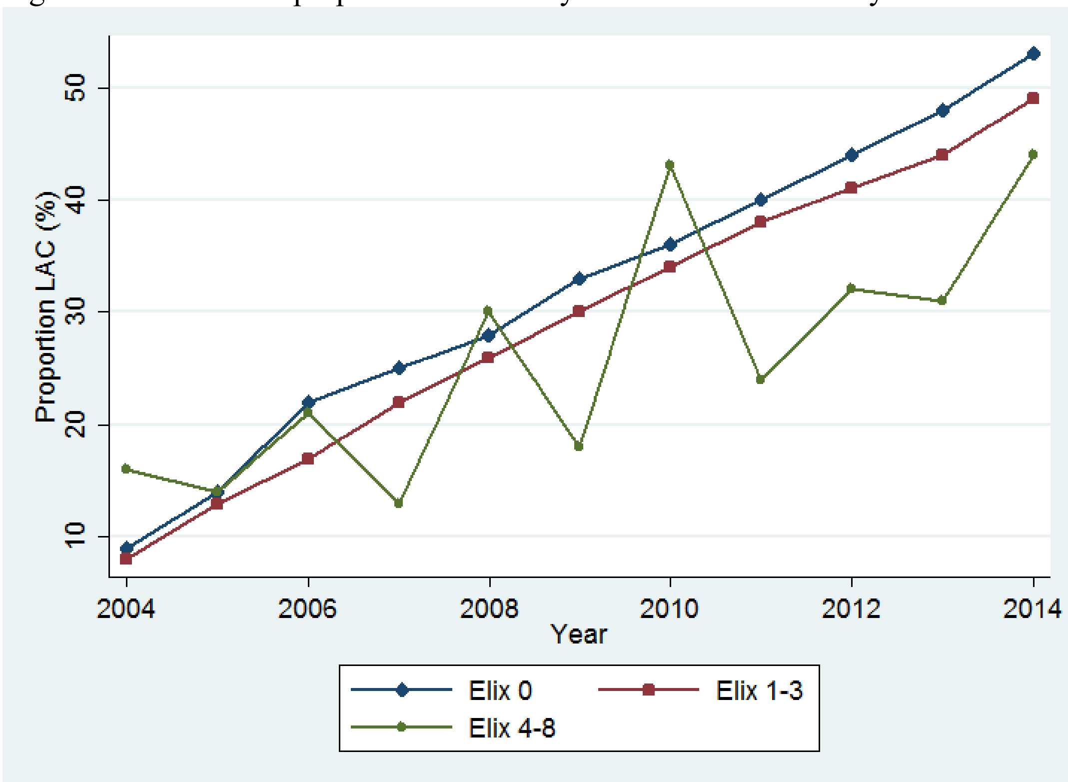


Figure 4.3.6 Annual proportion of LAC by segmental resection

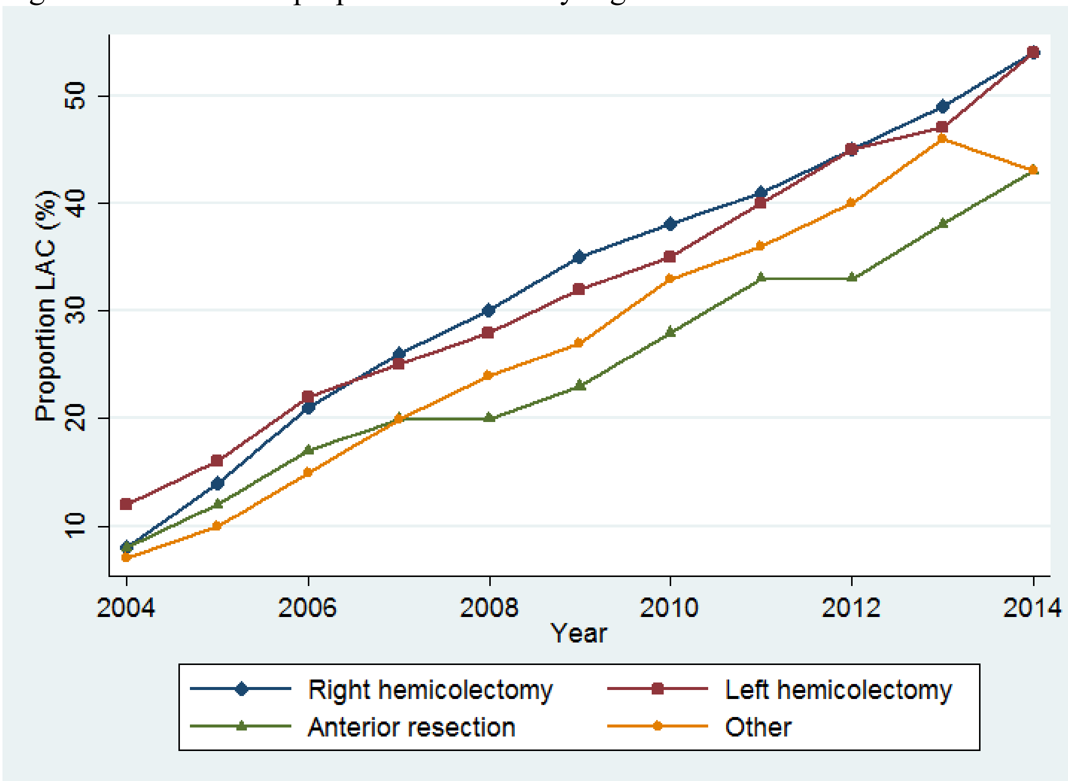


Figure 4.3.7 Annual proportion of LAC by surgeon volume

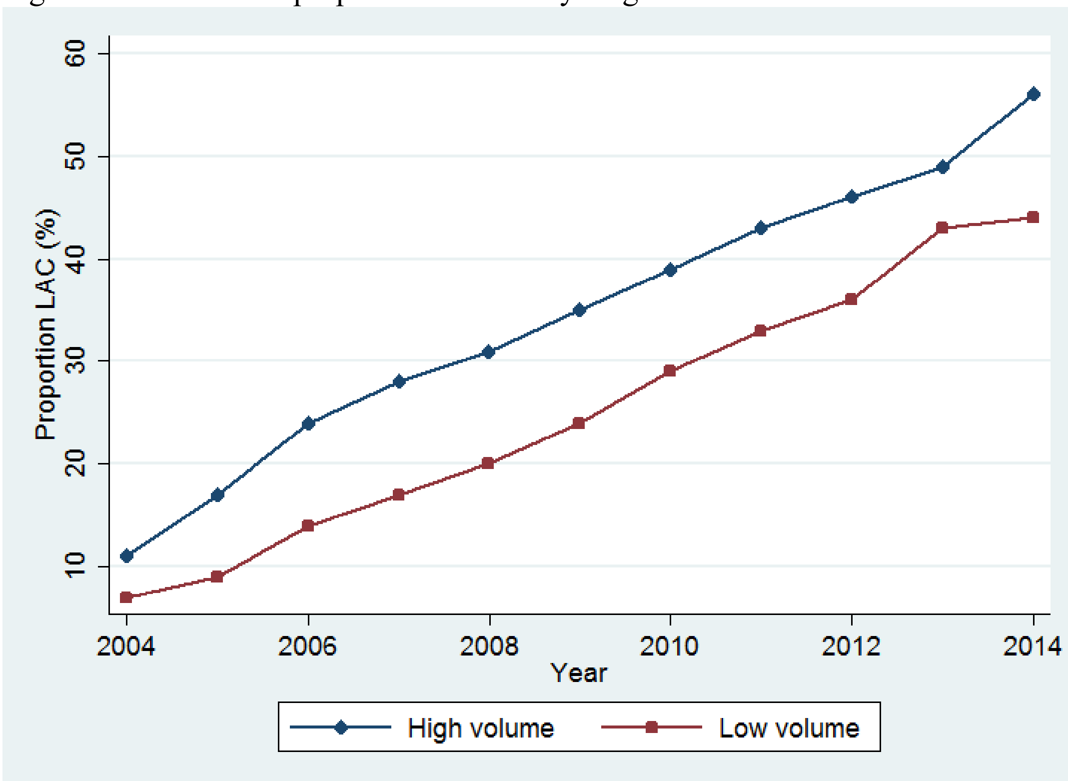


Figure 4.3.8 Annual proportion of LAC by hospital volume

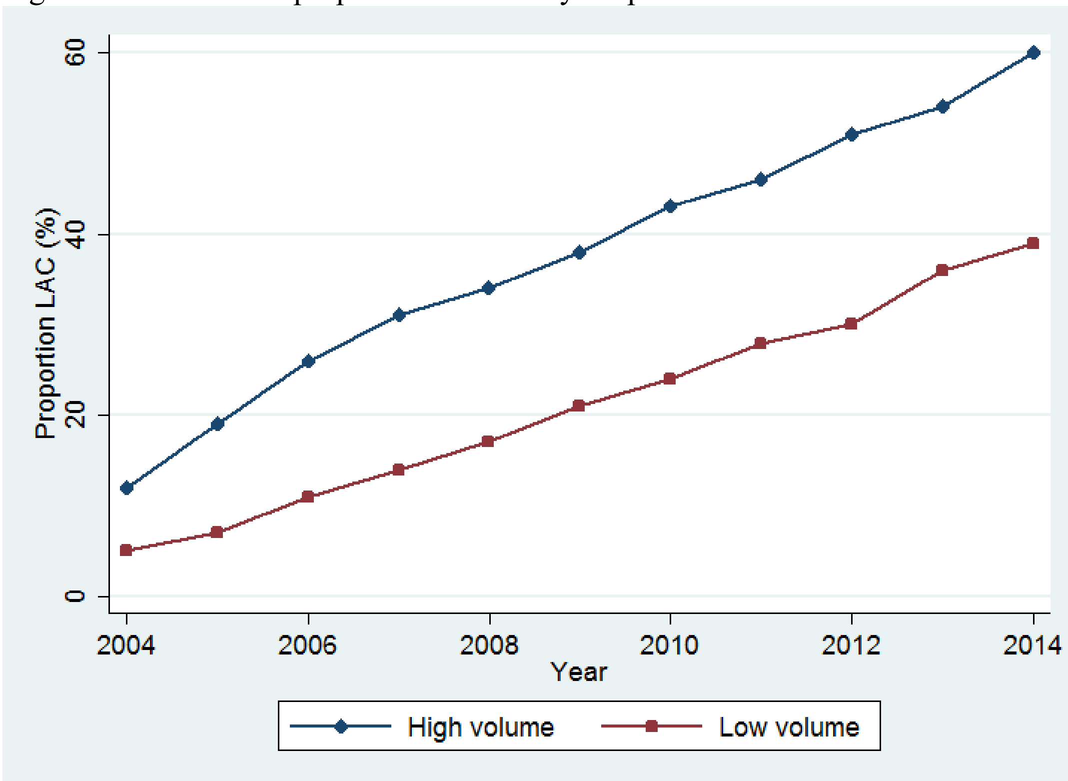
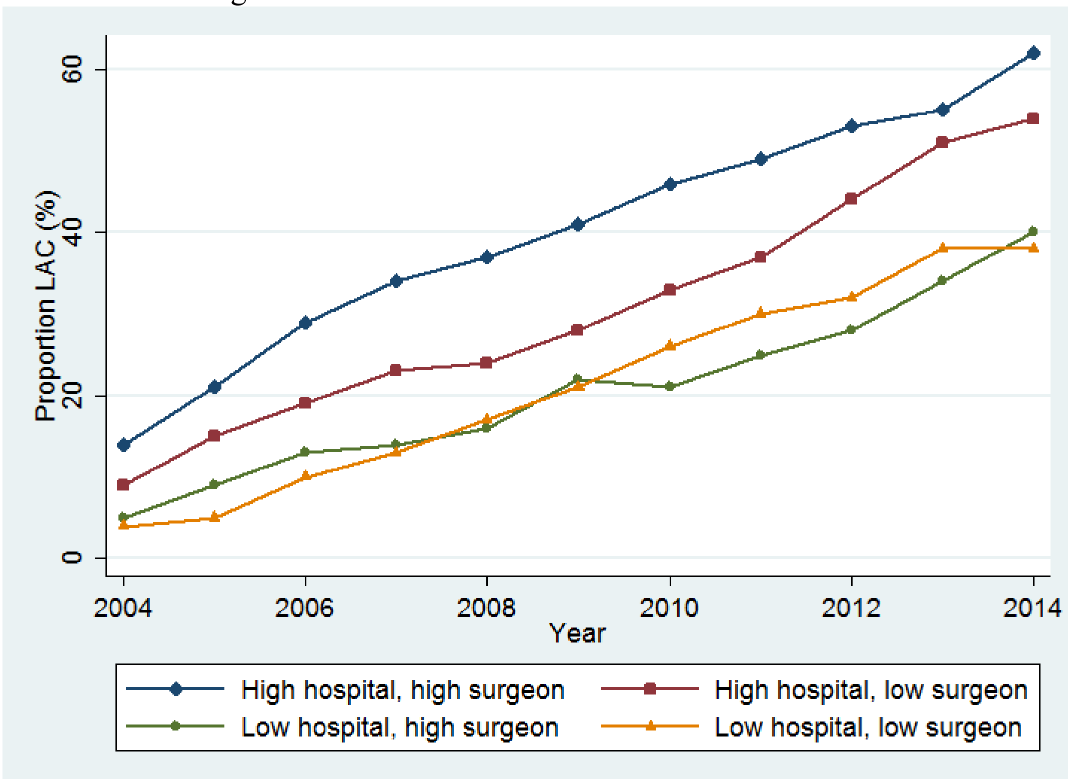


Figure 4.3.9 Annual proportion of LAC by combination of hospital and surgeon volume



CHAPTER 5 DISCUSSION

This study is the first to provide a national perspective on the proportional use and uptake of LAC in Canada for the decade following the COST trial. Overall, 31% of colectomies were performed laparoscopically. Use of laparoscopy increased from 9% in 2004 to 52% in 2014 in a relatively constant fashion at an average rate of 4% per year. The utilization of LAC in Canada is comparable with that of England and the Netherlands, where the proportion of LAC was 28% in 2008 and 44% in 2010 respectively, vs. 28% and 35% in Canada (107, 108). However, studies from the US reported the majority of colectomies for cancer being performed laparoscopically as early as 2009, reaching 54% in 2012, whilst Canada only passed the 50% mark in 2014 (24, 29). Although this study was not designed to predict future use, the national uptake of LAC did not show any signs of plateauing and can therefore be expected to continue to increase at least into the near future. However, given our current technology, there are patients who remain less suitable for a laparoscopic approach even in the hands of an expert laparoscopic surgeon working in a minimally invasive unit. These include patients who require complex resections for locally advanced cancer, who present as surgical emergencies with obstructing or perforating cancers, who underwent extensive prior abdominal surgeries and the morbidly obese (81, 113, 122). In 2017, a realistic goal for the proportion of LAC in Canada is therefore most likely in the range of 70-80%.

Year of surgery was the most significant predictor of LAC, with a patient requiring colectomy in 2014 being 9 times more likely to undergo a laparoscopic procedure compared to 2004. This reflects the advances in laparoscopic equipment, the cumulative experience of surgeons and perioperative teams and the positive effects of initiatives like the enhanced recovery after colorectal surgery pathway, that supports LAC by consolidating the efforts of the various disciplines involved in the surgical management of the colon cancer patient and by facilitating a coordinated team-based approach (16).

Regional variation in the use of LAC has been described. LAC rates ranged from

0-96% in hospitals in the Netherlands and from 0-67% across hospital referral regions in the US (61, 108). We found significant interprovincial variation in overall number of colectomies as well as in the proportional use and annual uptake of LAC. The majority of colectomies were performed in ON, as was the highest proportion of LAC (36%). Annual uptake followed a curve similar to that of Canada at a relatively constant rate of 5% per year, except for a steeper increase from 2005 to 2006. By 2014, proportional use of LAC reached 59% while uptake remained constant. The highest provincial LAC rate was 60% in BC in 2014. However, by the end of the study period uptake started to slow down, which may be an indication that utilization has neared its maximum. AB was the only other province in which laparoscopy became the preferred approach. With the exception of ON and NS, provincial use increased from east to west across Canada. The adoption rate was lowest in NL, where LAC odds was one seventh of what it was in ON. The challenges that laparoscopic surgery pose to older, established surgeons may have impeded the expansion of LAC in Atlantic Canada. In PE for example, although limited by the lowest overall colectomy volume (503), an increase in the proportion of LAC from 1.85% in 2012 to 26% in 2013 coincided with the successful recruitment of a recent graduate from the Dalhousie residency program.

Strategies to improve equity in access to LAC may need to be focused on provinces that had the lowest use and uptake over the entire study period, including NL, NB, NS, SK and MB. On the other hand, if the goal is to increase access by maximizing efficiency, use of LAC at the end of the study period should be considered and efforts directed toward provinces with the highest capacity to change, including ON, BC, AB and, owing to the radical increase in uptake since 2012, also PE.

In procedure sensitive care, where more than one acceptable treatment modality is available for a given condition, the most important determinants of variation are surgeon and patient preference (123). Surgeon preference is not only guided by training and experience but also by institutional culture and beliefs (124). Financial incentives may also play into decision making although its impact on the uptake of new technology has not been well studied (112).

Strategies for changing surgeon behavior may include re-affirming the safety and advantages of the laparoscopic approach, additional laparoscopic training and mentorship, development of practice and clinical care guidelines and placing emphasis on shared decision making (125). Newly qualified surgeons, who are more likely to incorporate LAC into their practices, can also be expected to bring about change in the culture of their surgical communities (98). Patients may also be empowered to make more informed decisions by decision guides, shared decision making tools and public awareness campaigns (125).

This study confirmed that patients older than 80 years were less likely to undergo LAC, compared to those aged 66-80 years. With an aging population the number of new cases of colon cancer is expected to rise. Early concerns regarding LAC in these patients have been refuted in the literature (126, 127). To the contrary, they stand to benefit more from the reduced surgical stress and consequent enhanced postoperative recovery (128, 129). It is therefore important that the safety and advantages of LAC in the geriatric patient be re-affirmed with surgeons.

As with older patients, there was initial concerns regarding the safety of LAC in patients with major medical comorbidities. However, the safety and feasibility as well as the benefits of LAC in terms of postoperative recovery have been confirmed in this patient group (78). The lower rate of LAC in more comorbid patients in our data is consistent with the literature (80, 81). The prevalence of chronic medical disease, including diabetes mellitus, hypertension, nonalcoholic steatohepatitis and pulmonary hypertension is increasing among younger patients, as is the incidence of colon cancer (9). It is therefore important to address the misconceptions around the use of LAC in patients with medical comorbidities.

In our study, the odds of undergoing LAC was related to the complexity of the segmental resection; patients who underwent right hemicolectomy were most likely to undergo LAC, followed by left hemicolectomy. The LAC odds was lowest for an anterior resection. For the more difficult segmental resections a larger number of cases are required to complete the learning curve (85). However, right hemicolectomy was the most common segmental resection performed in this study, and strategies focused on developing the skills of lower-volume surgeons to a level where they are comfortable performing a right hemicolectomy laparoscopically could potentially be most effective at enhancing population access to LAC.

This study found lower LAC odds in patients who live in rural communities. Rural patients are often of lower socio-economic status and have lower levels of education, both of which are associated with higher degrees of medical comorbidity and advanced or complicated disease at presentation (64). Smaller rural hospitals may be less likely to have modern laparoscopic equipment and surgeons who work in these communities are less likely to have the expertise to perform LAC (63). Although the universal healthcare system in Canada ensures equal access to care for patients with colon cancer, it does not imply equal access to advanced laparoscopic techniques. Therefore, socio-economic disparities in care may still exist for rural patients.

LAC odds was related to a surgeons' average annual overall volume of colectomies. To master the advanced laparoscopic techniques of LAC requires between 30 and 70 cases and, with only 25% of surgeons performing on average more than 7 colectomies per year, many may find it difficult to accumulate enough colectomies in an adequate time frame to complete the learning curve and to maintain their skills (88). Learning the technique can be especially challenging for practicing surgeons who may not have access to an experienced mentor and who work in community hospitals where operating room time comes at a premium (93). In order to advance LAC, surgeons may have to change their practice to ensure adequate volume for those who perform colon cancer surgery. This may be achieved by directing all colon cancer cases to 1 or 2 surgeons within the group, who have a special interest in advanced laparoscopy. With the current limited opportunities for employment for surgeons in Canada, it may become easier to recruit fellowship-trained laparoscopic and/or colorectal surgeons to smaller community hospitals where they may serve as mentors to surgical colleagues or be designated to perform all colon cancer surgeries in their institution.

In this study, hospital volume of colectomies was a strong predictor of LAC. Low-volume surgeons working in high-volume hospitals were more likely to perform LAC than high-volume surgeons in low-volume hospitals. This may partly be due to lack of advanced laparoscopic equipment in smaller hospitals. However, the importance of an experienced, multidisciplinary team that includes all aspects of perioperative management is essential to realizing the benefits of LAC in terms of enhanced postoperative recovery, and is well accepted as integral to a successful laparoscopic colorectal unit (101). Practical implications may be that management of colon cancer surgery be consolidated in selected hospitals with existing expertise or the capacity to develop it. An example from our own province is 2 fellowship-trained laparoscopic surgeons and an integrated laparoscopic suite in St. Martha's hospital in Antigonish that can also provide surgical care for colon cancer patients from neighbouring Pictou county, where the Aberdeen hospital does not have the same level of laparoscopic expertise.

5.1 Limitations

This study faces limitations inherent to a retrospective analysis of administrative data. The use of modifier codes to identify LAC is prone to underestimation of its use (105). Although the unique CCI codes for laparoscopy used in this study should mitigate this, it has not been validated with clinical datasources.

It is possible that additional potential clinical confounders were not included in our analyses. For example, obesity is not captured in the CIHI DAD. Although obesity is an important determinant of surgical approach and postoperative outcomes (130, 131), we were not able to consider it in our study. Similarly, neither stage of colon cancer nor history of prior abdominal surgeries are captured in data sources used for our study; both of which could have been important in the selection of surgical approach, especially during the earlier years of the study period.

Our data sources also limited our ability to fully examine several specific clinical issues. We were not able to identify reoperations for recurrent cancers. However, these represent a small number of colectomies that remain fairly stable over time so it is not expected to have had a significant impact on our primary outcome. Our definition of segmental resections relied on location of tumor according to ICD-10-CA code which could have resulted in a degree of misclassification: We included transverse colon tumors under right hemicolectomy, however, a small number of these may have been closer to the splenic flexure and therefore have been resected by left hemicolectomy. Similarly, some more distal sigmoid cancers may have required anterior resection instead of left hemicolectomy. We were not able to identify laparoscopic converted to open, hand assisted or single-incision surgeries, therefore LAC should be interpreted as colectomies at least partially approached in a minimally invasive manner.

Unfortunately, Quebec was not included in this pan-Canadian study as its health facilities are not required to report data for capture in the DAD. Findings from this study may therefore not be generalizable to Quebec.

Finally, our study did not evaluate strategies aimed at increasing the use of LAC. Potential strategies and targets of initiatives to increase LAC may be provider centered and include education on the advantages of LAC, additional training in advanced laparoscopic techniques, establishment of mentorship programs for practicing surgeons, recruitment of surgeons comfortable with LAC and development of practice and clinical care guidelines for modern management of colon cancer. Patient centered strategies may include providing tools and guides to allow for informed shared decision making and raising public awareness on the safety and benefits of LAC.

5.2 CONCLUSION

This study described the national and provincial use and year over year uptake of LAC in Canada from April 01, 2004 to March 31, 2015 and estimated the impact of patient (age, sex, degree of medical comorbidities, segmental resection), demographic (rural/urban residence, year of study, province) and system (average annual surgeon and hospital volume of colectomy) factors on the use of LAC. Overall, 31% of colectomies for cancer was performed laparoscopically, while the proportional use increased from 9% to 52% per year. The utilization and uptake of LAC in Canada compares well to that of the US, England and the Netherlands. However, there exists significant interprovincial variation with a greater and more marked increase in use of LAC moving from east to west across Canada. Several demographic, patient and system variables were found to be associated with the use of LAC, including provincial uptake, urban residence, year of surgery, sex, age, degree of medical comorbidities, segment of colon resected and average annual surgeon and hospital volume of colectomies. A full quantitative understanding of the use of LAC in Canada is foundational to designing strategies aimed at increasing its use and evaluating the impact of such strategies.

5.3 FUTURE RESEARCH

The effectiveness of LAC in terms of enhanced postoperative recovery has not been studied in Canada. We plan a follow-up study, using the same dataset, to compare short-term outcomes including LOS, in-hospital mortality and discharge disposition between LAC and open colectomy.

REFERENCES

1. Canadian Cancer Society. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2014. Toronto, ON: Canadian Cancer Society; 2014.

2. Hawk ET, Limburg PJ, Viner JL. Epidemiology and prevention of colorectal cancer. Surg Clin North Am. 2002 Oct;82(5):905-41.

3. Colorectal cancer: Canadian Cancer Society. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/colorectal/statistics/?region=on.

4. Statistics Canada. Life Tables, Canada, Provinces and Territories, 2007/2009 (Catalogue no. 84-537). Ottawa: Minister of Industry; 2013.

5. Surveillance, Epidemiology, and End Results (SEER) Program SEER*Stat Database: Mortality – All COD, Aggregated With State, Total U.S. (1969-2010), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2013. Underlying mortality data provided by NCHS 2013.

6. Surveillance, Epidemiology and End Results (SEER) Program SEER*Stat Database: NAACCR Incidence – CiNA Analytic File, 1995- 2010, for Expanded Races, Custom File With County, ACS Facts and Figures projection Project, North American Association of Central Cancer Registries, 2013.

7. American Cancer Society. Colorectal Cancer Facts & Figures 2014-2016. Atlanta: American Cancer Society, 2014.

8. Edwards BK, Ward E, Kohler BA, Eheman C, Zauber AG, Anderson RN, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Cancer. 2010 Feb 1;116(3):544-73.

9. Siegel RL, Jemal A, Ward EM. Increase in incidence of colorectal cancer among young men and women in the United States. Cancer Epidemiol Biomarkers Prev. 2009 Jun;18(6):1695-8.

10. Eddy DM. Screening for colorectal cancer. Ann Intern Med. 1990 Sep 1;113(5):373-84.

11. European Colorectal Cancer Screening Guidelines Working Group, von Karsa L, Patnick J, Segnan N, Atkin W, Halloran S, et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis: overview and introduction to the full supplement publication. Endoscopy. 2013;45(1):51-9.

12. Lin JS, Piper MA, Perdue LA, Rutter CM, Webber EM, O'Connor E, et al. Screening for Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016 Jun 21;315(23):2576-94.

13. Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM, et al. American College of Gastroenterology guidelines for colorectal cancer screening 2009. Am J Gastroenterol. 2009 Mar;104(3):739-50.

14. Surgery for colorectal cancer: Canadian Cancer Society [cited October, 2016]. Available from: https://www.cancer.ca/en/cancer-information/cancer-type/colorectal/treatment/surgery/?region=on.

15. Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). Surg Laparosc Endosc. 1991 Sep;1(3):144-50.

16. Delaney CP, Brady K, Woconish D, Parmar SP, Champagne BJ. Towards optimizing perioperative colorectal care: outcomes for 1,000 consecutive laparoscopic colon procedures using enhanced recovery pathways. Am J Surg. 2012 Mar;203(3):353,5; discussion 355-6.

17. Feroci F, Kroning KC, Lenzi E, Moraldi L, Cantafio S, Scatizzi M. Laparoscopy within a fast-track program enhances the short-term results after elective surgery for resectable colorectal cancer. Surg Endosc. 2011 Sep;25(9):2919-25.

18. Lacy AM, Garcia-Valdecasas JC, Delgado S, Castells A, Taura P, Pique JM, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet. 2002 Jun 29;359(9325):2224-9.

19. Laparoscopically assisted colectomy is as safe and effective as open colectomy in people with colon cancer Abstracted from: Nelson H, Sargent D, Wieand HS, et al; for the Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004; 350: 2050-2059. Cancer Treat Rev. 2004 Dec;30(8):707-9.

20. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet. 2005 May 14-20;365(9472):1718-26.

21. Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol. 2005 Jul;6(7):477-84.

22. Kuhry E, Schwenk WF, Gaupset R, Romild U, Bonjer HJ. Long-term results of laparoscopic colorectal cancer resection. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD003432. doi(2):CD003432.

23. Bardakcioglu O, Khan A, Aldridge C, Chen J. Growth of laparoscopic colectomy in the United States: analysis of regional and socioeconomic factors over time. Ann Surg. 2013 Aug;258(2):270-4.

24. Moghadamyeghaneh Z, Carmichael JC, Mills S, Pigazzi A, Nguyen NT, Stamos MJ. Variations in Laparoscopic Colectomy Utilization in the United States. Dis Colon Rectum. 2015 Oct;58(10):950-6.

25. National Health Expenditure Trends, 1975-2015. Ottawa, Ontario: Canadian Institute for Health Information; 2015.

26. Canadian Cancer Society. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/colorectal/statistics/?region=on.

27. Ota DM. Colon cancer. Cancer Treat Res. 1997;90:347-56.

28. Schwenk W, Haase O, Neudecker J, Muller JM. Short term benefits for laparoscopic colorectal resection. Cochrane Database Syst Rev. 2005 Jul 20;3(3):CD003145.

29. Sticca RP, Alberts SR, Mahoney MR, Sargent DJ, Finstuen LM, Nelson GD, et al. Current use and surgical efficacy of laparoscopic colectomy in colon cancer. J Am Coll Surg. 2013 Jul;217(1):56,62; discussion 62-3.

30. Burton D, Nicholson G, Hall G. Endocrine and metabolic response to surgery. Contin Educ Anaesth Crit Care Pain. 2004;4(5):144-47.

31. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. Am J Surg. 2002;183(6):630-41.

32. Sato H, Carvalho G, Lattermann R, Matsukawa T, Schricker T. The association of preoperative glycemic control, intraoperative insulin sensitivity, and outcomes after cardiac surgery. J Clin Endocrinol Metab. 2010;95(9):4338-44.

33. Noel JK, Fahrbach K, Estok R, Cella C, Frame D, Linz H, et al. Minimally invasive colorectal resection outcomes: short-term comparison with open procedures. J Am Coll Surg. 2007;204(2):291-307.

34. Leung KL, Kwok SP, Lam SC, Lee JF, Yiu RY, Ng SS, et al. Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. Lancet. 2004 Apr 10;363(9416):1187-92.

35. Pascual M, Alonso S, Pares D, Courtier R, Gil MJ, Grande L, et al. Randomized clinical trial comparing inflammatory and angiogenic response after open versus laparoscopic curative resection for colonic cancer. Br J Surg. 2011 Jan;98(1):50-9.

36. Teeuwen PH, Bleichrodt RP, Strik C, Groenewoud JJ, Brinkert W, van Laarhoven CJ, et al. Enhanced recovery after surgery (ERAS) versus conventional postoperative care in colorectal surgery. J Gastrointest Surg. 2010 Jan;14(1):88-95.

37. Gianotti L, Nelson JL, Alexander JW, Chalk CL, Pyles T. Post injury hypermetabolic response and magnitude of translocation: prevention by early enteral nutrition. Nutrition. 1994 May-Jun;10(3):225-31.

38. Fearon KC, Luff R. The nutritional management of surgical patients: enhanced recovery after surgery. Proc Nutr Soc. 2003 Nov;62(4):807-11.

39. Soop M, Carlson GL, Hopkinson J, Clarke S, Thorell A, Nygren J, et al. Randomized clinical trial of the effects of immediate enteral nutrition on metabolic responses to major colorectal surgery in an enhanced recovery protocol. Br J Surg. 2004 Sep;91(9):1138-45.

40. Alvarez MP, Foley KE, Zebley DM, Fassler SA. Comprehensive enhanced recovery pathway significantly reduces postoperative length of stay and opioid usage in elective laparoscopic colectomy. Surg Endosc. 2015 Sep;29(9):2506-11.

41. Kolozsvari NO, Capretti G, Kaneva P, Neville A, Carli F, Liberman S, et al. Impact of an enhanced recovery program on short-term outcomes after scheduled laparoscopic colon resection. Surg Endosc. 2013 Jan;27(1):133-8.

42. Faiz O, Warusavitarne J, Bottle A, Tekkis PP, Darzi AW, Kennedy RH. Laparoscopically assisted vs. open elective colonic and rectal resection: a comparison of outcomes in English National Health Service Trusts between 1996 and 2006. Dis Colon Rectum. 2009 Oct;52(10):1695-704.

43. Kennedy GD, Heise C, Rajamanickam V, Harms B, Foley EF. Laparoscopy decreases postoperative complication rates after abdominal colectomy: results from the national surgical quality improvement program. Ann Surg. 2009 Apr;249(4):596-601.

44. Steele SR, Brown TA, Rush RM, Martin MJ. Laparoscopic vs open colectomy for colon cancer: results from a large nationwide population-based analysis. J Gastrointest Surg. 2008 Mar;12(3):583-91.

45. She WH, Poon JT, Fan JK, Lo OS, Law WL. Outcome of laparoscopic colectomy for cancer in elderly patients. Surg Endosc. 2013 Jan;27(1):308-12.

46. Davis PJ, Bailey JG, Molinari M, Hayden J, Johnson PM. The Impact of Nonelective Abdominal Surgery on the Residential Status of Older Adult Patients. Ann Surg. 2016 Feb;263(2):274-9.

47. Lawrence VA, Hazuda HP, Cornell JE, Pederson T, Bradshaw PT, Mulrow CD, et al. Functional independence after major abdominal surgery in the elderly. J Am Coll Surg. 2004 Nov;199(5):762-72.

48. Robinson TN, Wallace JI, Wu DS, Wiktor A, Pointer LF, Pfister SM, et al. Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. J Am Coll Surg. 2011 Jul;213(1):37,42; discussion 42-4.

49. Pier A, Gotz F, Bacher C. Laparoscopic appendectomy in 625 cases: from innovation to routine. Surg Laparosc Endosc. 1991 Mar;1(1):8-13.

50. A prospective analysis of 1518 laparoscopic cholecystectomies. The Southern Surgeons Club. N Engl J Med. 1991 Apr 18;324(16):1073-8.

51. Fowler DL, White SA. Laparoscopy-assisted sigmoid resection. Surg Laparosc Endosc. 1991;1(3):183-8.

52. Corbitt JD,Jr. Preliminary experience with laparoscopic-guided colectomy. Surg Laparosc Endosc. 1992 Mar;2(1):79-81.

53. Monson JR, Darzi A, Carey PD, Guillou PJ. Prospective evaluation of laparoscopic-assisted colectomy in an unselected group of patients. Lancet. 1992 Oct 3;340(8823):831-3.

54. Phillips EH, Franklin M, Carroll BJ, Fallas MJ, Ramos R, Rosenthal D. Laparoscopic colectomy. Ann Surg. 1992 Dec;216(6):703-7.

55. Schwenk W, Bohm B, Muller JM. Postoperative pain and fatigue after laparoscopic or conventional colorectal resections. A prospective randomized trial. Surg Endosc. 1998 Sep;12(9):1131-6.

56. Walsh DC, Wattchow DA, Wilson TG. Subcutaneous metastases after laparoscopic resection of malignancy. Aust N Z J Surg. 1993 Jul;63(7):563-5.

57. Alexander RJ, Jaques BC, Mitchell KG. Laparoscopically assisted colectomy and wound recurrence. Lancet. 1993 Jan 23;341(8839):249-50.

58. O'Rourke N, Price PM, Kelly S, Sikora K. Tumour inoculation during laparoscopy. Lancet. 1993 Aug 7;342(8867):368.

59. American Society of Colon and Rectal Surgeons: Policy statement. Diseases of the Colon and Rectum. 1992;35(5A).

60. Bilimoria KY, Bentrem DJ, Nelson H, Stryker SJ, Stewart AK, Soper NJ, et al. Use and outcomes of laparoscopic-assisted colectomy for cancer in the United States. Arch Surg. 2008 Sep;143(9):832,9; discussion 839-40.

61. Reames BN, Sheetz KH, Waits SA, Dimick JB, Regenbogen SE. Geographic variation in use of laparoscopic colectomy for colon cancer. J Clin Oncol. 2014 Nov 10;32(32):3667-72.

62. Birkmeyer JD, Reames BN, McCulloch P, Carr AJ, Campbell WB, Wennberg JE. Understanding of regional variation in the use of surgery. Lancet. 2013 Sep 28;382(9898):1121-9.

63. Bach PB, Pham HH, Schrag D, Tate RC, Hargraves JL. Primary care physicians who treat blacks and whites. N Engl J Med. 2004 Aug 5;351(6):575-84.

64. Robinson CN, Balentine CJ, Sansgiry S, Berger DH. Disparities in the use of minimally invasive surgery for colorectal disease. J Gastrointest Surg. 2012 May;16(5):897,903; discussion 903-4.

65. Baldwin LM, Dobie SA, Billingsley K, Cai Y, Wright GE, Dominitz JA, et al. Explaining black-white differences in receipt of recommended colon cancer treatment. J Natl Cancer Inst. 2005 Aug 17;97(16):1211-20.

66. Polite BN, Dignam JJ, Olopade OI. Colorectal cancer and race: understanding the differences in outcomes between African Americans and whites. Med Clin North Am. 2005 Jul;89(4):771-93.

67. Taylor EF, Thomas JD, Whitehouse LE, Quirke P, Jayne D, Finan PJ, et al. Population-based study of laparoscopic colorectal cancer surgery 2006-2008. Br J Surg. 2013 Mar;100(4):553-60.

68. Delgado S, Lacy AM, Garcia Valdecasas JC, Balague C, Pera M, Salvador L, et al. Could age be an indication for laparoscopic colectomy in colorectal cancer? Surg Endosc. 2000 Jan;14(1):22-6.

69. Beart RW. Laparoscopic colorectal surgery. Monson JR, Darzi A, Eds., editors. London: ISIS Medical Media; 1995.

70. Evers BM, Townsend CM,Jr, Thompson JC. Organ physiology of aging. Surg Clin North Am. 1994 Feb;74(1):23-39.

71. Rebenson-Piano M. The physiologic changes that occur with aging. Crit Care Nurs Q. 1989 Jun;12(1):1-14.

72. Bannenberg JJ, Rademaker BM, Grundeman PF, Kalkman CJ, Meijer DW, Klopper PJ. Hemodynamics during laparoscopy in the supine or prone position. An experimental study. Surg Endosc. 1995 Feb;9(2):125-7.

73. Schwandner O, Schiedeck TH, Bruch HP. Advanced age--indication or contraindication for laparoscopic colorectal surgery? Dis Colon Rectum. 1999 Mar;42(3):356-62.

74. Frasson M, Braga M, Vignali A, Zuliani W, Di Carlo V. Benefits of laparoscopic colorectal resection are more pronounced in elderly patients. Dis Colon Rectum. 2008 Mar;51(3):296-300.

75. Martinek L, Dostalik J, Gunka I, Gunkova P, Zonca P. Is age a risk factor for laparoscopic colorectal surgery? Zentralbl Chir. 2011 Jun;136(3):264-8.

76. Grocott MP, Martin DS, Mythen MG. Enhanced recovery pathways as a way to reduce surgical morbidity. Curr Opin Crit Care. 2012 Aug;18(4):385-92.

77. Chau DL, Walker V, Pai L, Cho LM. Opiates and elderly: use and side effects. Clin Interv Aging. 2008;3(2):273-8.

78. da Luz Moreira A, Kiran RP, Kirat HT, Remzi FH, Geisler DP, Church JM, et al. Laparoscopic versus open colectomy for patients with American Society of Anesthesiology (ASA) classifications 3 and 4: the minimally invasive approach is associated with significantly quicker recovery and reduced costs. Surg Endosc. 2010 Jun;24(6):1280-6.

79. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care. 1998 Jan;36(1):8-27.

80. Guller U, Buhler L, Clavien PA. Statistics in medicine. Swiss Med Wkly. 2003 Oct 11;133(39-40):521.

81. Plocek MD, Geisler DP, Glennon EJ, Kondylis P, Reilly JC. Laparoscopic colorectal surgery in the complicated patient. Am J Surg. 2005 Dec;190(6):882-5.

82. da Luz Moreira A, Kiran RP, Kirat HT, Remzi FH, Geisler DP, Church JM, et al. Laparoscopic versus open colectomy for patients with American Society of Anesthesiology (ASA) classifications 3 and 4: the minimally invasive approach is associated with significantly quicker recovery and reduced costs. Surg Endosc. 2010 Jun;24(6):1280-6.

83. Billeter AT, Polk HC,Jr, Hohmann SF, Qadan M, Fry DE, Jorden JR, et al. Mortality after elective colon resection: the search for outcomes that define quality in surgical practice. J Am Coll Surg. 2012 Apr;214(4):436,43; discussion 443-4.

84. Masoomi H, Kang CY, Chen A, Mills S, Dolich MO, Carmichael JC, et al. Predictive factors of in-hospital mortality in colon and rectal surgery. J Am Coll Surg. 2012 Aug;215(2):255-61.

85. Dincler S, Koller MT, Steurer J, Bachmann LM, Christen D, Buchmann P. Multidimensional analysis of learning curves in laparoscopic sigmoid resection: eight-year results. Dis Colon Rectum. 2003 Oct;46(10):1371,8; discussion 1378-9.

86. Tekkis PP, Senagore AJ, Delaney CP, Fazio VW. Evaluation of the learning curve in laparoscopic colorectal surgery: comparison of right-sided and left-sided resections. Ann Surg. 2005 Jul;242(1):83-91.

87. Damle RN, Macomber CW, Flahive JM, Davids JS, Sweeney WB, Sturrock PR, et al. Surgeon volume and elective resection for colon cancer: an analysis of outcomes and use of laparoscopy. J Am Coll Surg. 2014 Jun;218(6):1223-30.

88. Wishner JD, Baker JW,Jr, Hoffman GC, Hubbard GW,2nd, Gould RJ, Wohlgemuth SD, et al. Laparoscopic-assisted colectomy. The learning curve. Surg Endosc. 1995 Nov;9(11):1179-83.

89. Simons AJ, Anthone GJ, Ortega AE, Franklin M, Fleshman J, Geis WP, et al. Laparoscopic-assisted colectomy learning curve. Dis Colon Rectum. 1995 Jun;38(6):600-3.

90. Agachan F, Joo JS, Weiss EG, Wexner SD. Intraoperative laparoscopic complications. Are we getting better? Dis Colon Rectum. 1996 Oct;39(10 Suppl):S14-9.

91. Agachan F, Joo JS, Sher M, Weiss EG, Nogueras JJ, Wexner SD. Laparoscopic colorectal surgery. Do we get faster? Surg Endosc. 1997 Apr;11(4):331-5.

92. Bennett CL, Stryker SJ, Ferreira MR, Adams J, Beart RW,Jr. The learning curve for laparoscopic colorectal surgery. Preliminary results from a prospective analysis of 1194 laparoscopic-assisted colectomies. Arch Surg. 1997 Jan;132(1):41,4; discussion 45.

93. Schlachta CM, Mamazza J, Seshadri PA, Cadeddu M, Gregoire R, Poulin EC. Defining a learning curve for laparoscopic colorectal resections. Dis Colon Rectum. 2001 Feb;44(2):217-22.

94. Hyman N. How much colorectal surgery do general surgeons do? J Am Coll Surg. 2002 Jan;194(1):37-9.

95. ASCRS position statement on Laparoscopic Colectomy for Curable Cancer. American Society of Colon and Rectal Surgeons [cited October 17, 2015]. Available from: http://www.fascrs.org/physicians/position_statements/laparoscopic_colectomy/.

96. Lynch J, Aughwane P, Hammond TM. Video games and surgical ability: a literature review. J Surg Educ. 2010 May-Jun;67(3):184-9.

97. Rosser JC,Jr, Lynch PJ, Cuddihy L, Gentile DA, Klonsky J, Merrell R. The impact of video games on training surgeons in the 21st century. Arch Surg. 2007 Feb;142(2):181,6; discusssion 186.

98. Moloo H, Haggar F, Martel G, Grimshaw J, Coyle D, Graham ID, et al. The adoption of laparoscopic colorectal surgery: a national survey of general surgeons. Can J Surg. 2009 Dec;52(6):455-62.

99. Kuhry E, Bonjer HJ, Haglind E, Hop WC, Veldkamp R, Cuesta MA, et al. Impact of hospital case volume on short-term outcome after laparoscopic operation for colonic cancer. Surg Endosc. 2005 May;19(5):687-92.

100. Billingsley KG, Morris AM, Dominitz JA, Matthews B, Dobie S, Barlow W, et al. Surgeon and hospital characteristics as predictors of major adverse outcomes following colon cancer surgery: understanding the volume-outcome relationship. Arch Surg. 2007 Jan;142(1):23,31; discussion 32.

101. Ihse I. The volume-outcome relationship in cancer surgery: a hard sell. Ann Surg. 2003 Dec;238(6):777-81.

102. Pieper D, Mathes T, Neugebauer E, Eikermann M. State of evidence on the relationship between high-volume hospitals and outcomes in surgery: a systematic review of systematic reviews. J Am Coll Surg. 2013 May;216(5):1015,1025.e18.

103. Kemp JA, Finlayson SR. Outcomes of laparoscopic and open colectomy: a national population-based comparison. Surg Innov. 2008 Dec;15(4):277-83.

104. Rea JD, Cone MM, Diggs BS, Deveney KE, Lu KC, Herzig DO. Utilization of laparoscopic colectomy in the United States before and after the clinical outcomes of surgical therapy study group trial. Ann Surg. 2011 Aug;254(2):281-8.

105. Kiran RP, El-Gazzaz GH, Vogel JD, Remzi FH. Laparoscopic approach significantly reduces surgical site infections after colorectal surgery: data from national surgical quality improvement program. J Am Coll Surg. 2010 Aug;211(2):232-8.

106. Surgical Care and Outcomes Assessment Program (SCOAP) Collaborative, Kwon S, Billingham R, Farrokhi E, Florence M, Herzig D, et al. Adoption of laparoscopy for elective colorectal resection: a report from the Surgical Care and Outcomes Assessment Program. J Am Coll Surg. 2012 Jun;214(6):909,18.e1.

107. National Bowel Cancer Audit Report 2015. London, England; 2015 [cited November 20, 2016]. Available from: http://content.digital.nhs.uk/catalogue/PUB19500/nati-clin-audi-bowe-canc-2015.pdf.

108. Kolfschoten NE, van Leersum NJ, Gooiker GA, Marang van de Mheen PJ, Eddes EH, Kievit J, et al. Successful and safe introduction of laparoscopic colorectal cancer surgery in Dutch hospitals. Ann Surg. 2013 May;257(5):916-21.

109. Dobbins TA, Young JM, Solomon MJ. Uptake and outcomes of laparoscopically assisted resection for colon and rectal cancer in Australia: a population-based study. Dis Colon Rectum. 2014 Apr;57(4):415-22.

110. Thompson BS, Coory MD, Lumley JW. National trends in the uptake of laparoscopic resection for colorectal cancer, 2000-2008. Med J Aust. 2011 May 2;194(9):443-7.

111. Chan BP, Gomes T, Musselman RP, Auer RC, Moloo H, Mamdani M, et al. Trends in colon cancer surgery in Ontario: 2002-2009. Colorectal Dis. 2012 Oct;14(10):e708-12.

112. Simunovic M, Baxter NN, Sutradhar R, Liu N, Cadeddu M, Urbach D. Uptake and patient outcomes of laparoscopic colon and rectal cancer surgery in a publicly funded system and following financial incentives. Ann Surg Oncol. 2013 Nov;20(12):3740-6.

113. Musselman RP, Gomes T, Chan BP, Auer RC, Moloo H, Mamdani M, et al. Laparoscopic Colorectal Surgery in the Emergency Setting: Trends in the Province of Ontario. Surg Laparosc Endosc Percutan Tech. 2015 Mar 19.

114. About CIHI: CIHI; 2014 [cited October 25, 2015]. Available from: https://www.cihi.ca/en/about-cihi.

115. DAD Metadata: Canadian Institute for Health Information; 2014 [cited October 25, 2015]. Available from: https://www.cihi.ca/en/types-of-care/hospital-care/acute-care/dad-metadata.

116. Canadian Classification of Health Interventions, Volume Three: Canadian Institute for Health Information; 2009 [cited September 27, 2015]. Available from: www.cihi.ca//en/cci_vol3_2009_en.pdf.

117. Canada Post. Addressing guidelines. Canada: Canada Post [cited September 25, 2016]. Available from: https://www.canadapost.ca/tools/pg/manual/PGaddress-e.asp?ecid=murl10006450#1449294.

118. Stukenborg GJ, Wagner DP, Connors AF,Jr. Comparison of the performance of two comorbidity measures, with and without information from prior hospitalizations. Med Care. 2001 Jul;39(7):727-39.

119. Southern DA, Quan H, Ghali WA. Comparison of the Elixhauser and Charlson/Deyo methods of comorbidity measurement in administrative data. Med Care. 2004 Apr;42(4):355-60.

120. Sharabiani MT, Aylin P, Bottle A. Systematic review of comorbidity indices for administrative data. Med Care. 2012 Dec;50(12):1109-18.

121. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005 Nov;43(11):1130-9.

122. Khoury W, Kiran RP, Jessie T, Geisler D, Remzi FH. Is the laparoscopic approach to colectomy safe for the morbidly obese? Surg Endosc. 2010 Jun;24(6):1336-40.

123. Urbach DR. Closing in on surgical practice variations. Ann Surg. 2014 Apr;259(4):628-9.

124. Westert GP, Groenewegen PP. Medical practice variations: changing the theoretical approach. Scand J Public Health. 1999 Sep;27(3):173-80.

125. Reames BN, Shubeck SP, Birkmeyer JD. Strategies for reducing regional variation in the use of surgery: a systematic review. Ann Surg. 2014 Apr;259(4):616-27.

126. Stocchi L, Nelson H, Young-Fadok TM, Larson DR, Ilstrup DM. Safety and advantages of laparoscopic vs. open colectomy in the elderly: matched-control study. Dis Colon Rectum. 2000 Mar;43(3):326-32.

127. Law WL, Chu KW, Tung PH. Laparoscopic colorectal resection: a safe option for elderly patients. J Am Coll Surg. 2002 Dec;195(6):768-73.

128. Abraham NS, Young JM, Solomon MJ. Meta-analysis of short-term outcomes after laparoscopic resection for colorectal cancer. Br J Surg. 2004 Sep;91(9):1111-24.

129. Scheidbach H, Schneider C, Hugel O, Yildirim C, Lippert H, Kockerling F. Laparoscopic surgery in the old patient: do indications and outcomes differ? Langenbecks Arch Surg. 2005 Aug;390(4):328-32.

130. Leroy J, Ananian P, Rubino F, Claudon B, Mutter D, Marescaux J. The impact of obesity on technical feasibility and postoperative outcomes of laparoscopic left colectomy. Ann Surg. 2005 Jan;241(1):69-76.

131. Senagore AJ, Delaney CP, Madboulay K, Brady KM, Fazio VW. Laparoscopic colectomy in obese and nonobese patients. J Gastrointest Surg. 2003 May-Jun;7(4):558-61.

APPENDIX A

Table A.1 Stepwise regression model building

Variables	Year	Sex	Age	Province	Residence
Model	A	B	C	D	E
Variables included	year	A + sex	B+ age	C + province	D + residence
-2loglik	73,588.84	73,613.77	73,682.04	73,750.31	73,994.01
df	1	2	5	13	14
Increase in -2 loglik	73,588.84	24.93	68.27	2908.07	243.70
Increase in df	1	1	3	8	1
LR p-value	*	*	*	*	*
H-L chi-square	149.89	137.77	128.14	61.88	65.82
H-L df	8	8	8	8	8
H-L p-value	*	*	*	*	*

*p<0.001

Table A.1 cont'd

Variable	Elixhauser	Hospital volume	Surgeon volume	Segmental resection
Model	F	G	H	I
Variables included	E + Elix	F + Hosp vol	G + Surg vol	H + Seg res
-2 loglik	74,032.05	75,492.81	75,632.57	76,065.99
df	16	17	18	21
Increase in -2 loglik	38.04	1460.76	139.76	433.42
Increase in df	2	1	1	3
LR p-value	*	*	*	*
H-L chi-square	62.09	51.60	37.45	10.01
H-L df	8	8	8	8
H-L p-value	*	*	*	*

*p<0.001

Figure A.1 Observed ratio of LAC and fitted line of regression model by year