Evaluation of an Enhanced Recovery After Surgery (ERAS) Initiative

by © Alexander Norman

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Abstract

Purpose: To determine if patient outcomes and compliance with best practice guidelines improved when an Enhanced Recovery After Surgery (ERAS) program was implemented for elective colorectal resections at St. Clare's Mercy Hospital (SCMH) in St. John's, Newfoundland and Labrador (NL).

Methods: Interrupted time-series analysis was utilized to compare patient outcomes and guideline compliance between surgeries that were performed under standard practice (April 1, 2014 to March 31, 2015) and those performed during the first year of the ERAS program (March 1, 2016 to February 28, 2017). An ERAS Coordinator supervised guideline compliance in the first six months of ERAS surgeries. Charts were manually reviewed to obtain patient outcomes and compliance with guidelines.

Results: Length of stay (LOS) decreased significantly from 7.26 days in the control (standard practice) group to 6.27 days in the ERAS group. LOS was shorter in the first six months of ERAS (5.44 days) than in the second six months of ERAS (7.10 days). There were no statistically significant differences in rates of complication, readmission, or mortality with implementation of ERAS. Overall compliance with guidelines increased significantly from 52.2% to 77.7% with implementation of ERAS. Postoperative compliance decreased (79.2% to 68.6%) from the first six months to the second six months of ERAS.

Conclusion: Implementation of ERAS was successful at reducing LOS, but not rates of complication, readmission, or mortality. The success of this program appears to have been largely dependent on guideline supervision by an ERAS coordinator in the first six months. Methods for ensuring postoperative compliance are vital to the success of similar programs in the future.

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List of Abbreviations

AHS - Alberta Health Services

AKI – Acute kidney injury

ASA - American Society of Anesthesiologists

BMI - Body Mass Index

CCC - Computerized clinical chart

CHIA - Center for Health Informatics and Analytics

CI - Confidence interval

CIHI - Canadian Institute for Health Information

CRC - Colorectal cancer

CT - Computerized tomography

CWC - Choosing Wisely Canada

CWNL - Choosing Wisely NL

DVT - deep vein thrombosis

ED - Emergency department

EH - Eastern Health

ERAS - Enhanced Recovery After Surgery

GP - General practitioner

HIM - Health Information Management Professionals

HREB - Health Research Ethics Board

IL-6 - Interleukin 6

IV - Intravenous

KDIGO - Kidney Disease Improving Global Outcomes

KT - Knowledge translation

LOS - Length of Stay

NL - Newfoundland and Labrador

NLMA - Newfoundland and Labrador Medical Association

NIS - Nationwide Inpatient Sample

NSAID - Nonsteroidal anti-inflammatory drugs

NSQIP - National Surgical Quality Improvement Initiative

MUN - Memorial University of Newfoundland

MBP - Mechanical bowel preparation

POD - Postoperative day

PONV - Postoperative nausea and vomiting

QoCNL - Quality of Care NL

QoL - Quality of life

RCT - Randomized Control Trial

RHA - Regional Health Authority

RIW - Resource Intensity Weight

ROI - Return on investment

RR - Relative risk

RTM - Regression to the mean

SCMH - St. Clare's Mercy Hospital

SCr – Serum creatinine

SD - Standard Deviation

SPREAD - Stroke Prevention and Educational Awareness Diffusion

SU - Stroke unit

TEA - thoracic epidural anesthesia

UHC - University Health System Consortium

UTI - Urinary tract infection

VTE - venous thromboembolism

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Chapter 1: Background

1.1. Colorectal Resections in Newfoundland and Labrador

The province of Newfoundland and Labrador (NL) has the highest incidence rate of colorectal cancer (CRC) in Canada with an incidence of 127 cases per 100,000 people (Green et al., 2007). NL also has the highest mortality rate from CRC in Canada. In 2015, the age standardized mortality rates from CRC per 100,000 people were 38 in males and 21 in females (Parfrey, 2017). Finally, NL has the highest rate of familial CRC in the world. Specifically, 31% of individuals with CRC in NL have a first degree relative who has also had CRC (Green et al., 2007). The volume of procedures for the removal and treatment of CRC in NL, and the efficiency of these procedures, are therefore important to evaluate.

Eastern Health (EH) is one of four regional health authorities (RHA) in NL and services more than 300,000 (Twells, 2016) of the approximately 530,000 people (Statistics Canada, 2017) in the province. Every year, approximately 1,000 colorectal resections are performed in NL (NLCHI, 2018). St. Clare's Mercy Hospital (SCMH) in St. John's performs approximately 160 annual elective colorectal resections. The vast majority of these procedures are resections for CRC, but others include resections for inflammatory bowel diseases such as Crohn's and colitis. The term *elective* refers to surgery that is non-emergent, meaning the procedure was planned and did not have to be performed immediately. Most colorectal surgeries at SCMH are, in this sense, elective (Ballah, 2017). In the case of CRC, emergent surgery may be required if the colon is obstructed, bleeding, or ruptured (Wilkinson and Scott-Conner, 2008). A colon resection takes only a portion of a day to perform, but a substantial amount of recovery time in hospital is usual. It is common for patients to spend approximately a week in hospital, including the initial procedure and subsequent recovery (Ballah, 2017).

1.2. Types of Elective Colorectal Resections

The most frequent colorectal resections performed at SCMH are for CRC (Ballah, 2017). This disease is usually diagnosed via colonoscopy or contrast radiography, however, the literature suggests that an increasing number of cases are being detected when a computerized tomography (CT) scan is performed of the abdominal region (Wilkinson and Scott-Conner, 2008). Factors such as location of cancer, clinical stage, comorbid conditions, patient frailty and previous surgery can influence both the timing of surgery and the type of surgery required. Many colon resections are based on the need to remove cancerous tissue in the bowel and eradicate all lymph nodes that drain the cancerous region to prevent further growth and metastasis (Wilkinson and Scott-Conner, 2008). At SCMH, three of the most common elective colon resections are open colorectal resections, laparoscopic colorectal resections, and colostomies (Ballah, 2016). It should be noted, however, that these three procedures are not mutually exclusive (in that a colostomy is performed via either laparoscopic or open surgery). This section provides a description of these three procedures and states the cost associated with each.

1.2.1. Open versus Laparoscopic Resection

Open surgery of the bowel is the most traditional method used to accomplish a colorectal resection, and was the only technique used until introduction of the laparoscopic method in the early 1990's (Morneau et al., 2013). In open surgery, large incisions to the abdominal region allow access to the cancerous portion of the bowel and associated lymph nodes (Wilkinson and Scott-Conner, 2008). This method of surgery has been associated with higher than necessary levels of surgical trauma and pain, and a longer than necessary time to postoperative bowel function and mobility, all of which lead to prolonged hospital stay (Gustafsson et al., 2012).

Technological advances eventually permitted the use of a much less invasive laparoscopic technique. The first laparoscopic procedure to be performed was in 1985 for the removal of a gallbladder (Reynolds, 2001), and in 1991 it was utilized to perform a colon resection (Blackmore et al., 2014). To perform a laparoscopic colon resection, the abdominal cavity is insufflated with carbon dioxide to create pneumoperitoneum and a small incision in the abdomen allows for the insertion of a laparoscope to view the colon. Insertion of trocars allows the surgery to be performed without incisions as large as would be necessary for a traditional open colonic resection (Jacobs, 1991). Introduction of laparoscopic surgery into mainstream practice was slow during the 1990's as the safety and efficacy of the procedure was unknown, and evidence for its use was scarce (Blackmore et al., 2014). Initial reports of laparoscopy for colon resection also demonstrated high recurrence rates at port sites (Ndukka et al., 1994), and although more recent studies fail to show these results (Buunen et al., 2009), uptake of laparoscopy for colon cancer is still slow. In 2013 it was estimated that half of general surgeons in Canada perform laparoscopic colorectal resections (Morneau et al., 2013). In comparison to open colonic resection, laparoscopy is associated with a reduction in length of stay (LOS) (Pedziwiatr et al., 2016), and has been shown to reduce pain, complications, and postoperative immunosuppression (Gustafsson et al., 2012).

1.2.2. Colostomy

Colostomy is a surgical procedure whereby a portion of the colon is diverted to the exterior of the body through the abdomen and is attached at the surface of the skin. It allows bowel contents to be emptied into a pouch when normal passage through the bowel is not possible. This is typically performed on the left side of the colon and is sometimes required after bowel surgeries including those for CRC and inflammatory bowel disease (Johns Hopkins

Medicine, 2017). Many patients undergoing a colon or rectal resection require a colostomy or an ileostomy (diversion of the small bowel), which may be a permanent or temporary diversion (Smith, 2018).

1.2.3. Cost of Surgery

Table 1.1 presents the estimated average cost per day in hospital for the three most common elective colorectal resections at SCMH. Data on hospital costs was received from the Canadian Institute for Health Information (CIHI), using the Patient Cost Estimator. These procedures are coded as (1) *Colostomy/Enterostomy* (2*) Open Large Intestine/Rectum Resection without Colostomy, Planned* and (3) *Endoscopic Large Intestine/Rectum Resection without Colostomy* (Ballah, 2017) by Health Information Management Professionals (HIM) at EH. CIHI provides the following information regarding calculation of cost of hospital stay: each patient case that is submitted by a health jurisdiction (province) to CIHI has an associated Resource Intensity Weight (RIW), a number indicating the relative resources consumed by the patient's total hospital stay, and the total LOS of that patient (CIHI Patient Cost Estimator, 2016). The major difference between cost associated with open versus endoscopic surgery (seen in the estimates in Table 1.1) is likely due to the following: (1) operative time for laparoscopic procedures are much higher than open procedures, and (2) laparoscopic surgery involves the use of disposable equipment not needed in open surgery. However, considering that LOS is usually shorter for laparoscopic procedures, laparoscopic surgery is much more economical in the long term (Alkhamesi et al., 2011).

As time spent recovering in hospital is expensive, even a marginal decrease in LOS would, hypothetically, result in substantial savings in health care expenditure. For example, for colostomy/enterostomy where the cost is $1,663 per day per patient, in a year where 160 patients

spent 7 days in hospital, approximately $1.86 million worth of healthcare resources would be utilized. If, however, LOS was decreased by just one day per patient, the cost would be approximately $1.59 million, a reduction of $266,080. This is only hypothetical, in that the early recovery and discharge of a patient would not result in one less occupied hospital bed (and a direct reduction of health care expenditure). Given the limited number of hospital beds that are available, the sooner a bed becomes vacant, the sooner it can be occupied by another patient. The ultimate outcome, then, is a reduction in the number of patients waiting for hospital beds, and a reduction in the wait times for such hospital beds (Pridham, 2018). Nevertheless, this would still be a very positive outcome.

Such a decrease in LOS would also be important from the patient perspective. A reduction in recovery time means that the patient can get back to his or her daily routine much quicker, and would be beneficial when considering the associated quality of life (QoL).

Table 1.1: Estimated cost per day in hospital for recovery after elective colorectal procedures (Ballah, 2016)

Procedure Code	**Cost/Day in Hospital**
Colostomy/Enterostomy	$1,663
Open Large Intestine/Rectum Resection without Colostomy, Planned	$1,599
Endoscopic Large Intestine/Rectum Resection without Colostomy	$2,641

1.3. Adverse Outcomes

Surgical complications and mortality are two adverse outcomes that may result during or after an elective colorectal resection. This section will describe these outcomes and state the prevalence of each.

1.3.1. Surgical Complications

One factor that is significantly associated with delayed discharge from hospital after major surgery is the occurrence of complications (Zogg et al., 2016). In 2016, a study evaluating the economic impact of elective colonic resections reported that of 68,462 patients undergoing an elective colonic resection, 16.4% developed a complication. Records were obtained from patients in the Nationwide Inpatient Sample (NIS) who had an elective colorectal resection between 2009 and 2011 and who were diagnosed with either colon cancer, diverticular disease, benign colonic neoplasm, or ulcerative colitis/regional enteritis. Complications were assigned using codes defined by the Minnesota Gastroenterology research department (Zogg et al., 2016). As the literature is not consistent regarding complication definitions, reported complication rates will never be completely generalizable.

A multicenter study published in 2012 considered all (1,721) patients who underwent resection for colorectal cancer between 2001 and 2008 in the western zone of Sydney South West Area Health Service. This study reported that of the 591 patients who received laparoscopic surgery, 190 (32.1%) developed one or more complications. Of the 1,130 patients who received laparoscopic surgery, 190 (16.8%) developed one or more complications. The most common complications reported were pyrexia, prolonged ileus, cardiac event (defined in this study as atrial fibrillation, congestive cardiac failure, or acute myocardial infarction), and wound

infection (McKay et al., 2012). This study considers both 30-day readmission and in-hospital mortality as complications rather than separate patient outcomes, providing an example of how definitions of complications are not consistent across studies.

Although it may be unclear what should be considered a surgical complication, some reported complications are certainly more common than others. A study of 181 hospitals in the NIS of the Healthcare Cost and Utilization database found that the five most frequent complications after an elective bowel resection, and their respective rates, were ileus (15.4%), fluid electrolyte abnormality (11.5%), atelectasis (6.6%), post-hemorrhagic anemia (5.1%), and pulmonary dysfunction/failure (4.8%) (Fry et al., 2012).

1.3.2. Postoperative Mortality

Mortality is another adverse outcome that may occur after an elective colorectal resection. Mortality rate is generally reported as 30-day mortality, meaning that the patient died within 30 days after surgery. However it may also be reported as in-hospital mortality, representing death before discharge from hospital. A study published in 2016 considered 59,986 elective colorectal resections from the American College of Surgeons National Surgical Quality Improvement Initiative (NSQIP) that occurred between 2006 and 2012 for colon cancer. A total of 1,096 (1.8%) patients died within 30 days after surgery (Murray et al., 2016).

As previously mentioned, the multicenter study published in 2012 by McKay et al. considered in-hospital mortality to be a complication. In this study, 15 (1.33%) patients undergoing an open resection died in hospital, and 7 (1.17%) patients who received laparoscopic surgery died in hospital (McKay et al., 2012). Another study which considered in-hospital mortality was published in 2012 and evaluated 85,260 elective colorectal resections from the

University Health System Consortium (UHC) that took place in 195 teaching hospitals. This study reported that 1,334 patients (1.56%) died while in hospital (Billeter et al., 2012).

1.4. Enhanced Recovery After Surgery

One program that has proven effective at reducing recovery time after surgery in many populations is Enhanced Recovery After Surgery (ERAS). ERAS, sometimes referred to as 'fast-track' surgery, is a set of perioperative (preoperative, intraoperative, and postoperative) guidelines of best practice in surgery. Each individual guideline is evidence-based, and the entire pathway aims to reduce surgical stress and improve postoperative function. Guidelines have been selected for inclusion in the pathway by an informed consensus of experts based on existing evidence in the literature (Gustafsson et al., 2012). Table 1.2 presents each of the guidelines arranged in their respective perioperative position. Appendix I defines, and provides rationale for, each of these guidelines.

One of the main goals of compliance with ERAS is to decrease LOS in hospital (Gustafsson et al., 2012). One of the best predictors of success with an ERAS program is the extent of guideline compliance (i.e., the proportion of all guidelines that are followed for a given patient). This includes the physician's willingness and the patient's ability to be compliant (Smart et al., 2012). For example, a patient who is not able to open their mouth would be unable to comply with the chewing gum intervention (Choi et al., 2014), a disabled patient in a wheelchair might be unable to comply with early mobilization, and a physician who is reluctant to change his or her previous habits would be less likely to comply with every guideline. Deviation from guideline compliance in ERAS pathways has been shown to significantly increase time to discharge from hospital (Smart et al., 2012). No literature currently exists to demonstrate the extent to which guidelines would be followed and patient outcomes would

improve with an ERAS quality improvement initiative in NL.

Table 1.2: Enhanced Recovery After Surgery (ERAS) Guidelines

Perioperative Position	Guideline
Preoperative	Preadmission counselling
	Carbohydrate loading
	No bowel preparation
	Antibiotic prophylaxis
	Venous thromboembolism (VTE) prophylaxis
Intraoperative	Short acting anesthetics; limited use of narcotics
	Thoracic epidural anesthesia (TEA) for open surgery
	Fluid therapy
	Laparoscopy
	Maintenance of normothermia
	Maintenance of normoglycemia
Postoperative	Discontinuation of intravenous (IV) fluids after 24 hours
	No nasogastric tube
	Postoperative nausea and vomiting (PONV) management
	Foley catheter removal postoperative day (POD)1
	Clear fluids administered POD0
	Diet as tolerated POD1
	Multimodal pain management
	Early mobilization
	Chewing gum

1.5. Adherence to ERAS Guidelines and Patient Outcomes

There is sizeable literature demonstrating that patient outcomes can be improved when ERAS guidelines are followed for colorectal surgery, such as a reduction in LOS and the biological stress response. Articles identifying such improvements will be examined. One article suggesting a potential drawback of ERAS compliance will also be mentioned.

1.5.1. Decrease in Length of Stay

One of the major objectives of an ERAS program is to decrease LOS in hospital after major surgery (Gustafsson et al., 2012). A randomized control trial (RCT) in which ERAS guidelines were implemented for radical resections of the colon was conducted in Zhongshan Hospital, China in 2012 (Ren et al., 2012).

At this hospital, more than 1,100 annual radical resections are performed for CRC. With limited medical resources, and in an attempt to accelerate recovery and allow more patients to receive treatment, ERAS guidelines are enforced. Patients in this study were randomized to receive either standard surgery (n=298) or ERAS (n=299) surgery using a random number generator on SPSS v11.0. Based on the nature of the intervention, and that patient and physician participation is required, neither patients nor physicians could be blinded to the intervention. It was determined that patients in control and intervention groups were not statistically different in any of the following demographic or prognostic factors: sex distribution, median age, body mass index (BMI), American Society of Anesthesiologist's (ASA) score, and specific operation.

The inclusion criteria for this study were: between the ages of 20 and 80 inclusive, had a single colorectal lesion, and were eligible for a radical colorectal surgery. Exclusion criteria for this study were: emergent surgery, concurrent resection of other organs, a history of abdominopelvic surgery, and presence of comorbidities that could affect recovery. Patients who

received surgery under ERAS guidelines were discharged at (mean ± SD) 5.7 ± 1.6 days, whereas those who received surgery under standard practice were discharged at (mean ± SD) 6.6 ± 2.4 days (significant at $p<0.001$). This study determined that implementation of an ERAS program did not significantly change rates of postoperative complication: 28 (9.4%) patients in the control group developed complications whereas 29 (9.7%) patients in the ERAS group ($P=0.900$). Criteria used to discharge patients in this study were: occurrence of bowel movement, good pain management with oral analgesia, ability to tolerate solid food, no need for intravenous fluids, and independent mobility.

Another study looking at the impact of compliance with ERAS guidelines in colorectal surgery was published in 2014. This was a prospective study considering a total of 241 consecutive patients undergoing colorectal surgery at Duke University Medical Center. The first 99 of these patients received their surgery before a change in practice to ERAS, whereas the remainder (142 patients) received surgery under ERAS guidelines. This study is important to consider as it divides patient outcomes (in both ERAS and standard care groups) into subgroups based on whether the surgery was performed as an open or laparoscopic procedure. Upon implementation of ERAS, median LOS decreased significantly ($P<0.0001$) from 7 to 5 days. Within the open procedures, median LOS decreased significantly ($P=0.0133$) from 7 to 6 days. Median LOS for laparoscopic procedures also decreased significantly ($P<0.0001$) with implementation of ERAS, from 6 days to 4 days (Miller et al., 2014). This study shows not only the importance of adherence to ERAS guidelines, but also the benefit on patient recovery time of performing colorectal surgery laparoscopically.

In 2013, a meta-analysis was published that considered RCTs where ERAS guidelines were implemented for colorectal surgery. Sixteen relevant trials were included in the review

(Greco et al., 2014). In total there were 2,376 patients (1,181 under ERAS and 1,195 under conventional care). The study reported the weighted mean difference in LOS between patients who received surgery under ERAS guidelines and those who received surgery under conventional care to be 2.28 days with a 95 % confidence interval (CI) of –3.09 to –1.47 days.

1.5.2. Reduction in Stress Response

A major constituent of the ERAS pathway is its ability to reduce the stress response associated with major surgery (Gustafsson et al., 2012). Interleukin 6 (IL-6) is a proinflammatory cytokine whose levels are associated with the magnitude of surgical injury (Mari et al., 2016). In 2016, a RCT was published by Mari et al. investigating the levels of IL-6 in patients who received laparoscopic colorectal surgery under ERAS guidelines and conventional guidelines.

This study considered 140 patients who were randomly assigned to receive laparoscopic surgery under ERAS or conventional guidelines; 70 patients were enrolled in each group. Inclusion criteria consisted of: indication for major colorectal surgery, between the ages of 18 and 80, ASA score of I, II, or III, able to mobilize, and eligible for laparoscopic surgery. None of the demographic factors considered were statistically significant between groups. Before surgery, there was no significant difference in the concentration of IL-6 between patients in the ERAS and conventional groups. However, at each of the three time points (POD1, POD3, POD5), patients in the ERAS group had significantly lower levels of IL-6. Although there was no postoperative difference between levels of prolactin, white blood cells, nor cortisol between groups, levels of C-reactive protein (another proinflammatory agent) were significantly lower in patients receiving surgery under ERAS guidelines. As all patients received laparoscopic surgery, the ERAS program seems to have reduce the biological stress response associated with colorectal surgery.

Patients who received surgery under ERAS were discharged from hospital earlier, 5±2.6 days, than patients who received surgery under standard guidelines, 7.2±3 days, statistically significant at $p<0.05$. There was no significant difference in overall complication rate (i.e., portion of patients who developed any given complication), nor rates of any specific complication.

1.5.3. Potential Negative Impact on Patient Outcomes

Although there is a great amount of literature demonstrating that compliance with ERAS guidelines can improve patient outcomes, it is important to consider one potential negative impact that this pathway may have. Marcotte et al. evaluated the association between ERAS implementation and development of postoperative acute kidney injury (AKI).

The study considered 132 patients undergoing an elective colorectal resection within an ERAS pathway at Cooper University Hospital and 379 propensity-matched patients undergoing the same procedure at the same institution during the three years prior ERAS (Marcotte et al., 2018). Patients were matched according to the following variables: age, sex, ASA score, procedure type, operative approach (laparoscopic or open surgery), presence of ostomy, and preoperative diagnosis. Additionally, there were no significant differences in BMI or preoperative comorbidities between the two groups.

A standard pathway of preoperative, intraoperative, and postoperative guidelines was followed. The pathway was consistent with many other evaluations of ERAS in the literature, however the pathway did include utilization of mechanical bowel preparation. Compliance with guidelines was unfortunately not reported. But as LOS in the intervention group was significantly shorter than in the control group (5.5 days vs. 7.7 days, $p<0.0001$), one can at least

speculate that compliance was relatively high.

The major finding in this study was that the rate of postoperative AKI in patients who received surgery during the ERAS program was significantly greater than in those patients who received surgery before the protocol was introduced (11.4% vs 2.3%, $p < 0.0001$). AKI was defined in accordance with the Kidney Disease Improving Global Outcomes (KDIGO) criteria (Table 1.3).

Table 1.3: Kidney Disease Improving Global Outcomes (KDIGO) staging for AKI severity (Marcotte et al., 2018)

Stage	**Serum creatinine (SCr)**	**Urine output**
1	1.5-1.9x increase from baseline SCr **OR** ≥0.3 mg/dL increase in SCr within 48 hours	<0.5 mL/kg/h for 6 h
2	2.0-2.9x increase from baseline SCr	<0.5 mL/kg/h for 12 h
3	≥3x increase from baseline SCr **OR** Increase in SCr to ≥4 mg/dL **OR** Initiation of renal replacement therapy	<0.3 mL/kg/h for 24 h **OR** Anuria for 12 h

The authors do not state an exact reason for the increased rate of AKI associated with introduction of an ERAS protocol. They note that chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease, and cardiovascular disease are known perioperative risk factors for AKI, and that hypotension, anemia, and the use of nephrotoxic agents can contribute to AKI development. However, in their study, only diagnosis of diverticulitis and increased intraoperative time were predictors of AKI. Although several potentially nephrotoxic drugs (ketorolac, celecoxib, and gabapentin) are a component of the ERAS pathway, they were not determined to be predictors of AKI development.

One concept that has been hypothesized in the literature is that the postoperative fluid restriction guideline within the ERAS pathway has the potential to lead to renal dysfunction. This was refuted in a randomized observer-blinded multicenter trial from 2017, demonstrating that implementation of a reduced intraoperative and postoperative fluid program decreased overall complication rate, and did not increase the rate of postoperative renal failure (Brandstrup et al., 2017). A retrospective review, also from 2017, evaluated the impact of ERAS implementation on postoperative renal function. The study showed no significant increase in postoperative creatinine or AKI associated with ERAS implementation (Horres et al., 2017).

More research is necessary to determine if there is truly an association between compliance with ERAS guidelines and the development of AKI, but special attention should be payed to the development of this adverse outcome, and any preventative measures should be taken. The Marco et al. paper is virtually the extent of publication on negative implications associated with adherence to ERAS guidelines. As adverse outcomes resulting from ERAS is an important and relatively unexplored area, it is an essential topic for future research.

1.6. Impact of Deviation from ERAS Guidelines

The ERAS pathway is a somewhat complex series of clinical guidelines that have been shown to improve the overall recovery process of a patient undergoing major surgery, and it is not realistic to assume that every guideline will be followed for all patients. It has been documented that deviation from preoperative guidelines is rare, but that postoperative guideline deviation is much more common (Smart et al., 2012). This section aims to review existing literature regarding the impact of deviation from guidelines in the ERAS pathway.

The first study to be discussed is a retrospective review of laparoscopic colorectal resections that took place under an ERAS pathway in Yeovil Hospital between 2002 and 2009.

The intention of the study was to determine which guidelines, when compliance was violated, are most associated with a delayed discharge from hospital. The study reviewed patient records from 385 colorectal resections and performed univariate and multivariate analysis.

Univariate analysis determined that prolonged length of stay was predicted by the following: operation time of five hours or longer, blood loss >500ml, IV infusion after POD1, lack of functioning epidural, failure to mobilize on POD1, vomiting requiring nasogastric insertion, and re-insertion of urinary catheter. Table 1.4 provides the odds ratios (OR) for each predictor of delayed discharge.

Table 1.4: Predictors of increased LOS from univariate analysis (Smart et al., 2012)

Predictor	Odds Ratio	P-Value
Operation time of 5 hours or longer	2.02	0.027
Blood loss >500 ml	3.11	0.002
Presence of a stoma	1.94	0.002
IV infusion after POD1	4.80	<0.001
Lack of functioning epidural	1.89	<0.001
Failure to mobilize on POD1	7.50	<0.001
Vomiting requiring nasogastric insertion	11.27	<0.001
Re-insertion of urinary catheter	4.07	0.001

A multivariate analysis was also performed which determined that presence of a stoma, continuation of intravenous (IV) fluids, failure to mobilize on POD1, vomiting requiring nasogastric tube, and re-catheterization together are predictors of prolonged hospital stay for colonic resections in an ERAS pathway. Table 1.5 presents the OR and p-values for each of these

predictors.

Table 1.5: Predictors of increased LOS from multivariate analysis (Smart et al., 2012)

Predictor	Odds Ratio	P-Value
Presence of a stoma	2.53	0.001
IV infusion after POD1	2.20	0.006
Failure to mobilize on POD1	4.31	<0.001
Vomiting requiring nasogastric insertion	6.71	<0.001
Re-insertion of urinary catheter	2.33	0.051

Another study demonstrating the impact, on patient outcomes, of deviation from the ERAS pathway was published in 2017 by Pisarska et al. This was a prospective cohort study that investigated 251 consecutive patients undergoing elective colorectal surgery within an ERAS quality improvement program in a Polish hospital between January 2013 and July 2016. Inclusion criteria were: over the age of 18, colorectal adenocarcinoma, laparoscopic resection of the colon and/or rectum, and perioperative ERAS care. Patients were excluded from the study if: surgery was initially open or emergent, patients were treated with transanal endoscopic microsurgery or transanal total mesorectal excision, patients had multivisceral resection or concomitant inflammatory bowel disease, or if they were admitted to intensive care directly after surgery.

As mentioned in section 1.4., there are many reasons for deviation from compliance (from mobility issues to simple reluctance). Although the ERAS protocol was enforced for the 251 patients considered in the Pisarska study, the protocol was by no means perfectly followed. For statistical analysis, patients were divided into three groups depending on the percent of

ERAS guidelines that were followed for their surgery. Group 1 consisted of 70 patients who received less than 70% of guideline compliance. Group 2 consisted of 65 patients who received between 70 and 90% of ERAS guideline compliance. Finally. Group 3 consisted of 116 patients who received greater than 90% guideline compliance. A major limitation in this study is that the specific guidelines which were adhered in each group are unknown. To simply divide the 251 surgeries into three groups based on proportion of overall guidelines followed is to assume that all guidelines would equally impact patient outcomes. This is certainly not the case, as was demonstrated in the Smart et al., 2012 study. However, the study will still be discussed as it presents further evidence for the need to strive for compliance with as many ERAS guidelines as is possible and realistic for a given patient.

The three groups were not significantly different in any of the patient demographics compared (age, sex, BMI, and ASA score). Mean length of stay decreased significantly from 7.81 to 4.94 to 4.54 in Groups 1, 2, and 3, respectively (with increasing compliance with guidelines). There was no significant relationship between guideline compliance and readmissions. 8.6% of patients in Group 1, 4.6% of Group 2, and 6.9% of Group 3 were readmitted after discharge from hospital. Although there was no significant difference in complication rate between patients in Group 1 or Group 2, the difference between Group 1 and Group 3, as well as between Group 2 and Group 3, was in fact significant. This study demonstrates that within an ERAS quality improvement initiative, the extent to which guidelines are followed can significantly predict patient outcomes (Pisarska et al, 2016).

1.7. Economic Impact of an ERAS Program

One factor that can drive implementation of an ERAS program is cost associated with major surgery and subsequent recovery time in hospital. It has been documented that after

implementing ERAS guidelines, cost of care associated with surgery can decrease significantly. This can be the result of a faster and more efficient postoperative recovery process, and a decrease in the number of readmissions to hospital (Thanh et al., 2016). An article published in 2016 by Thanh et al. demonstrates this economic impact as they evaluated an ERAS implementation program for colorectal surgeries in six Albertan hospitals.

Alberta Health Services (AHS) is a health system that is responsible for providing medical care to the entire population of Alberta, approximately 4 million people. In February 2013, an ERAS implementation program was initiated by AHS in which six hospitals adopted ERAS Society guidelines for all elective colorectal procedures. These six hospitals perform 75% of all colorectal surgeries in the province of Alberta. The study considered 331 colorectal surgeries that took place before the change in practice, and 1,295 colorectal surgeries that took place under ERAS guidelines. Patient outcomes of interest were LOS in hospital for the initial procedure, post-discharge readmissions, LOS for patients who were readmitted, post-discharge complications which did not require readmission but did require a visit to the emergency department (ED), and post-discharge visits to a general practitioner (GP). The study aimed to estimate the health care costs and savings associated with an implementation of the ERAS program.

It was determined that upon implementation of the ERAS program, compliance with guidelines reached 73% and LOS decreased significantly from a mean value of 9.04 days in the control group to 7.50 days in the ERAS group. This program also resulted in a decrease in the following outcomes within 30 days of discharge: rate of readmission, LOS for readmissions, and visits to ED and GP. Although these were not statistically significant, they were deemed clinically relevant and were therefore considered in the estimation of healthcare savings. Based

on these patient outcomes, it was estimated that the ERAS program resulted in a savings of $1,768 per patient, or a total of $2,290,000. Based on this estimate and the resources invested into the program, the return on investment (ROI) was $3.8 for every $1 invested.

Another study published in 2015 set out to evaluate the cost-effectiveness of an ERAS program for colorectal surgery happening at one university-affiliated teaching hospital in Montreal, Canada (Lee et al., 2015). It was a prospective cohort study that utilized in comparison another university-affiliated teaching hospital in the same city that managed perioperative care for colorectal patients with conventional guidelines. Although this might seem to be a fair comparison (as the hospital is in the same city and the procedures being performed are the same) there is a major opportunity for underlying differences between the quality of care provided by nurses, surgeons, anesthetists, and other health care providers at the two hospitals. This is a limitation that should at least be considered in the analysis of this study.

The study considered a total of 190 patients who received colorectal surgery: 95 patients from each hospital. Patients were followed forward for 60 days and patient outcomes considered were length of stay, complications, ED visits, and readmissions. The mean LOS was 6.5 days in the hospital that followed ERAS guidelines. This was significantly shorter than the LOS of 9.8 days in the hospital providing conventional care. Rates of complications and readmissions, and visits to ED within the 60-day follow up period were not significantly different between groups.

In terms of an economic evaluation, this article states that at this hospital the total annual cost of implementing the ERAS program is $108,770 including a full time ERAS coordinator, ERAS steering committee expenses, and patient education material (see Table 1.6). However, this includes procedures other than colon resections such as gastroesophagectomy, pulmonary resection, and prostatectomy. It was estimated that it costed $153 per patient to implement this

program. The primary finding in this study was that patients who received surgery under ERAS guidelines had significantly lower societal costs. Societal costs in this study was defined to include productivity loss, caregiver burden, and out-of-pocket expenses. The mean reduction in societal costs in the ERAS surgeries was $2,895. However, the study did not find any significant difference in institutional or health care system costs.

Table 1.6: Breakdown of ERAS implementation cost (Lee et al., 2015)

	Cost (2013 CAD$)
Full-time ERP nurse coordinator (annual salary)	81,225
Opportunity costs of ERP steering group (1 hr/meeting × 26 meetings)	14,320
Nurse specialists and managers, nutritionist, physiotherapist, librarian, clinical leaders from surgery and anesthesia ($550 per meeting)	
Patient education material (operating costs of work performed by a medical informatics centre)	13,225
Total	108,770

A final study to be discussed in this section is a single-center case-matched study to determine the extent to which cost can be minimized by adhering to ERAS guidelines and performing laparoscopic surgery rather than open surgery for colon resections. The study was published in 2016 and compared three groups of colon resections at Jagiellonian University Medical College in Krakow, Poland. Group 1 consisted of 33 patients who received laparoscopy under ERAS guidelines. Group 2 consisted of 33 patients undergoing laparoscopy under conventional guidelines. Group 3 consisted of 33 open surgery under conventional guidelines.

The median LOS was 3 days for patients in group 1, 6 days for patients in group 2 and 9 days for patients in group 3. The mean (± SD) cost per patient was $2,739 ±596.55 in Group 1, $3,532.95 ±630.15 in Group 2, and $3,689.25 ±863.55 in Group 3 (For consistency purposes, figures reported in Euros were converted to Canadian Dollars at a rate of 1.50). Each incremental cost was significantly different. This study demonstrates not only that adherence to ERAS guidelines significantly decreases cost associated with colorectal resection, but so does laparoscopy in comparison to open surgery (Pedziwiatr et al., 2016).

1.8. The ERAS Society

The ERAS Society is an association whose mission is to "develop perioperative care and to improve recovery through research, education, audit and implementation of evidence based practice" (ERAS Society, 2017). In 2001, at a nutrition symposium in London, England, Ken Fearon and Olle Ljungqvist met and considered the idea of starting a multidisciplinary group on perioperative surgical care. The ERAS Study Group was initially formed in 2001 to investigate and expand on ideas for multimodal surgical care, which were put forth by Dr. Henrik Kehlet in the 1990's. This group determined that the multimodal care provided in different units, and what was considered best practice, varied greatly. In 2005, the ERAS study group came to an evidence-based consensus protocol for best practice guidelines for colonic surgery. At a meeting in Amsterdam in 2010, the formation of the ERAS society was decided. Later that year, the society was fully registered as a non-profit medical society (ERAS Society, 2017).

1.9. ERAS in NL

In 2016, EH initiated a major change in practice for all elective colorectal resections taking place at SCMH. As of March 1, 2016, physicians agreed to comply with ERAS guidelines for elective colorectal resections. The ultimate long-term goal is to implement ERAS for other

surgeries at EH and eventually other regional health authorities (RHA) (Pridham, 2018). As ERAS is a well-established set of guidelines that has proven successful in many populations, it was deemed safe and acceptable to enforce ERAS guidelines for all forthcoming elective colorectal surgeries (Ballah, 2017). This thesis sets out to perform an evaluation of compliance with guidelines and patient outcomes from this quality improvement initiative. It is the first assessment of an ERAS program in NL, and is necessary as it will assist with the development and implementation of future ERAS initiatives in this province.

1.10. Research Question

1.10.1. General Research Question

At the broadest level, the research question is to determine if the ERAS quality improvement program at SCMH was successful at increasing compliance with best practice guidelines and improving patient outcomes for elective colorectal resections. It is also to determine whether more quality improvement initiatives should be implemented at other sites in NL, and how compliance and patient outcomes could be improved in such initiatives.

1.10.2. Specific Research Question

The specific research question is as follows:

"Was the Enhanced Recovery After Surgery (ERAS) quality improvement initiative for elective colorectal resections at St. Clare's Mercy Hospital (SCMH) associated with decreased length of stay in hospital compared to baseline when the program was not in existence?"

Chapter 2: Methods

The objective of Chapter 2 is to describe the study design and research methods that have been employed to conduct this project. Definitions will be provided for patient factors (demographic and prognostic) and patient outcomes. Procedures for collection and analysis of data will also be explained.

2.1. Research Design

This section defines experimental research, non-experimental research, and describes the particular study design employed in this project.

2.1.1. Experimental and Non-Experimental Research

At the broadest level, it is generally accepted that there are two branches of research design: experimental and non-experimental. In experimental research, the investigator is directly involved with the exposure of patients to either a control or intervention treatment. Patient assignment is typically performed in a randomized manner, and there is a high degree of evidence that patient outcomes are a result of the intervention. In non-experimental studies, however, the investigator does not decide which individuals will be exposed to a particular intervention. Rather, (i) the investigator evaluates patient outcomes of individuals based on a previous exposure, or (ii) the investigator evaluates the exposure status of patients based on the presence, absence, or degree of a particular outcome. Non-experimental studies are weaker in terms of their ability to suggest causation between the exposure and outcome (Murphy, 2015, p. 51-52). In this study, patient outcomes are evaluated based on the exposure status. Specifically, outcomes are compared between patients who received surgery during the ERAS program and those who received surgery before this period. For this reason, the study is non-experimental in

design.

2.1.2. Interrupted Time-Series Analysis

Interrupted time-series analysis was applied in this research project. Generally, this involves performing multiple observations of a population over time, before and after an intervention, to ascertain whether the intervention affected the outcome (National Center for Biotechnology Information, 2017). In this study, elective colorectal resection patients at SCMH were retrospectively examined for two years before the ERAS intervention and were monitored for one year after the intervention. The goal was to determine if this intervention changed patient outcomes.

2.1.3. Surgery Timelines

Data from three sets of elective colorectal resections were used to perform this analysis. The first group of surgeries were performed during the fiscal year of 2014 (from April 1, 2014 to March 31, 2015). As these surgeries took place before implementation of ERAS, this is the control group. A thorough rationale for selection of the control group in this study is described in *2.1.4. Choice of Control Group*. The next group of surgeries constitutes the intervention group. These surgeries took place in the first twelve months of the ERAS quality improvement initiative (March 1, 2016 to February 28, 2017). A full-time ERAS Coordinator, Erin Ballah, supervised and promoted compliance with guidelines for the first six months of this quality improvement program. There was no supervision of guideline compliance in the second six months of the initiative as her position changed, and she became involved with supervision of ERAS guidelines for other procedures.

Data from surgeries that took place in the 11 months between the control year and intervention year (April 1, 2015 - February 29, 2016) were also collected and will be referred to

as the intermediate year. These data were used to determine if patient outcomes in the control year were representative of patient outcomes before this change in practice. Table 2.1 below presents each surgery group and their respective timeline.

Table 2.1: Timelines for each surgery group

Surgery Group	Dates
Control	April 1, 2014 - March 31, 2015
Intermediate	April 1, 2015 - February 29, 2016
ERAS	March 1, 2016 - February 28, 2017
First six months of ERAS	March 1, 2016 - August 31, 2016
Second six months of ERAS	September 1, 2016 - February 28, 2017

2.1.4. Choice of Control Group

Choosing an appropriate control or comparison group is vital to research. It sets a benchmark from which intervention-related outcomes can be measured. A control group should be virtually identical to the intervention group in terms of demographic and prognostic factors that may influence the outcome variable, and should differ only in the variable being examined (Murphy, 2015. p.58). When selecting a group of control surgeries for this project, it was important that the surgeries took place before implementation of ERAS guidelines, and that the population was likely to have been similar to the intervention group in terms of demographic and prognostic factors. Surgeries at the same site (SCMH) and with the same general procedure (elective colorectal) were chosen for this reason.

Another consideration is that compliance with guidelines and patient outcomes should be a true representation of standard practice for elective colorectal resections at SCMH before ERAS implementation. It might seem that the most similar group of patients would be those

receiving surgery in the year leading up to the initiative. At this time, however, physicians were being trained in ERAS compliance and were learning the benefits of following the guidelines (Ballah, 2017). Compliance was likely greater than usual at this time.

The selected control group are elective colorectal surgeries that took place in the 2014 fiscal year at SCMH. As these surgeries were performed at the same site as the ERAS program, patients are likely to be demographically and prognostically similar. As the control surgeries took place before educating physicians on ERAS guidelines, compliance and patient outcomes are likely representative of routine practice before ERAS implementation.

2.1.5. Surgery Group Comparisons

Three main comparisons were performed for this thesis. The first is a comparison of control and intermediate group surgeries. If patient outcomes between these groups are not significantly different, we can confidently consider the control year as representative of elective colorectal resections performed before the change in practice to ERAS guidelines. The second comparison, but the primary comparison in this thesis, is between the control year and the ERAS year. This will determine the impact of introducing an ERAS quality improvement program on patient outcomes. Finally, patient outcomes were compared between the first and second six months of ERAS. As guidelines were supervised in the first six months, but not the second six months, this comparison served to indicate the impact of supervision on compliance with guidelines and on patient outcomes. With any quality improvement initiative or change in practice, the sustainability of the change is important to consider. If compliance with guidelines were to deteriorate in the second six months of ERAS (without supervision of compliance), this would suggest a need to consider methods for ensuring this initiative is sustainable in the long term.

Table 2.2: Summary of surgery groups compared

	Surgery groups to be compared		Comparisons
(1)	Control	Intermediate	● Patient factors ● Patient outcomes
(2)	Control	ERAS	● Patient factors ● Patient outcomes ● Guideline compliance
(3)	First six months ERAS	Second six months ERAS	● Patient factors ● Patient outcomes ● Guideline compliance

2.1.6. Choice of Primary and Secondary Outcomes

The primary outcome for this thesis is LOS, as the central purpose of the ERAS initiative was to reduce the amount of time necessary for patients to make a full recovery after an elective colorectal resection at SCMH (Ballah, 2017). All other outcomes were considered secondary.

Compliance with guidelines was monitored to determine the extent to which implementing a quality improvement initiative increased compliance with ERAS guidelines, and also to determine the impact of guideline supervision by an ERAS Coordinator in the first six months of the initiative. Rates of complication, 30-day mortality, and 30-day readmission were also evaluated to determine if these adverse outcomes occur more or less frequently when the ERAS quality improvement initiative was implemented. Although it is hypothesized that complications, readmission and mortality rates will decrease, as long as they did not increase it will be considered clinically relevant: if it is possible to decrease LOS without significantly increasing readmissions, mortality, or readmissions, then this would indicate that it is possible to decrease overall healthcare resources for these surgeries without impairing the patient recovery experience.

2.2. Definitions

This section provides a description of patient factors (sex, age, comorbidity) and patient outcomes (LOS, complication rate, 30-day readmission rate, and 30-day mortality rate) that will be reported in the results section of this thesis.

2.2.1. Patient Factors

Demographic factors (sex and age) and one prognostic factor (comorbidity) were compared between each group to determine the similarity of patient populations. The following is a description of each factor:

(1) Sex: Percent of males and females in each group were compared to determine if there was a difference in the distribution of sex between groups.

(2) Mean Age: The mean age of each group was compared to determine if one group was significantly older than the other.

(3) Comorbidity: Percent of patients in each comorbidity class were compared to determine if either group had significantly greater comorbidity (percent impact on resource consumption is coded by HIM). The four comorbidity classes are as follows:

0: No significant comorbidity (0 to 24% impact on resource consumption)

1: Level 1 comorbidity (25% to 49% impact on resource consumption)

2: Level 2 comorbidity (50% to 74% impact on resource consumption)

3: Level 3 comorbidity (75% to 124% impact on resource consumption)

4: Level 4 comorbidity (125% or higher impact on resource consumption)

2.2.2. Patient Outcomes

LOS in hospital, complication rate, 30-day readmission rate, and 30-day mortality rate were the four patient outcomes evaluated in this study. The following is a description of each outcome:

(1) Length of stay in hospital: date and time of patient admission and discharge was obtained for all procedures. LOS in hospital represents the number of days that a patient remained in hospital for the procedure and recovery.

(2) Complication rate: the proportion of patients in a particular surgery group that experienced a complication during surgery.

(3) 30-day readmission rate: the proportion of patients in a particular surgery group that were readmitted to hospital within 30 days of their initial discharge. These include readmissions to sites other than that of their initial procedure (SCMH).

(4) 30-day mortality rate: the proportion of patients that died within 30 days of their procedure.

2.3. Ethical Review

Ethics approval was sought from the Health Research Ethics Board (HREB). The HREB Application for General Research form was completed, and full approval was received on July 5, 2016.

2.4. Data Collection

This section describes the process of data collection for patient factors (demographic and prognostic), compliance with ERAS guidelines, and patient outcomes. Meditech is the electronic health record database used by EH (Ballah, 2017), and is the primary source of data for this

project.

2.4.1. Patient Factors and Patient Outcomes

When a patient arrives at the hospital on the day of surgery, date and time of admission is recorded as part of the normal administrative process. The same type of information is also recorded upon discharge from hospital. Preoperative, intraoperative, and postoperative notes are made by the resident or physician in a process informally referred to as "dictation". Descriptive notes include all pertinent information about the procedure and recovery process such as (but certainly not limited to) preoperative anesthesia, procedure description, postoperative food consumption, mobilization, and catheter removal. Information on admission and discharge, and dictation notes are later entered into Meditech.

A team of coders with EH, known as Health Information Management Professionals (HIM), are responsible for organizing and processing data from the surgical procedures. This includes organizing notes on adverse outcomes into specific complications such as "urinary tract infection", or "paralytic ileus". Table 2.3 provides a complete list of all coded complications considered in this study. HIM determine whether a patient was readmitted (to the same or a different hospital) within 30 days of discharge. This is coded as "30-day readmission". They also determine whether a patient died within 30 days of their initial procedure. This is coded as "30-day mortality". HIM also note the impact that a particular patient had on resource consumption which is coded as comorbidity. Complication, readmission, mortality, and comorbidity codes are entered directly into Meditech. The ERAS Coordinator retrieved data on admission and discharge dates, complications, readmissions, mortality, and patient factors for elective colorectal patients in the specified time periods. This was stored on an excel file on a secure computer.

Table 2.3: List of surgical and postoperative complications considered

Abnormal findings on diagnostic imaging of heart and coronary circulation	Cardiac arrest, unspecified	Flatulence and related conditions
Abnormal levels of other serum enzymes	Cerebral infarction, unspecified	Fluid overload
Accidental puncture and laceration during a procedure, not elsewhere classifie	Chest pain, unspecified	Foreign body in respiratory tract, part unspecified
Acidosis	Chronic cholecystitis	Gastroenteritis and colitis of unspecified origin
Acute and subacute hepatic failure	Congestive heart failure	Gastrointestinal haemorrhage, unspecified
Acute pain	Constipation	Generalized skin eruption due to drugs and medicaments
Acute peritonitis	Cough	Haemorrhage and haematoma complicating a procedure, not elsewhere classified
Acute posthaemorrhagic anaemia	Cutaneous abscess, furuncle and carbuncle, unspecified	Haemorrhage of anus and rectum
Acute pulmonary insufficiency following nonthoracic surgery	Dehydration	Hepatic failure, unspecified
Acute renal failure, unspecified	Delirium not superimposed on dementia, so described	Hyperglycaemia, unspecified
Acute subendocardial myocardial infarction	Delirium, unspecified	Hyperkalaemia
Acute vascular disorders of intestine	Depressive episode, unspecified	Hyperosmolality and hypernatraemia
Alkalosis	Disorders of magnesium metabolism	Hypokalaemia
Anaemia, unspecified	Disorientation, unspecified	Hypo-osmolality and hyponatraemia
Anaphylactic shock, unspecified	Disruption of operation wound, not elsewhere classified	Hypotension, unspecified
Anxiety disorder, unspecified	Dizziness and giddiness	Ileus, unspecified
Ascites	Duodenal ulcer, acute with haemorrhage	Infection and inflammatory reaction due to other and unspecified cardiac and v
Asphyxia, unspecified	Duodenal ulcer, chronic or unspecified with both haemorrhage and perforation	Infection and inflammatory reaction due to other internal prosthetic devices,
Atelectasis	Dyspnoea	Infection following a procedure, not elsewhere classified
Atrial fibrillation, unspecified	Dysuria	Iron deficiency anaemia secondary to blood loss (chronic)
Bacterial infection, unspecified	Enterocolitis due to Clostridium difficile	Iron deficiency anaemia, unspecified
Bloodstream infection and inflammatory reaction due to central venous catheter	Enterostomy malfunction, not elsewhere classified	Laceration of colon without open wound into cavity
Bronchopneumonia, unspecified	Fever, unspecified	Laceration of small intestine, excluding duodenum with open wound into cavity
Candidiasis of vulva and vagina	Finding of other specified substances, not normally found in blood	Lobar pneumonia, unspecified
Cardiac arrest with successful resuscitation	Fistula of intestine	Localized oedema

Table 2.3: List of surgical and postoperative complications considered (continued)

Malfunction of colostomy stoma, not elsewhere classified	Paralytic ileus	Syncope and collapse
Melaena	Paroxysmal atrial fibrillation	Systemic inflammatory response syndrome of infectious origin with acute organ
Mental and behavioural disorders due to use of alcohol, harmful use	Perforation of intestine (nontraumatic)	Tachycardia, unspecified
Nausea alone	Peritoneal adhesions	Transient alteration of awareness
Nausea with vomiting	Persistent postoperative fistula	Unspecified abdominal hernia with obstruction, without gangrene
Orthostatic hypotension	Phlebitis and thrombophlebitis of other deep vessels of lower extremities	Unspecified urinary incontinence
Other and unspecified abnormal results of cardiovascular function studies	Pleural effusion, not elsewhere classified	Urinary tract infection, site not specified
Other and unspecified dysphagia	Pneumonia, unspecified	Vascular complications following a procedure, not elsewhere classified
Other and unspecified intestinal obstruction	Pneumonitis due to food and vomit	Ventricular tachycardia
Other and unspecified polyuria	Postoperative intestinal obstruction	
Other and unspecified skin changes	Postoperative leak	
Other complications of anaesthesia	Postprocedural pelvic peritoneal adhesions	
Other complications of procedures, not elsewhere classified	Postprocedural pneumothorax	
Other delirium	Postprocedural renal failure	
Other disorders of electrolyte and fluid balance, not elsewhere classified	Pulmonary embolism without mention of acute cor pulmonale	
Other forms of acute ischaemic heart disease	Pyothorax without fistula	
Other pruritus	Resistance to methicillin	
Other specified abnormal findings of blood chemistry	Respiratory failure, unspecified, type I [hypoxic]	
Other specified complications of cardiac and vascular prosthetic devices, impl	Respiratory failure, unspecified, type II [hypercapnic]	
Other specified disorders of male genital organs	Restlessness and agitation	
Other specified disorders of muscle, multiple sites	Retention of urine	
Other specified disorders of penis	Seizure disorder, so described	
Other specified general symptoms and signs	Sepsis due to other Gram-negative organisms	
Other volume depletion	Sepsis, unspecified	
Painful micturition, unspecified	Septic shock	

2.4.2. Population Selection

The following International Classification of Diseases Version 10 (ICD-10) codes were used by the ERAS Coordinator to query Meditech and identify patients who received an elective colon resection:

Table 2.4: ICD-10 codes and definitions used to identify this study population

ICD Code	Definition
1NK87	Excision partial, small intestine
1NM87	Excision partial, large intestine
1NM89	Excision total, large intestine
1NM91	Excision radical, large intestine
1NQ87	Excision partial, rectum
1NQ89	Excision total, rectum
1NT87	Excision partial, anus
1NM82	Reattachment, large intestine
1NK82	Reattachment, small intestine
1NM77	Bypass with exteriorization, large intestine
1NK77	Bypass with exteriorization, small intestine
1NK80	Repair, small intestine

2.4.3. Compliance with ERAS Guidelines

The ERAS Coordinator reviewed charts of all patients in the control and ERAS surgery groups to determine compliance with each guideline. To ensure that this was objective, strict literature-based descriptions were used to define each guideline. Compliance or non-compliance was documented for each guideline, for every patient. The definitions used to determine compliance are listed below:

Table 2.5: Definitions for determination of compliance with ERAS guidelines

Guideline	Definition
Preadmission counselling	Was patient provided with written patient education material preoperatively?
Carbohydrate loading	Did patient consume carbohydrate beverage 3 hours before surgery?
No bowel preparation	Did patient receive bowel preparation (not including preoperative enema) – pico-salax or golytely?
Antibiotic prophylaxis	Did patient receive antibiotic prophylaxis treatment? Was the dosage repeated if surgery lasting > 4hrs?
Venous thromboembolism prophylaxis	Did patient receive thromboprophylaxis treatment – did patient receive low molecular weight heparin preoperatively and mechanical thromboprophylaxis via compression stockings or intermittent pneumatic compression?
Short acting anesthetics	Did patient receive short acting anesthetic agents, ie. short acting induction agents such as propofol combined with short acting opioid such as fentanyl, alfentanil remifentanil?
Thoracic epidural anesthesia for open surgery	Did patient receive intraoperative mid-thoracic epidural anesthesia/analgesia?
Fluid therapy	Was fluid administration guided by optimization of hemodynamic measurements including stroke volume, flow time corrected, pulse pressure variation, or stroke volume variation. This may include the use of non-invasive cardiac monitoring devices OR limited the total amount of intraoperative IV fluids to <= 8cc/kg/kr (*this amount is liberal, other hospitals have stricter guidelines)?
Laparoscopy	Did the patient receive laparoscopic surgery?
Maintenance of normothermia	Did patient remain normothermic – the first measured temperature on arrival to PACU >= 36.0^{o} C/96.8^{o} F?
Discontinuation of IV fluids after 24 hours	Were IV fluids discontinued within the first 24 hours following surgery (POD0-1)?

No nasogastric intubation	Did patient have any drains (ie. NG, JP, etc.) postoperatively?
Postoperative nausea and vomiting management	Did patient receive multimodal PONV management – only applicable if patient has >= 2 risk factors for PONV (female, nonsmoker, history of motion sickness, etc.), did patient receive intraoperative anti-emetic interventions including: anti-emetics, OR dexamethasone OR omission of nitrous oxide OR total IV anesthesia with propofol and remifentanil?
Foley catheter removal POD1	Was foley catheter removed within the first 24 hours following surgery (POD0-1)?
Clear fluids administered POD1	Did patient consume solids within the first 48 hours following surgery (POD1-2)?
Multimodal pain management	Did patient receive multimodal pain control approach – NSAID, acetaminophen, ketamine, glucocorticoids, IV lidocaine, TEA, spinal analgesia, regional blocks?
Early mobilization	Did patient mobilize BID POD1?
Chewing gum	Did patient chew gum x 5 minutes TID postoperatively?

2.4.4. Data Transfer

As previously mentioned, the initial data collected was stored on an excel file on a secure computer at EH. This was later transferred to the Center for Health Informatics and Analytics (CHIA) via a secure server. A Database Developer, Andrea Kavanagh, was responsible for de-identifying data: removing names and MCP numbers, and including a unique identifier for each patient. In order to access the data, a Translational and Personalized Medicine Initiative (TPMI) Statement of Confidentiality had to be completed. This indicated that the use of data would be only for the indicated research purpose, and that its contents would not be discussed outside of the expected role of a researcher. The Statement of Confidentiality has been attached as Appendix II.

2.5. Data Analysis

All data for this project was transferred from the Microsoft Excel file on which it was received, to the Statistical Package for the Social Sciences (SPSS) Version 23 for analysis. Primarily descriptive statistics were used in data analysis. The following six individual datasets were obtained:

- Baseline year procedures (April 1, 2014 - March 31, 2015)
- Intermediate year procedures (April 1, 2015 - February 29, 2016)
- First six months of ERAS procedures (March 1, 2016 - August 31, 2016)
- Second six months of ERAS procedures (September 1, 2016 - February 28, 2017)
- Guideline compliance for baseline surgeries
- Guideline compliance for ERAS surgeries

2.5.1. Data Organization and Inspection

Upon data acquisition, a thorough review was carried out to ensure that the specified population (surgery dates and procedures) was accurately captured. Initially, procedures in each of the four surgery periods (baseline, intermediate, first six months of ERAS, and second six months of ERAS) were sorted by date. As the entire fiscal year of 2015 was included in the intermediate surgery group, all procedures taking place after February 29, 2016 were removed: these were part of the ERAS program. All other surgeries received were within the timelines indicated above.

Procedure datasets were then inspected to ensure: they were elective procedures (as opposed to emergent), they were in fact resections of the colon, they took place at SCMH, there was one unique identifier representing each individual patient, and that there was no missing

data.

Compliance data was reviewed to determine that: there were the same number of patients in the baseline compliance dataset as the baseline procedure dataset, there were the same number of patients in the ERAS compliance dataset as the ERAS procedure dataset, the unique identifiers in the compliance datasets matched the unique identifiers in the procedure datasets, and that there was no missing compliance data for any patient.

2.5.2. Baseline Characteristics

Two of the baseline characteristics considered, sex and comorbidity, are categorical variables. A Pearson Chi-squared test was performed to determine if there was a significant difference in the distribution of these variables between groups. Age is a continuous variable, and therefore an independent sample t-test was performed to determine if there was a significant difference in mean age between any two given populations.

2.5.3. Primary Outcome: Length of Stay

Distribution of the continuous variable LOS (the primary outcome in this study) was considered. A frequency distribution was constructed. Also, the mean and median LOS were compared within each individual surgery group. The non-parametric nature of the outcome dictated the use of a Mann-Whitney U test to compare median LOS of any two groups.

2.5.4. Secondary Outcomes

The four secondary outcomes in this study (compliance with ERAS guidelines and rates of 30-day readmission, 30-day mortality, and complication) were categorical variables. For this reason, A Pearson Chi-squared test was performed to determine if there was a significant

difference in the distribution of these variables between groups.

2.5.5. Impact of Geography on LOS

A Kruskal-Wallis H test was performed to compare LOS of patients coming from each of the four provincial RHAs to determine if such travel was associated with a difference in recovery time.

Chapter 3: Results

This chapter presents research findings that have been obtained from all components of the study. Patient outcomes (LOS in hospital, complication rate, 30-day readmission rate, and 30-day mortality rate), demographic (sex and age) and prognostic (comorbidity) factors will be compared between groups of elective colorectal resections (control year, intermediate year, ERAS year, first and second six months of ERAS) as outlined in Chapter 2.

3.1. Control and Intermediate Year Surgeries

This section presents a comparison of the control and intermediate year surgeries.

3.1.1. Demographic and Prognostic Factors

Table 3.1: Demographic and prognostic factors for control and intermediate year surgeries

	Control (n=158)	**Intermediate (n=159)**	**Significance**	
			Statistical Test	P-value*
Sex **Male** **Female**	 87 (55.1%) 71 (44.9%)	 102 (64.2%) 57 (35.8%)	Pearson Chi-Squared	0.099
Age (mean ± SD)	60.76 ± 14.35	62.62 ± 13.96	Independent sample t-test	NS
Comorbidity **0** **1** **2** **3 or 4**	 102 (64.56%) 32 (20.25%) 15 (9.49%) 9 (5.60%)	 103 (64.77%) 21 (13.21%) 24 (15.09%) 11 (6.92%)	Pearson Chi-Squared	NS

NS: not significant; *Significance level is a=0.05 (P-value < 0.05: statistically significant difference)

Table 3.1 demonstrates that between patients in control and intermediate surgery groups, there is no significant difference in: distribution of sex; mean age; distribution of comorbidity.

3.1.2. Patient Outcomes

Table 3.2: Comparison of patient outcomes between control and intermediate surgeries

	Control (n=158)	**Intermediate (n=159)**	**Significance**	
			Statistical Test	P-value*
Median length of stay (IQR)**	7.26 (5.41-11.06)	7.20 (5.19-10.25)	Mann-Whitney U	NS
Total hospitalization time (days)	1797.1	1542.7	--	--
Complications (% of patients)	45.6%	39.0%	Pearson Chi-Squared	NS
30-day readmissions (% of patients)	8.86%	8.81%	Pearson Chi-Squared	NS
30-day mortality (% of patients)	1.27%	1.26%	Fisher's Exact	NS

NS: not significant; *Significance level is set at a=0.05(P-value < 0.05: statistically significant difference); **Days in hospital

Table 3.2 demonstrates that between patients in control and intermediate year surgery groups, there is no significant difference between: median LOS; complication rate, 30-day readmission rate; 30-day mortality rate.

3.1.3. Time to Event Analysis

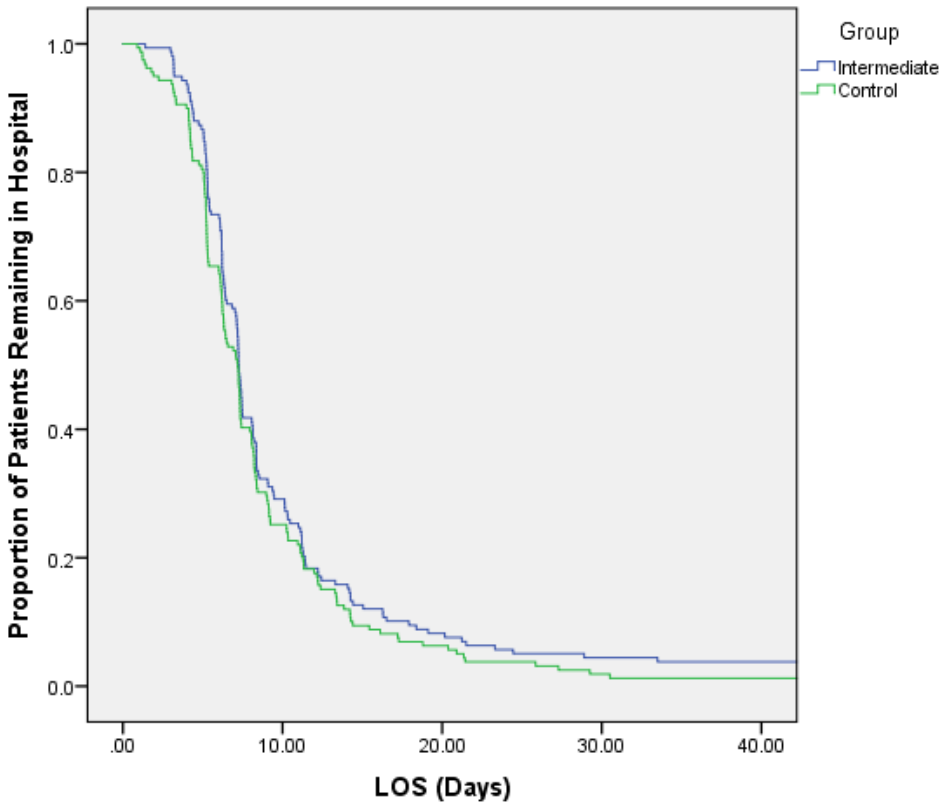


Figure 3.1: Time to event (discharge) analysis of control and intermediate surgeries

Figure 3.1 presents a time to event analysis of discharge from hospital for the control and intermediate groups. There is no significant difference between control and intermediate years. Median LOS (IQR) for the control year was 7.26 (5.41-11.06) and for the intermediate year it was 7.20 (5.19-10.25).

3.2. Control and Full ERAS Year Surgeries

This section provides a comparison of control and ERAS year surgeries.

3.2.1. Demographic and Prognostic Factors

Table 3.3: Comparison of demographic and prognostic factors between control surgeries and full year ERAS surgeries

	Control (n=158)	**ERAS (n=174)**	**Significance**	
			Statistical test	P-Value*
Sex **Male** **Female**	 87 (55.1%) 71 (44.9%)	 94 (54.0%) 80 (46.0%)	Pearson Chi-Squared	NS
Age (mean ± SD)	60.76 ± 14.35	64.71± 12.13	Independent sample t-test	0.007
Comorbidity **0** **1** **2** **3 or 4**	 102 (64.56%) 32 (20.25%) 15 (9.49%) 9 (5.60%)	 108 (62.1%) 24 (13.8%) 30 (17.2%) 12 (6.90%)	Pearson Chi-Squared	NS

NS: not significant; *Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference)

Table 3.3 demonstrates that between patients who received surgery in control and ERAS years, there was no significant difference in: distribution of sex; distribution of comorbidity. It also demonstrates that patients who received in the ERAS group were significantly older than those who received surgery in the control year.

3.2.2. Patient Outcomes

Table 3.4: Comparison of patient outcomes between control and ERAS year surgeries

	Control (n=157)	**ERAS Year (n=174)**	**Significance**	
			Statistical Test	P-value*
Median Length of Stay (IQR)**	7.26 (5.41-11.06)	6.27 (4.34-8.35)	Mann-Whitney U	0.002
Total hospitalization time (days)	1797.1	1597.0	--	--
Complications (% of patients)	45.6%	42.5%	Chi-Squared (Pearson)	NS
30-day Readmissions (% of patients)	8.86%	7.47%	Chi-Squared (Pearson)	NS
30-day Mortality (% of patients)	1.27%	1.15%	Fisher's Exact Test	NS

NS: not significant; *Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference); **Days in hospital

Table 3.4 demonstrates that patients who received surgery in the ERAS year had a significantly shorter LOS than those who received surgery in the control year. It also demonstrates that between patients who received surgery in the control and ERAS years, there was no significant difference in: complication rate; 30-day readmission rate; 30-day mortality rate.

3.2.3. Compliance with ERAS Guidelines

Table 3.5: Comparison of compliance with ERAS guidelines between control and ERAS surgeries

	Control	Full Year ERAS	P-Value*
Preoperative	63.9%	90.0%	0.00
Intraoperative	62.9%	72.3%	0.00
Postoperative	39.9%	73.9%	0.00
Overall	52.2%	77.7%	0.00

*Significance level is set at a=0.0 5 (P-value < 0.05: statistically significant difference); Pearson Chi-Squared was performed for all statistical analysis

Table 3.5 demonstrates that with introduction of the ERAS program, there was a significant increase in compliance with preoperative, intraoperative, and postoperative guidelines.

Table 3.6: Comparison of compliance with individual ERAS guidelines between control and ERAS surgeries

Guideline	Control	Full Year ERAS	P-Value*
Patient education	99.4%	100%	NS
Carbohydrate beverage	0.00%	70.7%	0.00
No bowel preparation	29.1%	81.0%	0.00
Antibiotic prophylaxis	98.1%	98.9%	NS
VTE prophylaxis	93.6%	98.8%	NS
Short acting anesthetic agents	98.7%	97.7%	NS
Epidural (for open surgery)	85.2%	84.7%	NS
Fluid restriction	22.3%	68.4%	0.00
Laparoscopy	12.1%	15.5%	0.00
Normothermia	99.4%	97.1%	NS
IV fluids discontinued POD1	15.2%	72.8%	0.00
No NG tubes	100%	100%	NS
Multimodal PONV management	93.6%	97.1%	NS
Foley catheter	14.7%	60.5%	0.00
Clear fluids POD0	43.6%	74.7%	0.00
DAT POD1	98.7%	63.2%	0.00
Multimodal pain management	79.1%	95.4%	0.00
Mobilization POD1	12.0%	54.3%	0.00
Chewing gum	0%	84.9%	0.00

*Significance level is set at a=0.0 5(P-value < 0.05: statistically significant difference); Pearson Chi-Squared was performed for all statistical analysis

Table 3.6 indicates percent compliance with individual guidelines before and after implementation of the ERAS initiative.

3.2.4. Time to Event Analysis

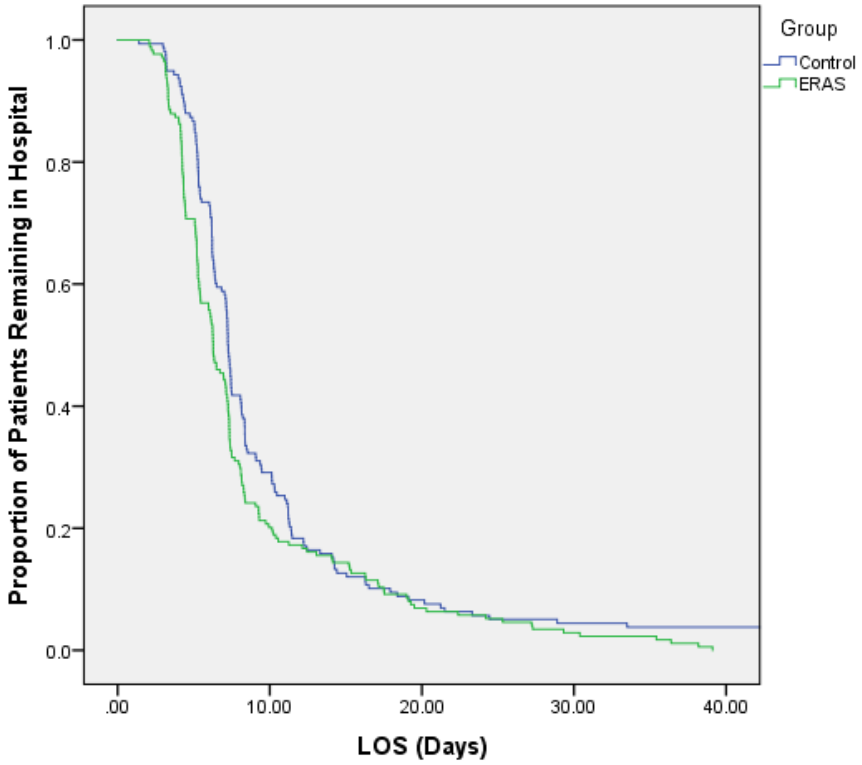


Figure 3.2: Time to event (discharge) analysis of control and full year ERAS surgeries

Figure 3.2 presents a time to event analysis of discharge from hospital for the control group and the full year of ERAS surgeries. There was a significant difference between control and ERAS years. Median LOS (IQR) for the control year was 7.26 (5.41-11.06) and for the ERAS year it was 6.27 (4.34-8.35).

3.3. First and Second Six Months of ERAS

This section provides a comparison of surgeries in the first and second six months of the ERAS program.

3.3.1. Demographic and Prognostic Factors

Table 3.7: Demographic and prognostic factors for the first and second six months of ERAS surgeries

	ERAS: First Six Months (n=87)	**ERAS: Second Six Months (n=87)**	**Significance**	
			Statistical test	P-Value*
Sex **Male** **Female**	 52 (59.8%) 35 (40.2%)	 42 (48.3%) 45 (51.7%)	Pearson Chi-Squared	NS
Age (mean ± SD)	63.87 ± 11.98	65.54 ± 12.28	Independent sample t-test	NS
Comorbidity **0** **1** **2** **3 or 4**	 54 (62.07%) 13 (14.95%) 15 (17.24%) 5 (5.75%)	 54 (62.07%) 11 (12.64%) 15 (17.24%) 7 (8.05%)	Pearson Chi-Squared	NS

NS: not significant; *Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference)

Table 3.7 demonstrates that between patients who received surgery in the first and second six months of the ERAS program, there was no significant difference in: distribution of sex; mean age; distribution of comorbidity.

3.3.2. Patient Outcomes

Table 3.8: Patient outcomes for the first and second six months of ERAS surgeries

	Control (n=157)	**ERAS: First Six Months (n=87)**	**ERAS: Second Six Months (n=87)**	**Significance**	
				Statistical Test	P-value*
Median length of stay (IQR)**	7.26 (5.41-11.06)	5.44 (4.29-7.35)	7.10 (5.07-13.06)	Mann-Whitney U	0.010
Total hospitalization time (days)	1797.1	699.1	928.0	--	--
Complications (% of patients)	45.6%	41.4%	43.7%	Chi-Squared (Pearson)	NS
30-day Readmissions (% of patients)	8.86%	10.3%	4.60%	Chi-Squared (Pearson)	NS
30-day Mortality (% of patients)	1.27%	0.00%	2.30%	Fisher's Exact	NS

NS: not significant; *Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference); **Days in hospital

Table 3.8 demonstrates that patients who received surgery in the second six months of the ERAS program had a significantly longer LOS than those who received surgery in the first six months of the ERAS program. It also demonstrates that between patients who received surgery in the first and second six months, there was no significant difference in: complication rate; 30-day readmission rate; or 30-day complication rate.

3.3.3. Compliance with ERAS Guidelines

Table 3.9: Compliance with ERAS guidelines in the first and second six months of ERAS surgeries

	Control (n=157)	**ERAS: First Six Months (n=87)**	**ERAS: Second Six Months (n=87)**	**P-value***
Preoperative	63.9%	90.3%	89.0%	NS
Intraoperative	62.9%	73.6%	71.0%	NS
Postoperative	39.9%	79.2%	68.6%	0.00
Overall	52.2%	80.7%	74.7%	0.00

NS: not significant; *Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference); Pearson Chi-Squared was performed for all tests

Table 3.9 demonstrates that between surgeries in the first and second six months of ERAS surgeries, there was no significant difference in compliance with preoperative and intraoperative guidelines. It also shows that in the second six months of ERAS surgeries, postoperative and overall guideline compliance decreased significantly.

Table 3.10: Comparison of compliance with individual ERAS guidelines between the first and second six months of ERAS surgeries

Guideline	First Six Months	Second Six Months	P-Value*
Patient education	100%	100%	NS
Carbohydrate beverage	71.3%	70.1%	NS
No bowel preparation	82.8%	79.3%	NS
Antibiotic prophylaxis	97.7%	100%	NS
VTE prophylaxis	100%	97.7%	NS
Short acting anesthetic agents	98.9%	96.6%	NS
Epidural (for open surgery)	87.8%	81.6%	NS
Fluid restriction	67.8%	69.0%	NS
Laparoscopy	17.2%	13.8%	NS
Normothermia	98.8%	95.4%	NS
IV fluids discontinued POD1	83.7%	62.1%	0.00
No NG tubes	100%	100%	NS
Multimodal PONV management	94.3%	96.6%	NS
Foley catheter	64.0%	57.0%	NS
Clear fluids POD0	80.5%	69.0%	0.08
DAT POD1	64.4%	62.1%	NS
Multimodal pain management	94.1%	96.6%	NS
Mobilization POD1	63.2%	45.3%	0.02
Chewing gum	69.0%	28.7%	0.00

*Significance level is set at a=0.0 5 (P-value < 0.05: statistically significant difference); Pearson Chi-Squared was performed for all statistical analysis

Table 3.10 indicates percent compliance with individual guidelines in the first and second six months of the ERAS initiative.

3.3.4. Time to Event Analysis

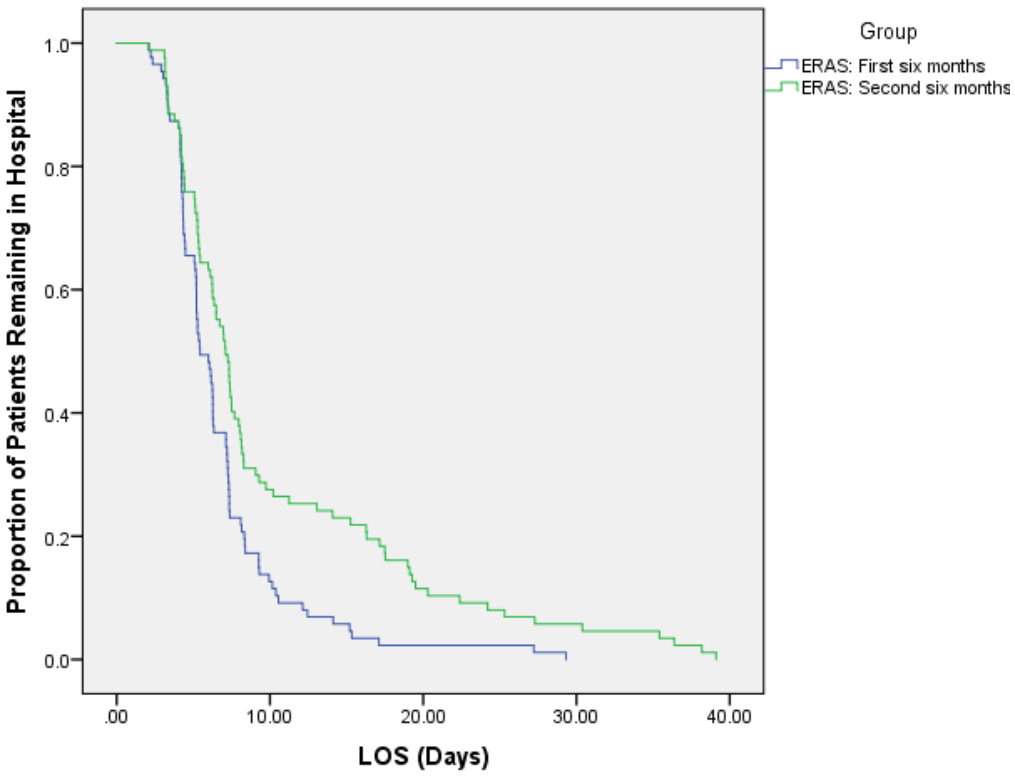


Figure 3.3: Time to event (discharge) analysis of first and second six months of ERAS

Figure 3.3 presents a time to event analysis of discharge from hospital for the first and second six months of ERAS surgeries. There was a significant difference between the first and second six months of ERAS. Median LOS (IQR) for the first six months was 5.44 (4.29-7.35) and for the second six months it was 7.10 (5.07-13.06).

3.4. Location of Patient Residence

Table 3.11: LOS for baseline surgeries partitioned into patients' RHA of residence

RHA	n	Median LOS (IQR)*	Significance (P-value**)
Eastern	140	7.24 (5.45-10.43)	NS
Central	4	5.28 (5.01-9.67)	
Western	11	8.34 (4.33-13.31)	
Labrador-Grenfell	2	8.46 (N/A***)	

LOS: length of stay; NS: not significant; RHA: Regional Health Authority; *Days in hospital; **Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference); ***inadequate number of patients to calculate IQR; Kruskal-Wallis H was performed for statistical analysis

Table 3.12: LOS for first six months of ERAS partitioned into patients' RHA of residence

RHA	n	Median LOS (IQR)*	Significance (P-value**)
Eastern	77	5.27 (4.25-7.27)	NS
Central	2	10.23 (N/A***)	
Western	2	9.73 (N/A)	
Labrador-Grenfell	6	8.80 (5.69-19.00)	

LOS: length of stay; NS: not significant; RHA: Regional Health Authority; *Days in hospital; **Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference); ***inadequate number of patients to calculate IQR; Kruskal-Wallis H was performed for statistical analysis

Table 3.13: LOS for second six months of ERAS partitioned into patients' RHA of residence

RHA	n	Median LOS (IQR)*	Significance (P-value**)
Eastern	76	7.29 (4.62-10.98)	NS
Central	2	11.73 (N/A***)	
Western	3	6.49 (N/A***)	
Labrador-Grenfell	5	6.36 (6.46-24.75)	

LOS: length of stay; NS: not significant; RHA: Regional Health Authority; *Days in hospital; **Significance level is set at a=0.05 (P-value < 0.05: statistically significant difference); ***inadequate number of patients to calculate IQR; Kruskal-Wallis H was performed for statistical analysis

Tables 3.11, 3.12, and 3.12 demonstrate that (in the baseline period, first six months of ERAS, and second six months of ERAS, respectively) there was no significant difference in LOS between patients who are residents of areas serviced by Eastern Health, Central Health, Western Health, and Labrador-Grenfell Health authorities.

3.5. Summary of Research Findings

The median LOS for colon resections that took place in the control year was 7.26 days. With implementation of the ERAS program, median LOS decreased significantly to 6.27 days. Interim analysis demonstrated that median LOS was 5.44 days after the first six months of ERAS and then regressed to 7.10 days in the second six months. Patients' RHA of residence did not significantly impact LOS. Overall compliance with ERAS guidelines increased significantly from 52.2% to 77.7% with implementation of the quality improvement program. However, there was a significant decrease in compliance with postoperative and overall guidelines between the first and second six months of the ERAS program.

Chapter 4: Discussion

This thesis investigated the impact, on patient outcomes and adherence to best practice guidelines, of implementing an ERAS quality improvement initiative for all elective colorectal resections at SCMH beginning in March 2016. Results revealed a significant decrease in LOS and a significant increase in compliance with best practice guidelines between surgeries that took place in the 2014 fiscal year (before the ERAS program was implemented) and those that took place in the first year of the ERAS program. There was a significant increase in LOS and a significant decrease in compliance with guidelines in the second six months of the ERAS program compared to the first six months of the ERAS program. Supervision of guideline compliance by a full-time ERAS Coordinator in the first six months could be an explanation for these findings. This chapter consists of a discussion of results, relevance and applicability of this research, and potential biases and limitations of the study.

4.1. Rationale for Selected Control Group

To ensure that the group of patients finally selected as the control group (April 1, 2014 to March 31, 2015) were indeed representative of patients receiving elective colorectal resections before implementation of the ERAS program, their outcomes were compared to patients who received surgery in the subsequent year (April 1, 2015 - February 29, 2016) who also did not receive surgery under ERAS guidelines. There were no significant differences in patient factors (age, sex, and comorbidity; Table 3.1) or patient outcomes (LOS, complication rate, 30-day readmission rate, and 30-day mortality rate; Table 3.2) between surgeries in the 2014 and 2015 fiscal years. The 2014 fiscal year was selected as the control group because ERAS compliance was a topic of discussion at SCMH in 2015 (Ballah, 2016), and thus guideline compliance may have been higher than usual.

4.2. Comparison of Control and ERAS Surgeries

Implementation of the ERAS program was associated with a significant increase in compliance with preoperative, intraoperative, postoperative, and overall ERAS guidelines (Table 3.5). With this increase in guideline compliance, a significant decrease in median LOS (0.99 days) was observed. However, there was no significant difference in rates of complication, 30-day mortality, or 30-day readmission. These results are relatively consistent with a meta-analysis of 13 RCTs of ERAS versus traditional care for colorectal cancer (Zhuang et al., 2013) which showed a decrease in LOS by 2.44 days, but no change in rates of readmission or mortality. The meta-analysis did, however, show a decrease in complication rate.

In this study, patients in the control and ERAS groups were distinct in terms of one demographic factor. Table 3.3 demonstrates that patients in the ERAS group were significantly older (64.71± 12.13) than patients in the control group (60.76 ± 14.35). It is unlikely that this age difference is exaggerating the observed difference in LOS. It might be expected that the older of the two groups would take longer to recover from surgery. In fact, the opposite result was observed. A study published in 2014 demonstrated an association between age and increased hospital stay in patients undergoing colorectal surgery (Bircan et al., 2014). Perhaps if the ERAS group was not significantly older than the control group, an increased difference in LOS would have been observed.

Although implementation of ERAS guidelines did not significantly decrease rates of complication, 30-day readmission, or 30-day mortality, the fact that these rates did not increase is clinically meaningful. Compliance with ERAS guidelines allowed patients to be discharged earlier without resulting in increased adverse outcomes (complications, readmissions, or mortality). This also indicates that the observed reduction in LOS is unlikely to be a result of bias

on the behalf of healthcare professionals in the ERAS program. If patients were discharged earlier than they should have been, due to the knowledge of a quality improvement program, one could plausibly expect increased rates of adverse outcomes. This was not the case.

Given the low mortality rate in our control group (1.27%), a very large sample size would have been needed to show that ERAS was successful at decreasing postoperative mortality. However, even the meta-analysis mentioned above, with a total of 1,910 patients, did not demonstrate a decrease in mortality rate with implementation of ERAS. Part of the reason that our study did not show a decrease in complication rate may have to do with the sheer number of events that were considered "complications" by HIM staff. Table 2.3 shows the 134 events that were considered complications in this study. Many of these seem to be incidental, and likely difficult to avoid, even with implementation of an ERAS program.

4.3. Comparison of First and Second Six Months of ERAS Surgeries

As mentioned in the methods section of this thesis, a full-time ERAS coordinator supervised guideline compliance in only the first six months of the ERAS quality improvement initiative. This makes a comparison of patient outcomes between the first and second six months necessary. There were no significant differences in patient factors (age, sex, or comorbidity) between the two groups, meaning that any difference in patient outcomes cannot likely be attributed to a difference between the patient populations. The only difference in patient outcomes was that patients in the second six months of ERAS had a significantly longer LOS (7.10 days) than those in the first six months of ERAS (5.44 days). In terms of compliance with guidelines, there was a significant decrease in postoperative and overall guideline compliance (Table 3.8). The decrease in guideline compliance can likely be attributed to the absence of the

coordinator in the second six months of the program whose role it was to supervise the use of guidelines.

4.4. Compliance with Postoperative Guidelines

To strengthen the argument that the increase in LOS observed in the second six months of ERAS was in part due to a decrease in postoperative guideline compliance, a discussion of current literature on the relationship of postoperative ERAS guideline compliance and patient outcomes is necessary.

In 2017, Aarts et al. published a paper based on a prospective analysis of ERAS programs in 15 academic hospitals in Ontario, Canada between September 2012 and April 2015 (Aarts et al., 2017). Inclusion criteria were: (i) patients undergoing elective colorectal surgery, (ii) age 18 or older. Exclusion criteria were: (i) patients undergoing multivisceral resection, ileostomy construction or reversal without bowel resection, or (ii) patients undergoing exclusively small bowel surgery. In total, 2,876 patients were considered for analysis. In addition to considering compliance with ERAS guidelines in the entire 2,876 patient cohort, patients were divided into an optimal recovery cohort (those who were discharged within five days after surgery, did not develop a major complication, were not re-admitted, and did not die within 30 days of surgery), and a delayed recovery cohort (those who did not meet the optimal recovery cohort criteria). Guideline compliance was highest in the preoperative period and was lowest in the postoperative period (Table 4.1).

Table 4.1: Guideline compliance for total, optimal recovery, and delayed recovery cohorts (Aarts et al., 2017)

Care Pathway	ERAS Recommendations	Compliance in Total Cohort n (%)	Compliance in Optimal Recovery Cohort (n = 1428)	Compliance in Delayed Recovery Cohort (n = 1448)	*P* Value
Compliance with each preoperative intervention	Received patient education booklet and counseling	2366 (82.3)	1214 (85.0)	1152 (79.6)	<0.001
	Instructed on length of stay	2415 (84.0)	1252 (87.7)	1163 (80.3)	<0.001
	Consumed fluid carbohydrate rich drink morning of surgery	1783 (62.0)	955 (66.9)	828 (57.2)	<0.001
	Appropriate bowel prep Fleet enema for left-sided resections, oral mechanical bowel prep for low anterior resections	2166 (75.3)	1054 (73.8)	1112 (76.8)	0.063
Compliance with each intraoperative intervention	Administration of acetaminophen and/or gabapentin prior to surgery	2007 (69.8)	1050 (73.5)	957 (66.1)	<0.001
	Use of fluid monitor intraoperatively	769 (26.7)	404 (28.3)	365 (25.2)	0.062
	Avoidance of abdominal drains and nasogastric tubes	2442 (84.9)	1299 (91.0)	1143 (78.9)	<0.001
	Use of Lidocaine infusion and/or Epidural	2182 (75.9)	1065 (74.6)	1117 (77.1)	0.11
Compliance with each postoperative intervention	Early enteral feeding—clear fluids day of surgery, offered solids POD1	1636 (56.9)	956 (67.0)	680 (47.0)	<0.001
	Early ambulation—dangling day of surgery, walking POD1	1367 (47.5)	796 (55.7)	571 (39.4)	<0.001
	Chewing gum 3×/d	1511 (52.5)	866 (60.6)	645 (44.5)	<0.001
	Avoidance and early removal of Foley catheters (POD1 for colon, POD3 for rectal surgery)	1543 (53.7)	880 (61.6)	663 (45.8)	<0.001
Compliance with each phase of care*	Preoperative care pathway	2147 (74.7)	1121 (78.5)	1026 (70.9)	<0.001
	Intraoperative care pathway	1627 (56.6)	866 (60.6)	761 (52.6)	<0.001
	Postoperative care pathway	1160 (40.3)	738 (51.7)	422 (29.1)	<0.001
Overall compliance†	Compliance with all 3 care pathways	578 (20.1)	390 (27.3)	188 (13.0)	<0.001

*Compliance was defined as adherence to 75% (3 out of 4) of these measured recommendations within each care pathway.
†Overall compliance was defined as compliance with all aspects of care.
POD1 indicates postoperative day 1; POD3, postoperative day 3.

Patients were considered compliant with guidelines of an operative period (i.e. preoperative, intraoperative, and postoperative) if they were compliant with 75% (3 of 4) of guidelines within that operative period. It was determined that the relative risk of being in the optimal recovery cohort was greatest for patients who were compliant with postoperative guidelines (RR=2.12), followed by preoperative (RR=1.30) and intraoperative guidelines (RR=1.14) (Table 4.2). This provides further support for the claim that the increase in LOS in the second six months of ERAS in this study was due to the decrease in postoperative guideline compliance in that period.

Table 4.2: Relative risk of optimal recovery by phase of compliance (Aarts et al., 2017)

Phase of Compliance	RR (95% CI)	*P* Value
Preoperative compliance	1.30 (1.02–1.64)	0.031
Intraoperative compliance	1.14 (0.92–1.41)	0.24
Postoperative compliance	2.12 (1.81–2.47)	<0.001

4.4.1. Compliance with Urinary Catheter Removal Guideline

One of the most important postoperative guidelines within the ERAS pathway is early removal of the urinary catheter (Okrainec et al., 2017). Compliance with this guideline increased significantly (from 14.7% to 60.5%) with implementation of ERAS. And although the decrease between the first and second six months of ERAS (from 64% to 57%) was not statistically significant, it may be considered clinically significant. The difference in LOS observed between the main surgery group comparisons in this thesis (control and ERAS; first and second six months of ERAS) may be in part due to compliance with this guideline. Evidence for this statement will now be discussed.

In 2017, Okrainec et al. published a paper based on data from the same 15 ERAS programs mentioned in section 4.4. Specific inclusion criteria were: patients receiving an elective small bowel, colon, or rectal resection. Patients were excluded if they were undergoing: construction, revision, or closure of a loop ileostomy or colostomy without a laparotomy, and were not undergoing bowel resection. In total, 2,927 patients were included. The aim of the paper was to determine the implications of compliance versus deviation from the early removal of urinary catheter guideline. This paper defined early removal of the Foley catheter as removal within 24 hours of a colon procedure and 72 hours of a rectal procedure.

Of the 2,927 patients in the study, 1,897 (66%) received a colon resection, and 1,030 (33%) received a rectal resection. In both groups of patients (colon resections and rectal resections), early removal of the urinary catheter was associated with a reduction in UTI development and a decreased LOS (Table 4.3.)

Table 4.3: Implications of early removal of urinary catheter (Okrainec et al., 2017)

	Colon procedures (n = 1897)				Rectal procedures (N = 1030)			
	Compliant	Non-compliant	p value	RR (95% CI)	Compliant	Non-compliant	p value	RR (95% CI)
UTI, n (%)	7 (0.8)	43 (4.1)	0.003	0.20 (0.07–0.58)	25 (3.5)	30 (9.6)	0.001	0.37 (0.20–0.68)
LOS, median (IQR)	4 (3 to 6)	5 (4 to 8)	<0.001	0.73 (0.66–0.82)	5 (4 to 7)	8 (6 to 13)	<0.001	0.54 (0.49–0.59)
Short LOS (<5 days), n (%)	584 (69.5)	566 (53.6)	<0.001	1.32 (1.20–1.46)	378 (52.8)	46 (14.7)	<0.001	2.82 (2.27–3.50)
Reinsertion of urinary catheter, N (%)	40 (4.9)	20 (1.9)	<0.001	2.51 (1.62–3.87)	48 (6.8)	14 (4.8)	0.15	1.37 (0.89–2.12)

Selection bias (i.e. that patients with delayed catheter removal were truly sicker than those with early catheter removal) is a possibility in the Okrainec et al. study and should be considered. Table 4.4. Provides a list of variables that were tested as predictors of compliance with the urinary catheter guideline. Early mobilization (ambulation), early feeding, and a number of postoperative complications were significantly associated with early catheter removal. There is a possibility that patients who had delayed catheter removal were not as healthy overall (i.e. were unable to eat and mobilize earlier, for example). If this were the case, the delayed recovery of patients who were not compliant with the urinary catheter guideline may simply be a result of their health condition rather than the result of deviation from this one particular guideline. However, it may be just as likely that the association suggests that a physician who is negligent in removing the catheter at the appropriate time would also be negligent in having her patient comply with other guidelines (such as early feeding and ambulation). It is uncertain whether this selection bias exists, but it must be taken into consideration when interpreting results from this study.

Table 4.4: Multivariable analysis of factors associated with compliance with catheter guideline (Okrainec et al., 2017)

Predictor	RR (95% CI)[a]	*p* value[a]
Sex (male vs female)	1.00 (0.88–1.14)	0.99
Age (continuous in years)	1.00 (0.99–1.00)	0.30
Procedure type (colonic vs rectal)	0.21 (0.15–0.30)	<0.001
Laparoscopic/converted vs open	1.91 (1.41–2.58)	<0.001
Epidural vs others	0.49 (0.40–0.60)	<0.001
Compliance with ambulation guideline	1.27 (1.09–1.48)	0.003
Compliance with eating guideline	1.63 (1.32–2.01)	<0.001
Ileus	0.82 (0.70–0.95)	0.011
Leak	0.61 (0.46–0.81)	0.001
Reoperation	0.50 (0.31–0.78)	0.003
Any other complication[b]	0.69 (0.57–0.84)	<0.001

[a] Estimates derived from log-binomial generalized estimating equations

[b] Anesthesia related complication, bleeding, clostridium difficile, cardiac, confusion, fascia dehiscence, high ileostomy output, ileostomy, myocardial infarction, pneumonia, renal failure, renal other, sepsis, small bowel obstruction, stroke, stoma, surgical site infection, urinary retention, venous thromboembolism, wound, respiratory

The evidence for compliance with this guideline is clear, and the need to evaluate current practice and provide feedback is crucial. A local initiative to provide such academic detailing has been proposed and, if successful will begin in March 2018. This will be described in more detail in section 4.9.

4.4.2. Compliance with Early Removal of IV Fluids Guideline

Another crucial postoperative guideline in the ERAS pathway is removal of IV fluids on POD1. Both the increase in compliance upon implementation of ERAS (from 15.2% to 72.8%) and the decrease in compliance between the first and second six months of ERAS (83.7% and 62.1%) were statistically significant. This may, in part, help explain the difference in patient outcomes between these surgery groups. Evidence for this statement will now be presented.

A randomized trial in 2002 compared the use of standard postoperative IV fluids (defined as ≥3 L water and 154 mmol sodium per day) with a restricted postoperative IV fluid protocol (defined as ≤2 L water and 77 mmol sodium per day) after elective colorectal resections in 20 patients (10 per group) at University Hospital in Nottingham, UK. Patients were not significantly different in any of the baseline demographic factors measured (such as age, sex, and BMI). The most pertinent finding in this study was that patients who received restricted postoperative IV fluids had a significantly shorter LOS (6.0 days) than patients who received standard postoperative IV fluids (9.0 days). Table 4.5 demonstrates other improvements in patient outcomes that were associated with restricting postoperative IV fluids (Lobo et al., 2002).

Table 4.5: Comparison of patient outcomes between standard and restricted IV Fluids (Lobo et al., 2002)

	Standard group (n=10)	Restricted group (n=10)	Difference (95% CI)	p
Endpoints				
Day on which flatus first passed	4·0 (4·0–5·0)	3·0 (2·0–3·0)	2 (1–2)	0·001
Day on which stool first passed	6·5 (5·8–8·0)	4·0 (3·0–4·0)	3 (2–4)	0·001
Day on which intravenous infusion discontinued	6·0 (4·8–6·3)	4·0 (3.8–4·0)	2 (1–3)	0·001
Day on which solid food intake resumed	6·5 (5·5–7·0)	4·0 (4·0–4·3)	2 (1–3)	0·002
Postoperative hospital stay (days)	9·0 (7·8–14·3)	6·0 (5·0–7·0)	3 (1–8)	0·001

Values are median (IQR), Mann Whitney *U* test applied.

4.4.3. Compliance with Postoperative Mobilization

Compliance with postoperative mobilization increased significantly with implementation of the ERAS program (from 12.0% to 54.3%) and decreased significantly from the first to second six months of ERAS (from 63.2% to 45.3%). This is another postoperative guideline that may be, in part, responsible for the change in LOS observed between these groups.

In the 2012 study by Smart et al., which was discussed in the introduction chapter of this thesis, the odds of prolonged LOS (defined as greater than 8 days in hospital) in patients who did not mobilize on POD1 was 7.5 times greater than the odds of prolonged LOS in patients who did mobilize on POD1 (Smart et al., 2012). Another study from 2013 by Cook et al. evaluated the

relationship between number of steps taken after surgery and recovery time. Patients in this study were scheduled for an elective surgery, were greater than 50 years old, and were expected to recover in five to seven days. There was a significant association between increased number of steps taken after surgery, and reduction in LOS (Cook et al., 2013). This evidence helps support that the decrease in LOS observed in the ERAS group, and the increased LOS observed in the second six months of ERAS, may be partially due to compliance with this guideline. A specific suggestion to improve compliance is discussed in section 4.8.3.

4.5. Alternate Explanations for Research Findings

Regression to the mean (RTM) is a major threat to the validity of non-randomized interventional studies (such as interrupted time-series analysis), and is an element that is often overlooked when interpreting the results of such research. RTM suggests that if the first (or any given) measurement of a particular outcome is significantly different than the mean value of that outcome, then the subsequent measurement is expected be closer to the mean than the initial measurement (Skinner et al., 2016). It is necessary to consider if such a change is different than what would be expected with normal variation (Barnett et al., 2004). In this study, LOS was 7.26 days in the 2014 fiscal year, 7.20 days in the 2015 fiscal year, 5.44 days in the first six months of ERAS, and 7.10 days in the second six months of ERAS. Although the substantial increase in compliance with guidelines in the first six months of ERAS, compared to both the 2016 fiscal year and second six months of ERAS, is quite compelling, the threat of RTM is acknowledged.

Selection of an appropriate, and representative, control group has been noted as one of the most effective ways to avoid erroneous conclusions that are simply the result of RTM (Yudkin and Stratton, 1996). The control group selection in this study, which was described in section 4.1, was thorough and valid - the 2014 fiscal year surgeries are likely to be a true

representation of colorectal resections before implementation of the ERAS program. As such, the reduction in LOS and subsequent increase is very likely a result of the corresponding increase and subsequent decrease in compliance with guidelines. However, data regarding the second year of ERAS surgeries would help strengthen this argument.

4.6. Knowledge Translation

The intention of this thesis is not simply to validate the ERAS pathway. Sufficient evidence exists to this effect (Gustafsson et al., 2012). Nor is this the first study of ERAS implementation in colorectal surgery (Zhuang et al., 2013). However, it is a study of the first ERAS program in NL. The primary purpose of this research is to determine the success and effectiveness of this particular quality improvement program. The aim is to provide local evidence, and point to areas that must improve as this initiative progresses. It will also assist with implementation of future ERAS programs in NL. For this reason, knowledge translation (KT) and provision of academic detailing is necessary to make this research consequential.

The Faculty of Medicine at Memorial University of Newfoundland (MUN) and the Newfoundland and Labrador Medical Association (NLMA) have partnered to form Quality of Care NL/Choosing Wisely NL, a program that address issues regarding overutilization of healthcare resources in NL. Quality of Care NL (QoCNL) is aimed at the appropriateness of healthcare, ensuring the “right patient” gets the “right intervention” at the “right time”. Choosing Wisely NL (CWNL) is aimed at reducing the unnecessary use of tests, medications, and other health resources (QoCNL Practice Points Volume 2, 2017). Evaluation of the ERAS initiative at SCMH falls under the QoCNL group of projects.

Practice Points are a set of one-page reports generated by QoCNL/CWNL which provide academic detailing on the utilization of a number of different drugs and medical procedures,

some of which include antibiotics, antipsychotics in nursing homes, and regional rates of coronary catheterization and revascularization (QoCNL Practice Points Volume 2, 2017). These are circulated to physicians throughout NL. In the winter of 2017, a one-page report detailing compliance with guidelines and patient outcomes in the first six months of the ERAS initiative was generated under QoCNL (Figure 4.1). The intention was to provide concrete feedback on the change in practice, demonstrating the marked improvement in patient outcomes due to compliance with ERAS guidelines. In the fall of 2017, a similar report was generated with data from the full year of ERAS surgeries (Figure 4.2). Differences in the first and second six months of ERAS (i.e., compliance with guidelines and patient outcomes) were emphasized, demonstrating deterioration of postoperative guideline compliance and the regression of LOS. Only an evaluation of the second year ERAS colorectal surgeries will indicate the impact of this KT, but the hope is that it will provide a reminder of the need to be compliant with as many guidelines, specifically postoperative guidelines, as is possible.

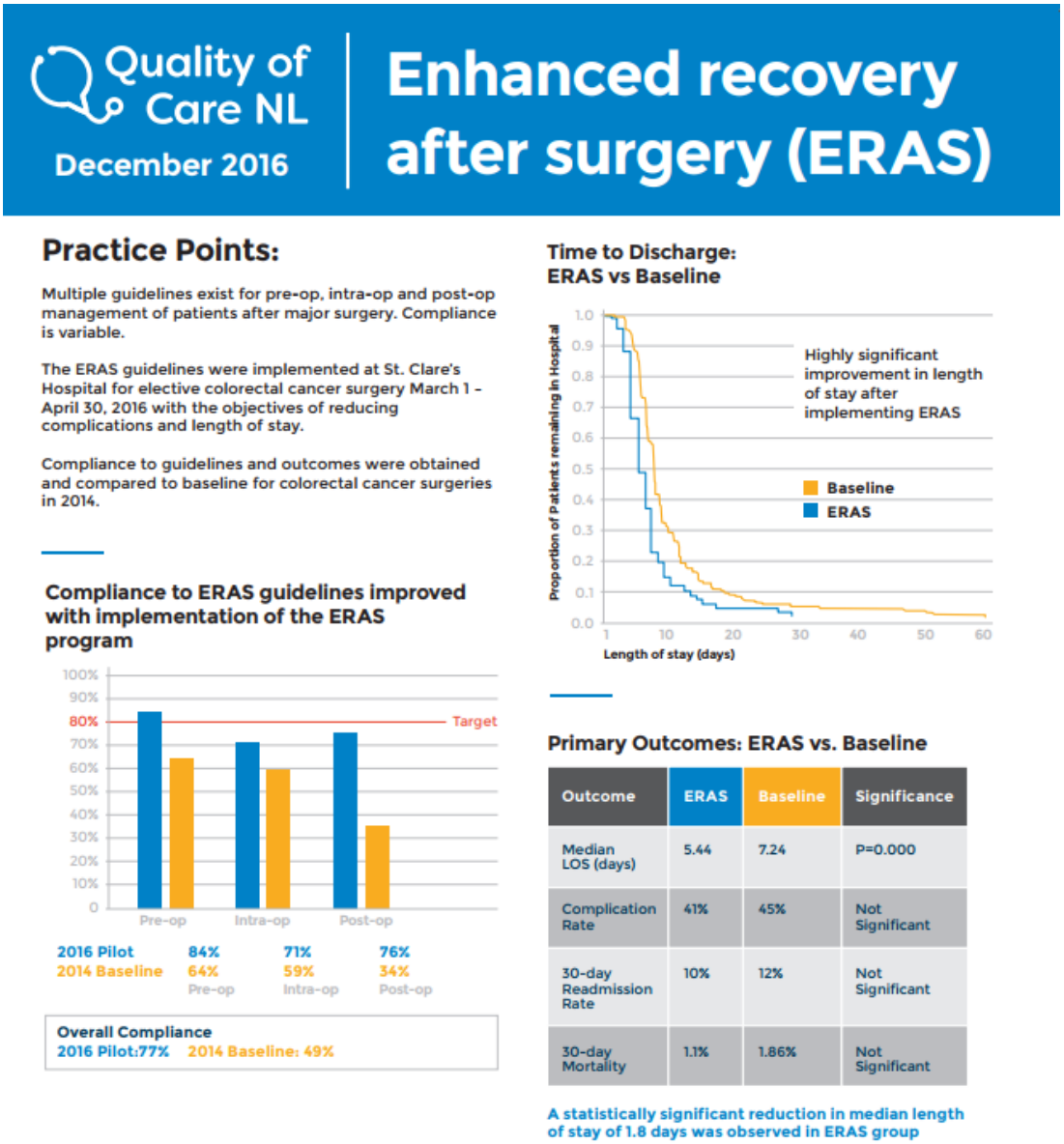


Figure 4.1: ERAS Practice Points report released in the winter of 2017 (QoCNL Report 1, 2017)

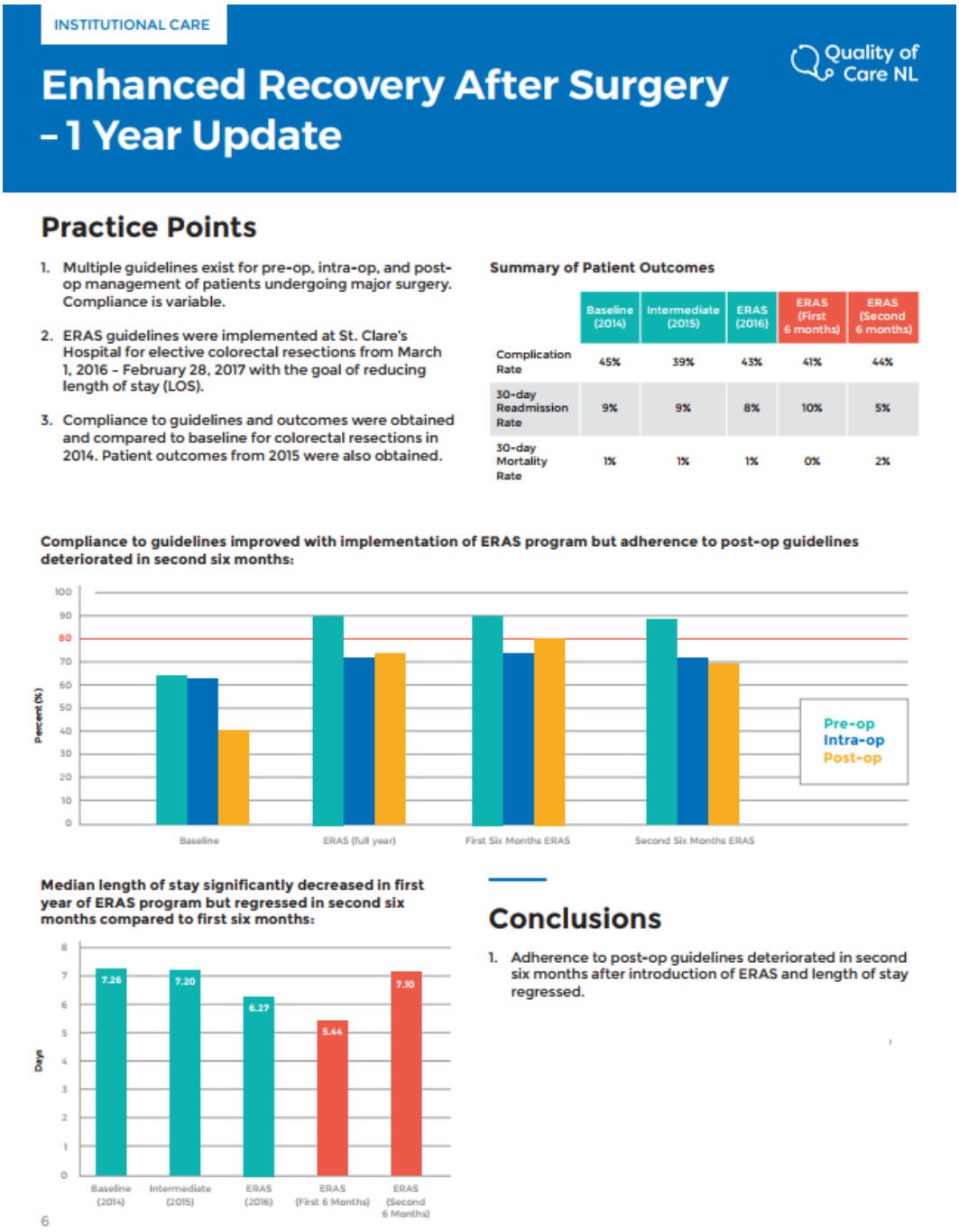


Figure 4.2: ERAS Practice Points one year update released in the fall of 2017 (QoCNL Practice Points Volume 2, 2017)

4.7. Biases and Limitations

In virtually any research, limitations and some degree of bias are inevitable. One of the most significant limitations in this study was the lack of a patient randomization process. The study design which most effectively determines causation between intervention and outcome is a RCT (Curtis et al., 2015, p.159). However, as this study evaluated a quality improvement program implemented by a RHA, randomization of patients into ERAS and standard practice surgery groups was not possible. This means that only known demographic and prognostic factors can be accounted for in data analysis. In a RCT, both known and unknown demographic and prognostic factors are likely to be similar in both groups (Foley, 2015, p.180). However, in this study, the only demographic and prognostic factors compared were sex, age, and comorbidity. Any other factors that could influence patient outcomes were not accounted for. This makes causation (i.e. that ERAS caused a decrease in LOS) impossible as there may be unknown confounding variables impacting patient outcomes that are not taken into consideration.

Another limitation in this study is the lack of a blinding process for surgeries that took place in the ERAS program. As the change in practice under evaluation involves physician compliance with guidelines of best practice, physicians and other health care workers were evidently not blinded to the intervention that they were implementing. This may be an issue in that the health care team may be more inclined to release patients early in this program as they know that the guidelines are supposed to decrease recovery time. Therefore, the decrease in LOS determined in this study may not be completely representative of the true effect of an ERAS initiative. However, evaluation of rates of complication, 30-day readmission, and 30-day mortality were beneficial in determining the extent of this bias. If patients were being released too early, it would be expected that mortality, readmission or postoperative complications would

increase. However, this was not the case. As there were no significant differences between rates of these adverse outcomes between control and ERAS surgeries, the premature release of patients in the ERAS group is unlikely.

4.8. Improving Compliance with ERAS Guidelines

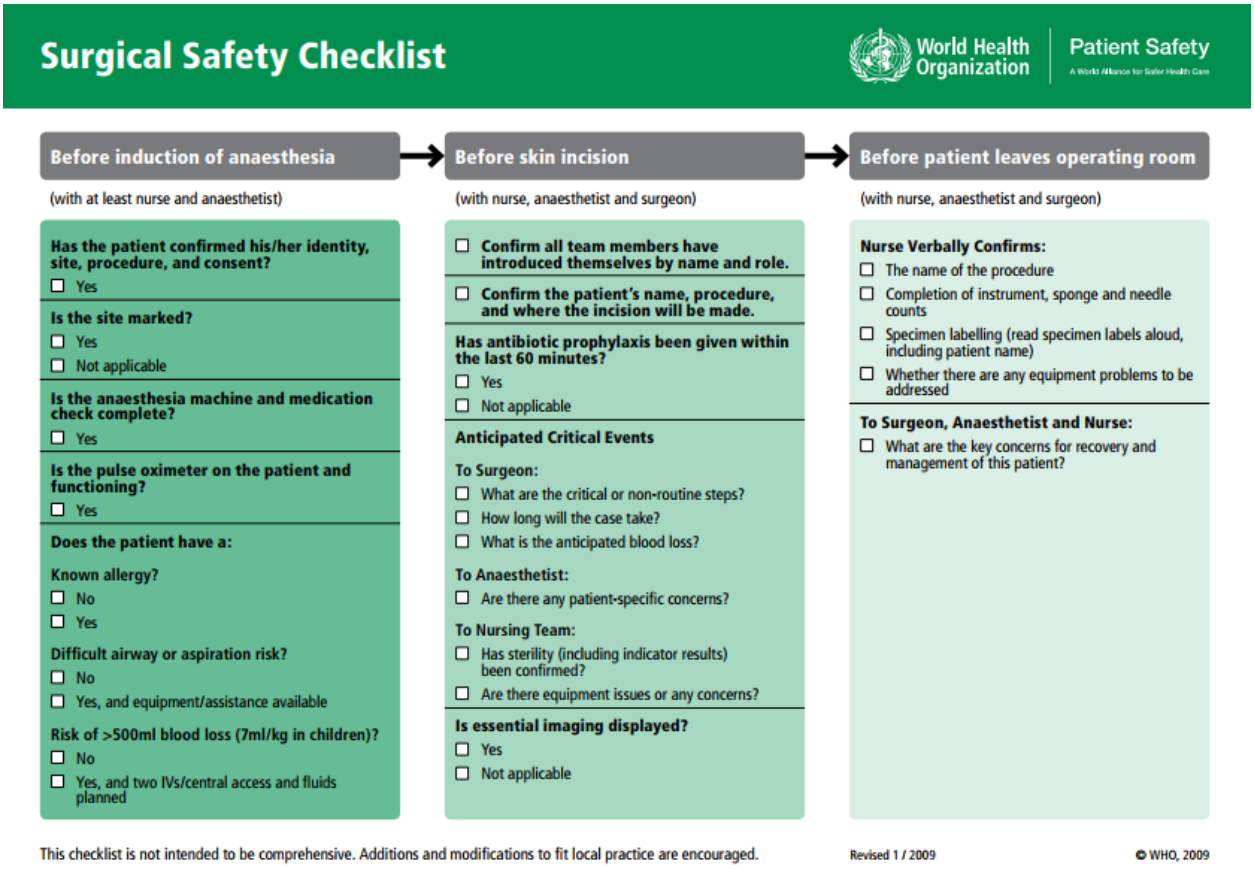
ERAS programs are beginning to expand to other procedures in NL (orthopedic, thoracic, vascular, and head and neck) and at other sites (HSC, and eventually throughout EH and then provincially) (Pridham, 2018). Issues have been demonstrated in this thesis regarding implementation of guidelines without supervision. Therefore, it is necessary to discuss several approaches which may facilitate compliance with guidelines as the protocol expands in this province.

4.8.1. ERAS Checklist

One rather simple method that might incite increased compliance with ERAS guidelines, and at the very least would expedite measurement of guideline compliance, would be to introduce a very simple checklist of appropriate ERAS guidelines for the specific surgical procedure (for example colorectal, orthopedic, thoracic, et cetera). This would consist of a list of preoperative, intraoperative, and postoperative guidelines, and a Yes or No (if no provide specific reason) check box. The idea for such a checklist comes from literature on the success of the World Health Organization (WHO) Safer Surgery checklist.

In June 2008, a Safer Surgery checklist was established by the WHO with the goal of ensuring safety of patients throughout all phases (preoperative, intraoperative, and postoperative) of their surgery (Figure 4.3). The checklist consists of a number of processes that must take place and actions that must be performed in order to proceed with the procedure (Keijzer et al., 2017). The initial and most significant study pertaining to the success of this checklist was published in

2009 by Haynes et al. It considered 3,733 consecutive patients, 16 years of age or older, undergoing noncardiac surgery in eight cities (Toronto, Canada; New Delhi, India; Amman, Jordan; Auckland, New Zealand; Manila, Philippines; Ifakara, Tanzania; London, England; and Seattle, WA) before the intervention and 3,955 consecutive patients (from the same cities and using the same inclusion criteria) after the intervention. The 30-day mortality rate decreased from 1.5% to 0.8% ($P=0.003$) when the checklist was introduced. The complication rate decreased from 11.0% to 7.0% ($P<0.001$) with adherence to the checklist protocol (Haynes et al., 2009).



Surgical Safety Checklist

World Health Organization | Patient Safety
A World Alliance for Safer Health Care

Before induction of anaesthesia → **Before skin incision** → **Before patient leaves operating room**

(with at least nurse and anaesthetist)

Has the patient confirmed his/her identity, site, procedure, and consent?
- ☐ Yes

Is the site marked?
- ☐ Yes
- ☐ Not applicable

Is the anaesthesia machine and medication check complete?
- ☐ Yes

Is the pulse oximeter on the patient and functioning?
- ☐ Yes

Does the patient have a:

Known allergy?
- ☐ No
- ☐ Yes

Difficult airway or aspiration risk?
- ☐ No
- ☐ Yes, and equipment/assistance available

Risk of >500ml blood loss (7ml/kg in children)?
- ☐ No
- ☐ Yes, and two IVs/central access and fluids planned

(with nurse, anaesthetist and surgeon)

- ☐ **Confirm all team members have introduced themselves by name and role.**
- ☐ **Confirm the patient's name, procedure, and where the incision will be made.**

Has antibiotic prophylaxis been given within the last 60 minutes?
- ☐ Yes
- ☐ Not applicable

Anticipated Critical Events

To Surgeon:
- ☐ What are the critical or non-routine steps?
- ☐ How long will the case take?
- ☐ What is the anticipated blood loss?

To Anaesthetist:
- ☐ Are there any patient-specific concerns?

To Nursing Team:
- ☐ Has sterility (including indicator results) been confirmed?
- ☐ Are there equipment issues or any concerns?

Is essential imaging displayed?
- ☐ Yes
- ☐ Not applicable

(with nurse, anaesthetist and surgeon)

Nurse Verbally Confirms:
- ☐ The name of the procedure
- ☐ Completion of instrument, sponge and needle counts
- ☐ Specimen labelling (read specimen labels aloud, including patient name)
- ☐ Whether there are any equipment problems to be addressed

To Surgeon, Anaesthetist and Nurse:
- ☐ What are the key concerns for recovery and management of this patient?

This checklist is not intended to be comprehensive. Additions and modifications to fit local practice are encouraged.

Revised 1 / 2009

© WHO, 2009

Figure 4.3: World Health Organization (WHO) Surgical Safety Checklist (WHO, 2017)

Evidently, the introduction of a physical checklist that required the operating team to indicate their own usage of, or adherence to, best practices was successful at ensuring that they truly followed such practices. The introduction of a similar checklist of ERAS guidelines (in essence, to demand self-assessment) would likely provoke more thorough compliance with an ERAS pathway. This is a suggestion for this ERAS initiative (and other similar initiatives) in the future.

4.8.2. Technological Facilitation

Recent and ongoing advances in technology could also be utilized to promote adoption of ERAS guidelines. For example, a workflow management system (WfMS), could potentially be adapted for use within an ERAS pathway to strengthen guideline compliance. Broadly stated, a WfMS is an automated, software-driven, method of using definitions and data to guide actions and decision making (Gooch and Roudsari, 2011). Such a process has proven effective at improving patient care (Panzarasa et al. 2007). Although published more than a decade ago, Panzarasa et al. describe the success of one particular WfMS program for acute care of patients within a stroke unit (SU). Specifically, they suggest that the system improves both evidence-based practice and patient outcomes.

In this particular SU, before introduction of the WfMS, a computerized clinical chart (CCC) was already in place with the intention of limiting paper-based communication and facilitating future retrieval of patient data. Introduction of the WfMS did not consist of an additional interface, which would have been perceived as a barrier to efficient practice, rather it was a modification to the already satisfactory CCC. The WfMS described in this study is simply a more dynamic and informative version of the CCC, providing guidance on the specifics of care to be provided. The central component of the WfMS is the Smart graphical user interface (Figure 4.4). It provides "to-do" lists that physicians must follow, which are patient-specific (based on the patient's specific conditions). This would be valuable in an ERAS pathway for patients who cannot comply with certain guidelines (i.e., patients that are unable to chew gum or mobilize post-surgery; whether or not a patient should receive TEA depending on if the surgery is open or laparoscopic; special considerations for administration of drugs depending on other medication or allergies, et cetera). A valuable element of the WfMS is the method which directs completion

of a given task. A green happy smiley face represents a task that has been completed, an orange thoughtful smiley face represents a task that is in the process of being completed, a red sad smiley face represents a task that has not been completed due to a specific exception, and a task that still has to be completed has no icon.

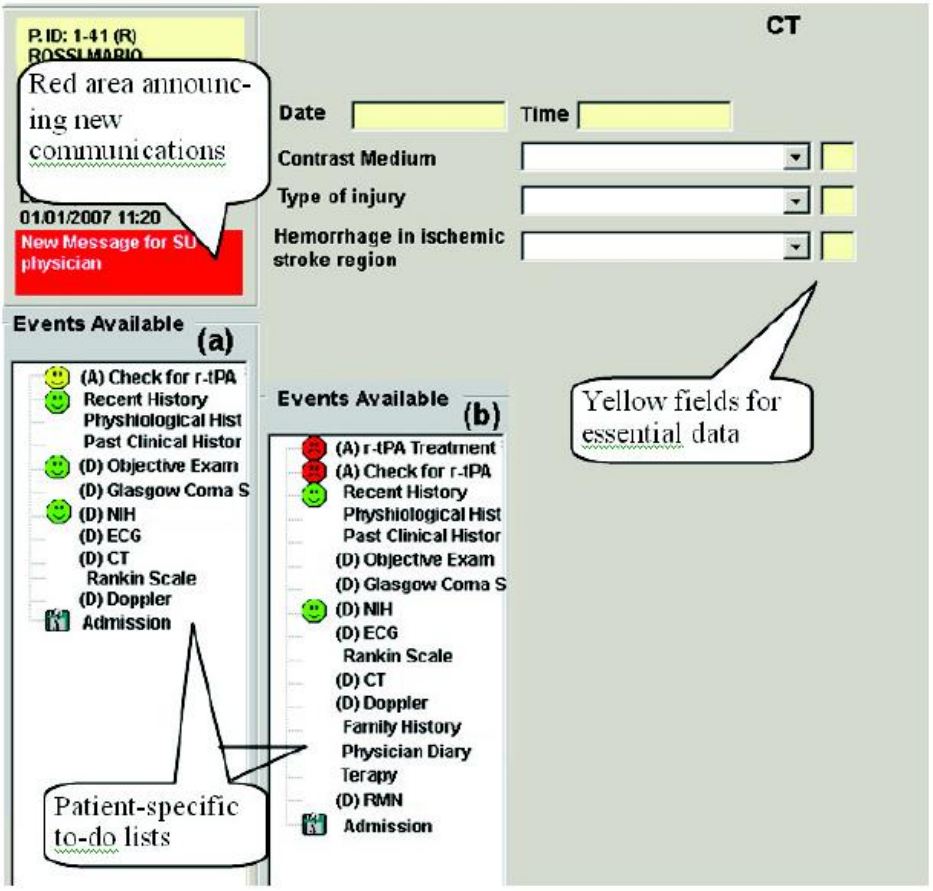


Figure 4.4: Smart graphical user interface from the workflow management system (WfMS) (Panzarasa et al. in 2007)
(a) and (b) are two different to-do lists for the same patient shown in two different points in time

The study states that before the WfMS was introduced, all practice was performed based on the physician's expert opinion, and that it was not necessarily best practice. There is a parallel to be drawn here, to the practice performed in the second six months of the ERAS initiative when there was no strict guidance provided (as would be the case under a WfMS) or supervision of

guideline compliance. Upon introduction of the WfMS in this study, compliance with Stroke Prevention and Educational Awareness Diffusion (SPREAD) increased significantly. It would not be unrealistic to imagine that compliance with ERAS guidelines would also increase if a similar WfMS interface were implemented, prompting adherence with specific guidelines in the preoperative, intraoperative, and postoperative periods.

4.8.3. Compliance with Postoperative Mobilization

Another recommendation, though much more specific, has to do with the potential for increasing compliance with postoperative mobilization on POD1. The evidence is clear that beginning mobilization on POD1 leads to improved patient recovery, and a reduced LOS. The suggestion is that each patient be provided with a simple pedometer or fitness tracker as a means to encourage postoperative physical activity.

As patients are educated preoperatively regarding all components of the ERAS pathway (including the rationale for POD1 mobilization) (Gustafsson et al., 2012), this awareness combined with a means for tracking that mobilization would potentially increase the level of physical activity after surgery. A study in 2015 demonstrated that a wrist-worn physical activity monitor was successful at increasing levels of physical activity in young healthy men in Finland (Juaho et al., 2015). Although this population is by no means representative of patients in the postoperative phase of a colorectal resection, it is evidence that a fitness tracker can potentially motivate increased physical activity. At the very least, it is hard to imagine that this additional intervention would have any negative consequences. With the cost of pedometers being relatively low (in comparison to the overall cost of hospital care as discussed in Chapter 1), their use after colorectal surgery within an ERAS pathway may be worth an attempt, even in a small pilot study.

4.9. Urinary Catheterization, Potential for Future Research

In a 2016 study, it was demonstrated that 18% of hospitalized patients in Sunnybrook Health Sciences Centre, Toronto, were catheterized. However, in 69% of these patients, there was no evidence based guideline for the use of a catheter. Staff were trained to comply with a new medical directive (Figure 4.5): to remove catheters without a pre-specified reason and follow a post-catheter algorithm for management of urinary retention. The rate of catheterization has decreased by 50%, an outcome that was sustainable beyond 12 months (Leis et al., 2015).

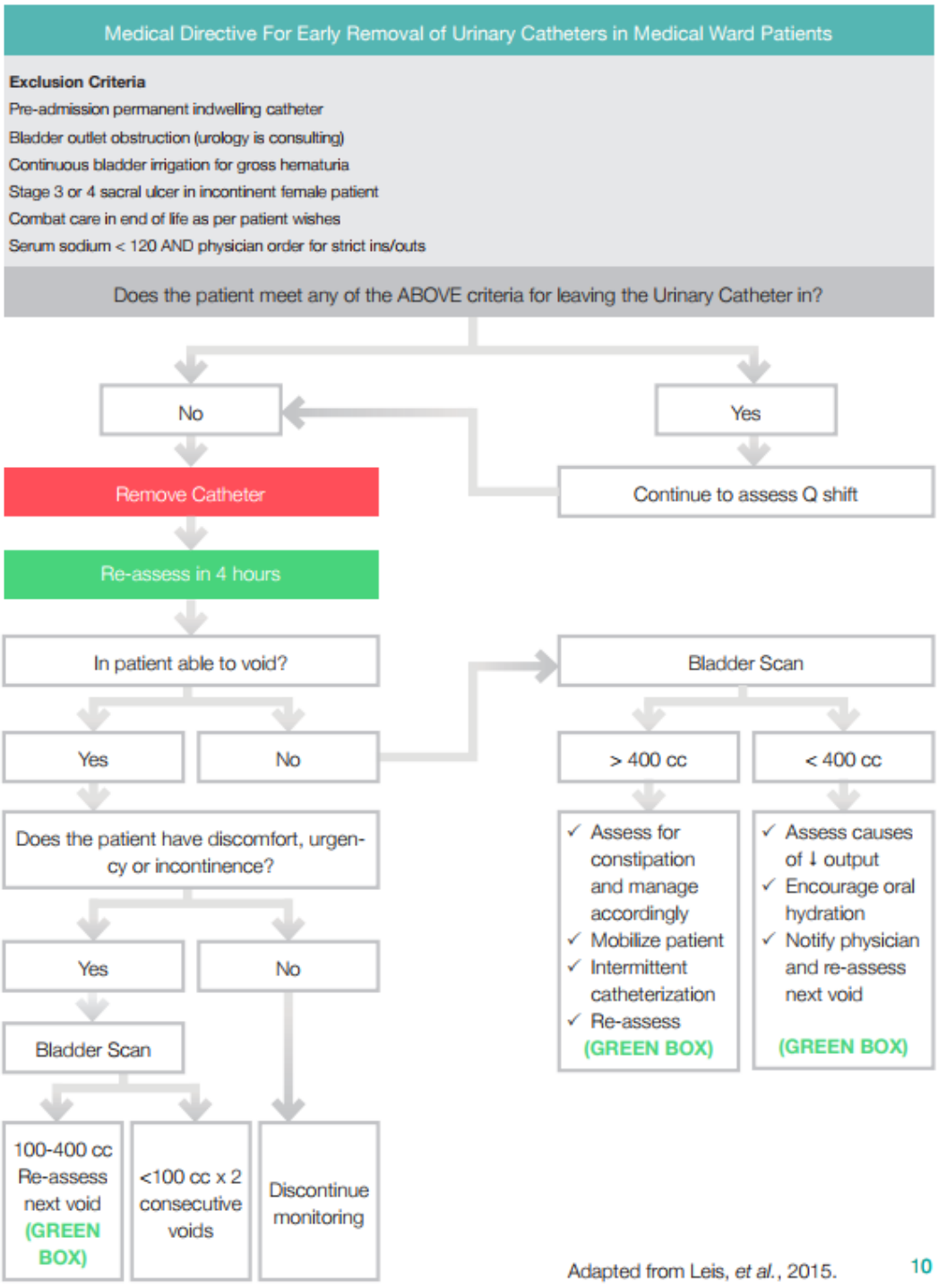


Figure 4.5: Catheterization medical directive (adapted from Leis et al., 2015)

As a result of this initiative and research, Choosing Wisely Canada (CWC) has partnered with Sunnybrook Health Sciences Centre to develop a toolkit, "Lose the Tube", with two recommendations (CWC Lose the Tube, 2017):

1) **Don't place, or leave in place, a urinary catheter without reassessment**
2) **Don't place, or leave in place, urinary catheters without an acceptable indication (such as critical illness, obstruction, palliative care).**

A recently proposed CWNL project suggests that NL should adopt these recommendations and also adhere to the medical directive decision tree (Figure 4.5). A research team would evaluate volume and duration of use of urinary catheters at SCMH between April 1, 2016 and March 30, 2017 as a baseline group. After implementation, number of admissions, rate and volume of catheterizations, and length of time of catheterization would be evaluated. Report cards would be generated every three months. The long-term goal of this project is to demonstrate, locally, the evidence for proper use of urinary catheterization and eventually roll these recommendations out to the HSC and then other sites in NL (Mahoney, 2018).

4.10. Conclusion

This thesis has demonstrated the benefit of supervised compliance with ERAS guidelines at one site in NL. It has also demonstrated the likely result of eliminating that supervision. There is a clear opportunity in this province to improve patient outcomes after surgery, and we hope that this thesis will be a motivating factor. However, we suggest that as this ERAS initiative and other future ERAS programs progress, a proper system (either technological or a simple physical checklist) is put into place to ensure guidelines are truly being followed. While supervision is important, this supervision needs to be translated into a culture change in the institution in which ERAS is implemented.

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Appendix

Appendix I: Description and Rationale for ERAS Guidelines*

***Definitions and rationale are from Gustafsson et al., 2012 unless otherwise noted*

Preadmission counselling: Providing preadmission information, education, and counselling to patients is the first preoperative guideline of the ERAS pathway. This involves an explanation, either oral or written, of the surgical and anesthetic procedures that the individual will undergo. It should also outline postoperative pathway components such as early feeding, mobilization, and gum chewing, to facilitate implementation of such guidelines. This intervention also aims to reduce patient anxiety, which has been shown to improve recovery. Adherence to this guideline is particularly important for patients who demonstrate higher than usual levels of fear or anxiety (Fearon et al., 2005).

Carbohydrate loading: The second guideline in the ERAS pathway is administration of a carbohydrate beverage before surgery. Fasting after midnight the night before surgery has been standard practice to prevent aspiration and regurgitation. However, recent research does not support the belief that complete fasting after midnight is necessary (Ren et al., 2012). One meta-analysis of 22 RCTs showed that fasting from midnight did not reduce gastric content in comparison to patients who consumed clear fluids only two hours before surgery (Brady et al., 2003). The carbohydrate loading intervention usually involves consumption of a clear fluid with 12.5% maltodextrins two to three hours before anesthesia. This intervention will allow the patient to undergo surgery in a metabolically fed state which has been shown to reduce thirst, hunger, and anxiety before surgery, and to reduce postoperative insulin resistance. This will prevent the body from entering a catabolic state during and after the procedure, preventing

postoperative muscle deterioration.

No bowel preparation: The third preoperative intervention is to withhold mechanical bowel preparation (MBP). MBP involves consumption of an oral substance that clears colonic contents before surgery. Traditionally, MBP has been carried out for colonic resections under the assumption that it is important for reducing infectious complications. It was believed that spillage of bowel contents during surgery and anastomotic leakage after surgery were the cause of such complications. One meta-analysis showed that this is not the case (Cao et al., 2012). There are several reasons that mechanical bowel preparation is avoided as part of the ERAS initiative. Manipulation of the bowel can result in some physiological symptoms associated with dehydration. Patients are also more likely to have prolonged obstruction of the bowel if MBP is performed. One Cochrane review performed in 2011, which included 18 RCTs with 5,805 elective colorectal resections, did not detect a significant difference in anastomotic leakage, mortality rate, requirement for follow up operation, or postoperative infection, between those who received and did not receive MBP (Guena et al., 2003). Although many surgeons have noted that MBP makes the surgery easier, especially for laparoscopic surgery, MBP is not necessary and colonic resection without it is safe and very effective.

Antibiotic prophylaxis: The next intervention is the administration of antibiotic prophylaxis. This is implemented to prevent infections from occurring at the site of incision. If an intravenous antibiotic is used, it should be administered 30-60 minutes before the incision is made. Repeated doses may be favorable for longer procedures. Timing protocol for oral antibiotics in the ERAS pathway is much less certain, especially because oral antibiotics have not been studied extensively in patients who have not received bowel preparation.

Venous thromboembolism (VTE) prophylaxis: The next intervention in the ERAS pathway, and the final preoperative guideline, is the administration of venous thromboembolism (VTE) prophylaxis. Heparin, an anticoagulant, is administered once or twice daily to help prevent deep vein thrombosis (DVT), the formation of a deep vein blood clot. In patients who do not receive VTE prophylaxis, approximately 30% will develop DVT, and 1% of patients will develop fatal pulmonary embolus. These rates are substantially higher in patients who have a malignant form of cancer, have had previous pelvic surgery, are taking corticosteroids preoperatively, are extensively comorbid, or are in a hypercoagulable state (Fleming et al., 2010). It is recommended that VTE prophylaxis in conjunction with well-fitted compression stockings be used for colorectal patients in order to reduce the prevalence of DVT.

Short acting anesthetics: The first intraoperative guideline in the ERAS pathway is utilization of short acting anesthetics. Although evidence for this intervention is scarce, it is recommended that short acting induction agents (e.g., propofol) be used in conjunction with short acting opioids (e.g., fentanyl, alfentanil). The rationale is simply that if the effects of an aesthetic agent wear off quicker, the recovery process may begin sooner (Lassen et al., 2009).

Thoracic epidural analgesia (TEA) for open surgery: The second intraoperative guideline is the use of thoracic epidural analgesia (TEA) for open surgery. This involves the administration of a low concentration local an aesthetic combined with a short-acting opiate. Although hypotension is possible with adherence to this guideline, vasopressors may be used in patients who are not hypovolemic. The epidural should be removed 48-72 hours after surgery once the patient has had their first postoperative bowel movement. It has been demonstrated that TEA for open surgery results in an earlier recovery of the bowel and reduces pain, complications, postoperative nausea and vomiting (PONV) and insulin resistance.

Fluid management: The next guideline in the ERAS pathway is the use of goal directed fluid management. It is recommended that patients receive intraoperative fluids regulated by flow measurements (including stroke volume, flow time, pulse pressure) to improve cardiac output (Ballah, 2017). As intravascular volume is a significant determinant of cardiac output which influences rate of oxygen delivery to tissues, fluid delivery is vital to efficient recovery after surgery. Systems may include the use of a non-invasive cardiac monitoring device, and limitation of intraoperative IV fluids to 8cc/kg/kr (Ballah, 2017).

Laparoscopy: Laparoscopy is a minimally invasive surgical technique that was used to carry out a colorectal resection for the first time in 1991. The pneumoperitoneum is inflated with carbon dioxide and a small incision in the abdomen allows for the insertion of a laparoscope to view the colon. Insertion of trocars allows the surgery to be performed without an incision as large as would be necessary in traditional open colonic surgery (Jacobs, 1991). Laparoscopy is an important component of the ERAS pathway as it has been associated with a reduction in LOS when used for colorectal resections. It has also been shown to reduce pain, complications, and postoperative immunosuppression.

Maintenance of Intraoperative Normothermia: Maintenance of intraoperative normothermia is vital to ensure proper body functions and homeostasis. Hypothermia is defined as having a body temperature of <36℃ and has been associated with an increased rate of wound infection, morbid cardiac events, and bleeding. A warm air blanket to pre-warm a patient has been used as one successful strategy to increase body temperature. Other methods have included heating mattresses and circulating water garments. Intravenous fluids may also be heated before administration. It is recommended that active warming be continued postoperatively until a patient's temperature has reached or exceeded 36℃. To avoid hyperpyrexia in prolonged

procedures, temperature should be monitored throughout so that heating can be adjusted.

Maintenance of intraoperative normoglycemia: Maintaining a reasonable level of glucose in surgery is vital. Research has demonstrated that hyperglycemia and insulin resistance are associated with postoperative mortality and complications. The combination of (i) epidural use, (ii) preoperative carbohydrates, and (iii) postoperative continuous complete enteral feeding has proven effective at maintaining normal blood glucose levels.

Discontinuation of IV fluids after 24 hours: The first postoperative guideline aims to maintain a normal blood volume and avoid fluid overload after surgery. This intervention is the removal of intravenous fluids within the first 24 hours after surgery. Evidence has suggested that providing excess intravenous infusions can result in an increase in postoperative complications and recovery time in hospital (Fearon, 2005). Potentially, the removal of the intravenous drip could prevent an excess of fluid administration and may prevent these adverse outcomes.

No nasogastric tube: The next ERAS guideline is the avoidance of nasogastric intubation postoperatively. A nasogastric tube is inserted through the nose into the stomach to decompress the stomach by removing excess air through vacuum action. Traditionally, physicians believed that nasogastric intubation reduces the risk of PONV, aspiration, wound dehiscence, and anastomotic leak (Cheatham et al., 1995). However, evidence suggests that nasogastric decompression actually increases the risk of complications including fever, atelectasis, and pneumonia (Fearon et al. 2005). It is recommended that if a nasogastric tube was inserted during surgery, it should be removed before the reversal of anesthesia.

Management of PONV: Between 25 and 35 percent of all surgery patients experience postoperative nausea and vomiting. Those who have the highest risk of PONV are females, non-

smokers, and individuals with a history of motion sickness. Certain drugs such as volatile anesthetics, nitrous oxide, and parenteral opiates can also increase the risk of PONV. A commonly used method for dealing with PONV involves a multimodal approach. This means that both non-pharmacological and pharmacological interventions are implemented. These include but are not limited to: avoidance of inhalational anesthetics, increased use of propofol, carbohydrate loading, reduced preoperative fasting, and sufficient hydration.

Removal of urinary catheter: The next intervention in the ERAS pathway is to remove the Foley catheter on POD1. A Foley catheter is a device inserted into the urinary bladder from the urethra to allow drainage of urine. It is used to monitor urine output during and after the surgery as a predictor of renal function, but minimal evidence exists to show that it is actually an effective predictor. Traditionally, the Foley catheter has been left in until POD4; however, it has been demonstrated that an early removal can result in reduced rates of UTI. One study determined that the rate of UTI can be reduced from 14% to 2% if the catheter is removed on POD1 rather than POD4.

Clear fluids on POD0: The next guideline is administration of clear fluids postoperatively on the day of surgery. It is recommended that patients begin consuming fluids 2 hours after surgery with a targeted total consumption of 800 ml on the day of surgery. The goal of this intervention is to reduce the need for administration of IV fluids postoperatively (Fearon et al., 2005). Excess IV fluids can result in complications (Brandstrup et al., 2003) and increased hospital stay (Lobo et al, 2002). As IV fluids can be discontinued as soon as oral intake is adequate (Fearon et al., 2005), administration of clear fluids 2 hours after surgery is recommended.

Diet as tolerated on POD1: The next protocol in the ERAS pathway is administration of food as tolerated on the first day after surgery. It is suggested that consuming 1,200-1,500 calories from drink and hospital food immediately after recovery from anesthesia is safe. Evidence suggests that early feeding, either through the enteral or oral route, reduces LOS and risk of infection, and is not associated with an increased risk of anastomotic leak.

Multimodal Pain Management: An effective pain management regimen after major surgery should be able to relieve pain, allow early mobilization, and promote gut function without causing complications. A multimodal approach to pain management is central to the ERAS pathway and is capable of achieving these outcomes. This approach involves the utilization of multiple pain management modalities such as nonsteroidal anti-inflammatory drugs (NSAID), acetaminophen, ketamine, glucocorticoids, IV lidocaine, TEA, spinal analgesia, and regional blocks (Ballah, 2017). It is recommended that opioids be avoided as evidence suggests that their use may be associated with adverse outcomes such as postoperative nausea and vomiting (Kehlet and Wilmore, 2002).

Early Mobilization: Postoperative mobilization is a vital component of the ERAS pathway and has several beneficial outcomes. Studies have shown that prolonged bed rest can result in insulin resistance, muscle deterioration, reduced tissue oxygenation, and thromboembolism (Fearon et al., 2005), and that combining early mobilization with nutritional support improves muscle strength in the early postoperative phase. It is suggested that patients spend two hours out of bed on the day of surgery, and six hours each subsequent day until discharge (Fearon et al., 2005). Factors such as inadequate pain control, continuation of IV fluids, extended use of urinary catheter and patient motivation can influence the compliance with this guideline. Failure to mobilize early is quite common and has been shown to increase

recovery time after surgery.

Chewing Gum: The final postoperative intervention to be discussed is the use of chewing gum. One of the major contributing factors to increased length of stay in standard practice colonic resections is intestinal obstruction, or ileus. Chewing gum has been shown to significantly reduce the incidence of this major complication. Mimicking food consumption, the chewing motion stimulates the vagus nerve and results in a release of hormones which stimulate gastrointestinal motility (Chan and Law, 2007). As a simple and inexpensive intervention that assists in reducing one of the most prominent complications in colonic resections, it is a vital component of the ERAS pathway.

Appendix II: TPMI Statement of Confidentiality

Translational & Personalized Medicine Initiative

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STATEMENT OF CONFIDENTIALITY

I, _____, having access to information from the Translational & Personalized Medicine Initiative (TPMI) which will identify research projects, outcomes, collaborations and possible personal identifiable information, agree that I am bound to confidentiality of all matters within TPMI. During my involvement with TPMI as a researcher I agree the content of information that I may be privy to in this role will not be discussed or disclosed in any means outside the normal parameters of the project and my role. I will consider myself liable to legal action if confidentiality is breached.

Date:_____

Signature:_____

Address:_____