2022-06-17

A Cost-Utility Analysis of Robotic vs. Laparoscopic-assisted Rectal Cancer Resection

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A Cost-Utility Analysis of Robotic vs. Laparoscopic-assisted Rectal Cancer Resection

by

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A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE

DEGREE OF A MASTER OF SCIENCE

GRADUATE PROGRAM IN COMMUNITY HEALTH SCIENCES

CALGARY, ALBERTA

JUNE, 2022

Abstract

Robotic-assisted colorectal surgery is a novel minimally invasive approach to cancers of the rectum and rectosigmoid. Compared to the more established laparoscopic-assisted technique, the robotic platform offers three-dimensional visualization and greater degrees of instrument mobility. While the robotic technique has gained widespread use in the United States and Europe, implementation in Canada remains limited due to high costs. Although there is some evidence for improved robotic outcomes, there is minimal reporting of Canadian outcomes after robotic rectal and rectosigmoid cancer resection. Further, there is a paucity of economic evaluations informing the cost-effectiveness of robotic rectal cancer resection. We assessed clinicopathologic outcomes and surgeon learning curve associated with robotic-assisted rectal and rectosigmoid cancer resection in an Alberta setting. We then systematically reviewed existing economic evaluations on robotic-assisted colorectal surgery. Finally, we performed a cost-utility analysis to inform the robotic technology's cost-effectiveness compared to the laparoscopic approach in rectal cancer care. Our Canadian outcomes study included 67 patients who underwent robotic-assisted rectal and rectosigmoid cancer resection in Alberta's first robotic colorectal surgery program. We found that the Alberta clinicopathologic results are comparable to existing international studies despite surgeons in the Alberta program being robotic novices at the start of the series. Robotic operating time decreased significantly as surgeon experience increased. We found four economic evaluations in the literature reporting on cost-effectiveness of robotic-assisted colorectal surgery. Two studies found it to be cost-effective whereas the other two found the contrary. Due to significant inter-study heterogeneity and contradicting results, there is no definitive conclusion to robotic cost-effectiveness without further research. Our cost-utility analysis found that robotic-assisted rectal cancer surgeon is cost-effective compared to the laparoscopic approach at a Canadian cancer care-specific cost-effectiveness threshold of CAD $100,000, assuming high case volumes on the robot. The wider adoption of robotic technology in Canadian rectal cancer care should be considered at high volume centres.

Keywords: robotic surgery, laparoscopic surgery, colorectal surgery, rectal cancer, economic evaluation, cost-effectiveness, cost-utility

Preface

This thesis is manuscript-based and composed of three manuscript chapters, as outlined below. One manuscript has been submitted for consideration of publication whereas the other two are pending submission. MYL led the study design, data collection, data analysis and interpretation of results with support from co-supervisors. MYL completed initial drafts of all manuscripts. All co-authors contributed to critical analysis of results and critical review of manuscripts.

Submitted:

Li MY, Daigle RJ, Clement F, Niven DJ (2022). Economic evaluations of robotic versus laparoscopic-assisted colorectal surgery: A systematic review. (Submitted to *Dis Colon Rectum*)

Pending submission:

Li MY, Muncner S, Dosanjh J, Dykstra MA, Snelgrove R, Rennert-May E, Crump T, Datta I, Dixon E, Wang H (2022). Robotic-assisted rectal and rectosigmoid cancer resection: early results from the Edmonton robotic colorectal surgery program. (Pending submission to *Surg Endoscopy*)

Li MY, Dykstra MA, Snelgrove R, Wang H, Dixon E, Rennert-May E, Crump T (2022). Robotic vs laparoscopic-assisted rectal cancer resection: A cost-utility analysis. (Pending submission to *Ann Surg*)

Acknowledgements

I would like to acknowledge my supervisory committee members, Dr. Elijah Dixon, Dr. Trafford Crump, Dr. Elissa Rennert-May and Dr. Indraneel Datta for their support and steady encouragement throughout this undertaking. Bringing this thesis to fruition while completing a full-time surgical fellowship has certainly been challenging but your flexibility and understanding have been instrumental in making this possible.

I would also like to thank my colorectal surgical colleagues from the University of Alberta, Dr. Haili Wang, Dr. Ryan Snelgrove and Dr. Mark Dykstra for your expertise in robotic colorectal surgery. I have benefited from your mentorship during surgical residency and have enjoyed the continued opportunity to collaborate with you during my Master's degree. My graduate experience has been enhanced by its dual-institutional nature and the consequent benefit of working with people like yourselves.

I must also extend my sincere gratitude to Dr. Paul Ronksley, Dr. Alexander Leung and Dr. Eldon Spackman. Dr. Ronksley and Dr. Leung, thank you for guiding me through a systematic review of economic evaluations before I learned how to perform economic evaluations! Dr. Spackman, thank you for your patience during the many e-mails and Zoom calls spent troubleshooting my decision analytic model.

I am grateful to the clinical faculty of my colorectal surgery fellowship as well as my program director, Dr. Don Buie, for checking in on me during my graduate journey and for helping to shape me into the surgeon I am.

Finally, I would like to thank my family and friends; particularly Sam, for tolerating me during the last two years, during the ones before that, and for the many more to come. You are the bestest and deserve the highest degree for expertly navigating the stress nugget that I can be.

This work was financially supported by the Government of Alberta through the Alberta Graduate Excellence Scholarship and by the Royal College of Physicians and Surgeons of Canada through the Royal College Bridging Grant. This work received data support from the Alberta Health Services Financial Planning, Activity and Costing department.

Dedication

For 妈妈.

Thank you for having imparted your wisdom, for having believed in me, and for continuing to look out for me in all that I do.

Table of contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations

US	United States
MIS	Minimally invasive surgery
RACS	Robotic-assisted colorectal surgery
LACS	Laparoscopic-assisted colorectal surgery
CEA	Cost-effectiveness analysis
CUA	Cost-utility analysis
CBA	Cost-benefit analysis
ICER	Incremental cost-effectiveness ratio
QALY	Quality-adjusted life year
CADTH	Canadian Agency for Drugs and Technologies in Health
RCT	Randomized controlled trial
CE threshold	Cost-effectiveness threshold
OCS	Open colorectal surgery
LOS	Length of stay
HUI 2	Health Utilities Index 2
WTP	Willingness-to-pay
UAH	University of Alberta Hospital
LAR	Low anterior resection
APR	Abdominal perineal resection
BMI	Body mass index
LARS	Low anterior resection syndrome
DLI	Diverting loop ileostomy
AHS	Alberta Health Services
OR	Operating room
CEAC	Cost-effectiveness acceptability curve
UAH	University of Alberta Hospital
STROBE	Strengthening the Reporting of Observational Studies
LAR	Low anterior resection
APR	Abdominoperineal resection
HP	Hartmann's procedure
TME	Total mesorectal excision
CCI	Charlson comorbidity index
BMI	Body mass index
AJCC	American Joint Committee on Cancer
MRI	Magnetic resonance imaging
LOS	Length of stay
REDCap	Research Electronic Data Capture
ANOVA	One-way analysis of variance
CRM	Circumferential resection margin
ROLARR	RObotic vs. LAparoscopic Resection for Rectal Cancer
ERAS	Enhanced recovery after surgery
COREAN	Comparison of Open versus laparoscopic surgery for mid or low REctal cancer After Neoadjuvant chemoradiotherapy
COLOR II	COlorectal cancer Laparoscopic or Open Resection

ACOSOG Z6051	American College of Surgeons Oncology Group Z6051
ALaCaRT	Australasian Laparoscopic Cancer of the Rectum Randomized Clinical Trial
COVID-19	Coronavirus Disease 2019
OCS	Open colorectal surgery
CHEC	Consensus on Health Economic Criteria
NICE	National Institute for Health and Care Excellence
HUI-2	Health Utilities Index 2
SF-36	Short Form 36
QOL	Quality of life
DLI	Diverting loop ileostomy
CAD	Canadian Dollars
USD	US Dollars
CEAC	Cost-effectiveness acceptability curve
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
NSQIP	National Surgical Quality Improvement Program

CHAPTER 1. Introduction and Overview of Thesis

1.1. Research Problem

1.1.1. Burden of disease and colorectal cancer management

In 2020, colorectal cancer is estimated by Canadian Cancer Statistics to be the third most commonly diagnosed malignancy and the second leading cause of cancer death in Canada [1]. It is estimated that in the past year, 26,900 Canadians will have been diagnosed with colorectal cancer and 9,700 would have died from this disease [2]. Cancers of the rectum and rectosigmoid colon are the most challenging colorectal cancers to remove due to their location in the narrow, bony pelvis, where visualization and instrumentation are limited. These challenges are significantly increased in obese patients and males with a narrow pelvis [3].

Surgery remains the gold standard cancer therapy [4]. Surgery could be performed open or via minimally invasive surgery (MIS). Open surgery involves a single large incision through which surgeons handle tissue directly. MIS involves several keyhole incisions through which surgeons handle tissue indirectly by using instruments inserted through trocars in the abdominal wall. MIS results in decreased post-operative complications including pain, wound infection, bleeding and length of hospital stay [5,6]. Use of MIS technique has surged, with United States (US) data demonstrating an increase in its use from 44% of elective colorectal resections in 2011 to 75% in 2018 [7].

1.1.2. Economic burden

Despite advances in treatment and outcomes, the financial burden of colorectal cancer to the healthcare system remains significant. According to year 2000 estimates, the average lifetime cost of managing a case of colorectal cancer in Canada ranged from CAD $20,319 to $39,182[8], which is similar to that for breast cancer (CAD $23,275 to 36,340 depending on stage)[9]. These costs increased in rectal cancer and more advanced cancer stages [8]. Although recent estimates specific to colorectal cancer are not available, the general economic burden of cancer care in Canada has more than doubled and this trend likely applies to colorectal cancer given its prevalence [10]. This increase is driven by a rise in hospital expenditure, of which technology is a major cost driver. Most experts agree that technological change is the most important driver of health care spending increases over time [11]. Thus, the cost-effectiveness of health technology, such as the approach used in colorectal cancer resection, needs to be evaluated.

1.1.3. Robotic vs laparoscopic rectal and rectosigmoid cancer

Given the increasing adoption of MIS techniques, our study will focus on the comparison of different MIS techniques. The two main types of MIS techniques are laparoscopic and robotic colorectal surgery, which have differing costs and outcomes. In laparoscopic-assisted colorectal surgery (LACS), the surgeon operates using two laparoscopic instruments at a time while looking at a 2D video feed [12]. In the more novel robotic-assisted colorectal surgery (RACS), the surgeon uses a robotic console to simultaneously control 4 arms of the robot while looking at a 3D video feed capable of magnification and depth perception [13,14]. In addition, RACS offers 7 degrees of wristed movement at the tips of its instrument compared to the 4 degrees in LACS. Clinically, these technical advantages have been associated with decreased length of stay, blood loss and need to convert to open surgery in RACS compared to LACS [15–17]. These advantages have led to the rapid adoption of RACS during the past decade in Europe and the US [18]. However, two points of contention in choosing RACS over LACS in rectal and rectosigmoid cancer surgery remain: 1) as evidence in RACS grows, there are conflicting studies regarding whether the improved clinical outcomes in RACS apply to all patients or only some subgroups (e.g. male, obese); and 2) since RACS costs are significantly higher, it remains unclear whether its potential benefits justify its price tag.

The issue of conflicting RACS vs LACS outcomes is especially important to settings like Canada where RACS uptake is sporadic. In Canada, RACS adoption is limited to a handful of academic centres in Ontario, Quebec, and Alberta[19,20]. Low surgical volumes and limited data to inform outcomes make it difficult to determine whether RACS implementation in Canada should be expanded or scaled back. Additional studies, even if limited in sample size, would contribute to the evidence on clinical outcomes of RACS in a Canadian setting.

With regards to the high costs of using RACS, there is a paucity of economic evaluations worldwide to assess the cost-effectiveness of RACS vs LACS in rectal and rectosigmoid cancer. In addition, the few existing economic evaluations have significant design flaws that preclude adequate assessment of the costs and effectiveness of RACS compared to LACS. Thus, the value of RACS in rectal and rectosigmoid cancer resection remains unclear. There is a lack of robust economic evaluations to guide the funding decisions for RACS in a rectal and rectosigmoid cancer setting, both in Canada and internationally.

1.1.4. Value for money and the role of economic evaluations

Healthcare resources are finite, thus value for money is an important concept. Value for money is determined by health system output and its associated expenditure[21]. Given that value for money is composed of health output and economic input, it is important to study both in order to appropriately assess value for money and increase healthcare system efficiency.

The types of study that focuses on the dual assessment of health output and economic input are known as economic evaluations [22]. It is important to perform economic evaluations rather than to use clinical trials or costing studies in isolation because economic evaluations are the only type of analyses that assesses health care costs and outputs in the context of each other. Economic evaluations offer systemic analysis of the relevant alternatives, clearly identify the perspective from which healthcare choices are made, quantifies the costs and effectiveness of healthcare programs, and approaches the assessment of value for money with explicitness and accountability [23].

There are several types of full economic evaluations, but all must compare different alternatives and evaluate their costs and clinical consequences. Main types of economic evaluations are cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). The outcome for all types of economic evaluations is the incremental cost-effectiveness ratio (ICER), which is the ratio of costs to effectiveness. However, the various types of economic evaluations differ by how effectiveness is measured [24]. CEAs measure effectiveness in natural units (e.g. millimetres of mercury when studying blood pressure). Although these units are most intuitive to clinicians, studies of different diseases or studies using different units cannot be compared [25]. CUAs is a sub-type of CEAs and measure effectiveness in only one unit, most commonly the quality-adjusted life year (QALY). The QALY is a function of time spent in a health state and one's preference for that health state [26]. This preference is represented by a utility value, which usually ranges from negative infinity to 1. In this context, a value of zero represents the health-related quality of life associated with death, a negative value represents health states felt to be worse than death, and a value of 1 represents perfect health [27]. QALYs allow comparison across different studies. For this reason, CUAs are preferred over

CEAs as the recommended type of economic evaluation by the Canadian Agency for Drugs and Technologies in Health (CADTH) [28]. Finally, CBAs measure effectiveness in monetary values of health gained or lost. There is controversy regarding whether it is ethical to quantify human life and suffering in dollar amounts, thus CBAs are infrequently utilized to perform economic evaluations [29].

Economic evaluations can be conducted alongside a clinical trial or using decision-analytic modelling. The advantage of using trial data is high quality evidence and the need for fewer assumptions [30]. However, a trial may not capture all the variables or have the follow-up duration needed in an economic evaluation. Using a model circumvents these problems by allowing the use of multiple sources of evidence, including but not limited to randomized controlled trials (RCTs), observational studies and the grey literature. The disadvantage of model-based studies is that assumptions are often made when good data aren't available, which could lower the accuracy of the results [31].

In line with the transparent and accountable nature of economic evaluations, each evaluation is defined by a decision problem which outlines the following: the alternatives being compared, the setting of comparison (including the specific health jurisdiction), the perspective, time horizon, discounting rate, cost-effectiveness threshold, and the target population of the analysis. Perspective refers to the point of view adopted when deciding which costs to include[32]. CADTH recommends a healthcare system perspective, which includes costs borne by the public health payer. On the other hand, a societal perspective would include all social opportunity costs, such as costs associated with patients' lost days of work, drug costs borne by the patient, and costs of productivity loss when family members take on caregiving. The time horizon refers to the period over which costs and effectiveness are accounted for. Discounting refers to the idea in economic theory that individuals prefer to have consumption abilities now rather than the future. This time preference applies both to costs and effectiveness. Thus, when the time horizon is longer than one year, future costs and effectiveness are discounted to reflect this time preference. Finally, the cost-effectiveness (CE) threshold is what the ICER, the outcome of an economic evaluation, is compared to. The CE threshold has the same units as the ICER and is jurisdiction-specific. It represents the amount of money the decision-maker is willing to pay in exchange for one unit of effectiveness, such as a QALY. When the ICER of a healthcare programme is lower than the CE threshold, the programme is considered cost-effective. In health economics language, the CE threshold is distinct from the willingness-to-pay (WTP) threshold, but they are sometimes used interchangeably in the clinical literature.

As aforementioned, RACS is a costly technology and its clinical benefits are controversial. There is also a paucity of Canadian data to inform the limited use of RACS in Canada and a general lack of robust economic evaluation on RACS vs LACS. The following section will review the literature on these topics with the goal of highlighting the importance and relevancy of our work.

1.2. Literature Review

1.2.1. Costs and benefits of robotic-assisted colorectal cancer surgery

Considerations in choosing RACS vs LACS include RACS costs and clinical benefits. With regards to cost, RACS has been shown to be significantly more costly than LACS[33–35]. One main cost driver is RACS equipment cost, which includes high initial purchase price of the surgical robot, expensive consumable instruments and high annual maintenance costs[36]. Two Canadian studies on RACS costs exist in the literature and both have omitted the initial purchase and annual maintenance costs. In Ramji et al.'s 2015 rectal cancer study comparing RACS and LACS costs, 26 RACS and 27 LACS cases completed between 2007-2013 in Toronto [19] were compared. The median cost per episode of care was CAD $18,273 for RACS compared to CAD $11,493 for LACS (p=0.029) [19]. This led to the conclusion that RACS in rectal cancer is associated with significantly increased costs. A more recent RACS study published in 2022 by Patel et al. compared costs before and after robotic program implementation. A total of 129 RACS cases were included in the post-robotic implementation phase. The study found no significant difference between total cost of care between the two MIS approaches. However, surgical costs of RACS exceeded that of LACS by $2,549 per case. Unlike Ramji et al., this study was not target anatomy or diagnosis-specific (both colon and rectal resections as well as all pathologies were included). RACS costs in both studies must be interpreted in the context of omitted upfront equipment and maintenance costs, which averaged USD $1.47 million and USD $80,000-170,000 per year in 2017, respectively. These costs have increased since then with newer models[37]. Thus, both studies likely underestimate the true cost of RACS.

Another major RACS cost driver is longer operating times associated with docking and repositioning of the robot [13]. Docking refers to setting the robot up in the operative field once the patient is placed under general anesthetics and the sterile field is established. This includes positioning the robot, setting up the camera and connecting the different arms of the robot to trocars placed in the patient's abdominal wall. Repositioning refers to the need to repeat this process when the operation needs to be performed in more than one quadrant in the abdomen[13]. Older generations of the robot were designed to operate in only one quadrant, thus if the operative field involves a different quadrant, the docking process needs to be repeated, incurring additional operative time. In addition to docking and re-positioning, operating times may be prolonged in RACS compared to LACS due to relative surgeon inexperience [38]. Given RACS is a more novel technology, practicing surgeons may still be on their learning curve. In a 2018 systematic review and meta-analysis, Prete et al. included 5 trials of moderate quality comparing RACS vs LACS for rectal cancer[15]. The mean overall operating time was longer in RACS by 38.43 minutes. Although there are similar findings of longer RACS operating times in the literature [34,39], research has shown that operating time could be shortened with increasing surgeon experience and the introduction of newer generation robots that simplify repositioning and eliminate the need for re-docking [13,40–42].

Lastly, there is controversy regarding the clinical benefits of RACS. While many observational studies have reported decreased hospital stay, blood loss and conversion rate [15–17], the landmark ROLARR trial by Jayne et al. randomizing 237 patients to RACS vs 234 patients to LACS found no significant difference between the RACS and LACS groups in these outcomes[33]. The lack of difference is especially notable in conversion rate. Conversion to open surgery occurs when a surgery cannot be completed minimally invasively due to poor visualization or lack of working space. This lack of working space may be a result of obese body habitus, difficult anatomy (e.g. narrow male pelvis or advanced tumour) and/or scar tissue from previous surgery. In these cases, the decision to switch from a minimally invasive to open approach would be made. However, outcomes will be similar to those of open surgery, which is associated with worse postoperative pain, higher rates of surgical infections, higher blood loss and longer length of stay [5,6]. As a result, low conversion rates are preferred and the ability of RACS to reduce conversion rates has garnered much attention. As the largest RCT to date on RACS in a rectal cancer population, ROLARR showed no significant difference between the two approaches with regards to conversion. However, there was a trend towards lower conversion in RACS than LACS (8.1% vs 12.2%). Further, this difference was statistically significant in subgroups of male patients and patients with obesity. Although ROLARR did not show a difference in conversion rate or any of the other outcomes studied, systematic reviews conducted on this subject have continued to show clinical benefits such as shorter length of stay and lower conversion rate with RACS, even when ROLARR was included[15]. Thus, the debate on clinical benefits between RACS and LACS has not been definitively concluded.

1.2.2. Canadian data on RACS vs LACS clinical outcomes

The lack of consensus in outcomes after RACS is demonstrated by two Canadian RACS studies, which analyzed outcomes in addition to the aforementioned costs. Ramji et al. did not find a statistically significant reduction in conversion rate in RACS whereas Patel et al. found the contrary. Ramji et al. compared clinicopathologic outcomes between RACS, LACS and open colorectal surgery (OCS) in rectal cancer resection. The authors found that compared to LACS, RACS was associated with significantly lower estimated blood loss (mean 296 vs 524 mL, $p = 0.04$) and trended towards a lower incidence of conversion (12% vs. 37%, $p = 0.05$). There was no difference between RACS and LACS in complication rate, length of stay (LOS), 30-day readmission or 30-day mortality rates. No differences were observed in short-term pathologic outcomes such as the quality of mesorectal excision or number of lymph nodes harvested. However, the median cost per episode of care was significantly higher in RACS than in LACS, solely due to differential costs incurred in the surgical suite. Operative time was also significantly longer in RACS than LACS (mean 407 min vs 240 min, $p < 0.01$), which the authors attribute to docking/undocking of the robot and the operating room staff's relative unfamiliarity with the RACS set-up.

This study echoes some of the RACS clinical benefits seen in other studies and report higher RACS costs and longer operating times as one would expect. However, the study's sample size was small, findings are dated (from years 2011-2013) and the greater RACS clinical benefits were not discussed in the context of higher costs. Although the more recent study by Patel et al. improved on some of these limitations such as sample size (RACS n=129 and LACS n=105), Patel et al.'s study was not specific to rectal cancer resection and thus its results are not applicable to this subject. Also, significant RACS capital equipment and maintenance costs were again omitted in Patel et al. Finally, statistically significant clinical benefits in Patel et al. were the result of a three-way comparison between RACS, LACS and OCS with no post hoc analyses.

Such an omnibus test is unable to confirm whether the statistically significant difference in length of stay and surgical time is related to RACS, since the difference could be between any two of the three approaches. Finally, despite both Canadian studies reporting on costs and clinical outcomes, neither was an economic evaluation and thus neither could not comment on the value of RACS vs LACS in rectal cancer resection.

1.2.3. Existing cost-effectiveness studies on robotic-assisted colorectal cancer surgery

There are two existing economic evaluations comparing RACS vs LACS rectal surgery. Both evaluations are CUAs published in 2021. One study is a trial-based CUA by Quijano et al. while the other is a model-based CUA by Simianu et al. The trial-based study was a Spanish analysis conducted alongside a retrospective cohort study comprising 81 RACS patients and 104 LACS patients [43]. The indication for surgery was rectal cancer and surgeons in this study had baseline experience in RACS (40 RACS cases performed at the authors' centre prior to data collection). Costs considered included that of the index operation and hospital stay, but not robotic equipment or maintenance costs. Effectiveness was measured at 3 months postoperatively. This was done by deriving utilities from the SF-36, a health-related quality of life questionnaire. Eight subscales of the SF-36 were used to calculate the Health Utilities Index 2 (HUI 2) using the Nichol method. Quijano et al. used a healthcare sector perspective with a one year time horizon and a willingness-to-pay (WTP) threshold of €20,000-30,000/QALY. RACS had higher mean costs and higher mean QALY at 1 year, resulting in an ICER of €1555.90/QALY, which is below the WTP threshold. Thus, the authors concluded that RACS is cost-effective.

The other CUA on RACS vs LACS by Simianu et al. was a US model-based study examining RACS and LACS for all rectal pathologies, rather than in cancer care alone [44]. The model was a decision tree which included decision branches for conversion to open as well as a variety of health states that describe possible complications. Many postoperative complications are possible, but this study selectively considered three of them: ileus (temporary arrest of bowel function after surgery), surgical site infection and incisional hernia. Model inputs for cost were US-based whereas inputs for effectiveness were derived from studies performed in a variety of countries, including the US, United Kingdom and Korea. Analysis was undertaken for both the healthcare system and societal perspectives. A one year time horizon was adopted and a US-specific WTP threshold of US$100,000 was used. The model found that RACS was associated with higher costs compared to LACS but a very minimal increase in QALY (0.00066), resulting in an ICER of $751,056/QALY in the societal perspective and $1,485,139/QALY in the healthcare system perspective. Regardless of perspective, the ICER of RACS vs LACS surpassed the WTP threshold. Thus, the authors concluded that RACS was not cost-effective.

Strengths and weaknesses in the existing CUAs on RACS vs LACS in rectal surgery are as follows. The trial-based CUA by Quijano et al. used real-world data in the form of a cohort study to inform their inputs. In this sense, the costs and effectiveness included in this study were specific to their decision problem and fully generalizable to their target population. However, this study did not include all relevant costs such as the significant cost of robotic equipment and maintenance. Inclusion of such costs may have made the ICER much higher, in which case the ICER could have surpassed the WTP and the study would conclude that RACS is not cost-effective compared to LACS. Exclusion of such an important cost factor has the potential to change the outcome of the study and is therefore a major weakness. Further, Quijano et al. only measured utilities derived using HUI 2 at 3 months postoperatively. This would fail to capture late complications associated with surgery such as incisional hernias. In addition, some surgical complications are permanent, such as bowel, bladder and sexual dysfunction due to pelvic nerve damage during dissection. A time horizon of one year would not capture these important permanent reductions in quality of life and hence is unlikely to accurately reflect the real value of RACS vs LACS.

The model-based CUA by Simianu et al. included the important capital equipment and maintenance costs. In addition, the study included both the healthcare system perspective and the broader societal perspective to explore whether results change based on the types of costs included. The adoption of both perspectives is a more comprehensive analysis. However, Simianu et al. only considered three postoperative complications in their model, which failed to capture other common complications for which there may be differences in cost and effectiveness between RACS and LACS. Examples of this are costly complications such as intraabdominal sepsis from abscess or anastomotic leak, which could influence the ICER due to the additional costs required to treat them. Other examples are permanent bowel, bladder or sexual dysfunction which may significantly influence health-related quality of life and thus impact the ICER due to their role in determining effectiveness. Finally, Simianu et al. used a short time horizon of one year. Again, a one year time horizon would not capture important long-term factors associated with cost or effectiveness.

1.2.4. Significance of the research problem

Whether the clinical outcomes of RACS are superior to those of LACS in rectal cancer resection remains unclear. This is especially true in the Canadian setting where RACS adoption and outcomes are limited. Given a paucity of Canadian outcome data on RACS in rectal and rectosigmoid cancer, the following questions remain: what are updated outcomes in Canadian RACS rectal cancer resection? Are the clinical benefits of RACS reported in outcome studies from other countries seen in a Canadian population? The single existing Canadian study on RACS rectal cancer resection is not enough to answer these important questions and the more recent study cannot appropriately answer these questions given its broad inclusion criteria beyond rectal resection and cancer surgery.

From a health economics perspective, many costing studies report on the significantly higher cost associated with using RACS for rectal cancers. However, there are few economic evaluations assessing the value associated with using the RACS vs LACS. The two existing evaluations are flawed in their study design and are unlikely to capture all relevant differences in cost and effectiveness between RACS and LACS. Further, they draw different conclusions on RACS cost-effectiveness. As healthcare resources are precious and finite, more comprehensive economic evaluations must be performed to allow efficient delivery of surgical care to patients with rectal and rectosigmoid cancers.

1.2.5. Purpose of the study

In order to address the knowledge gap in Canadian RACS clinical outcomes and the lack of economic evaluations informing the choice between adopting robotic vs laparoscopic technology for rectal cancer resection, the purpose of this study include the following:

1) To report on updated short-term clinicopathologic outcomes after RACS rectal and rectosigmoid cancer resection. This will be accomplished using retrospective chart review of patients who have undergone RACS for a diagnosis of rectal or rectosigmoid cancer in Edmonton, Alberta. Rectosigmoid cancers will be included due to rectosigmoid

cancers being a continuum of high rectal cancers, with similar surgical management options.

2) To summarize current literature involving economic evaluations of RACS vs LACS
3) To evaluate the cost-effectiveness of RACS compared to LACS in the setting of rectal cancer.

1.3. Thesis Outline

The following chapters in this manuscript-based thesis is composed of three studies to address our three objectives. Each manuscript has been formatted for publication in peer-reviewed journals. The overall aim is to improve Canadian reporting on RACS in rectal and rectosigmoid cancer, assess the knowledge gap in economic evaluations of RACS vs LACS and to use Canadian data to inform cost-effectiveness of RACS in rectal cancer care.

We evaluated short-term clinicopathologic outcomes after rectal and rectosigmoid cancer resection using data from Alberta's first robotic colorectal program. We also studied the associated surgeon learning curve given the effect of operating time on RACS costs, both of which are described in chapter 2. As part of this study, we assessed operating time and length of hospital stay in this Alberta cohort, which will be used in chapter 4.

In chapter 3 we describe a systematic review summarizing the existing literature on economic evaluations of RACS vs LACS. We review the four existing studies in detail and carefully interpret their quality and results by breaking down nuances of interstudy heterogeneity for clinical audiences. This chapter also better informs our subsequent economic assessment of the robotic technology by addressing limitations in existing studies.

We then built a decision analytic model using inputs from chapter 2 and the literature. We report on a cost-utility analysis of RACS vs LACS rectal cancer resection in chapter 4. Our results contribute to the paucity of economic evaluations on RACS and could help guide decision-making regarding funding of this technology in Canada and abroad.

Finally, in chapter 5 we address the implications of our work especially as they relate to healthcare decision-making. We discuss strengths, limitations and directions for future research to better improve our choices in healthcare given the precious healthcare resources available to us.

CHAPTER 2. Robotic-assisted rectal and rectosigmoid cancer resection: early results from the Edmonton robotic colorectal surgery program

This chapter will be submitted as **Li MY**, Muncner S, Dosanjh J, Dykstra MA, Snelgrove R, Rennert-May E, Crump T, Datta I, Dixon E, Wang H (2022). Robotic-assisted rectal and rectosigmoid cancer resection: early results from the Edmonton robotic colorectal surgery program. (Pending submission to *Surg Endoscopy*).

In this chapter we study a cohort of patients under RACS for rectal and rectosigmoid cancer resection. The cohort is derived from Alberta's first robotic colorectal surgery program and provides short-term clinicopathologic outcomes as well as information about surgeon learning curve. The former highlights Canadian results and allows comparison to international studies, while the latter provides institutions without prior robotic experience with information about salient trends, especially if they are looking to adopt RACS.

2.1. Abstract

Background: Robotic-assisted surgery could be advantageous in rectal and rectosigmoid cancer resection due to improved visualization and instrument mobility. However, implementation in Canada is limited by high cost and little evidence. We report on Canadian short-term clinicopathologic outcomes and compare differences in operating time by procedure type and surgeon learning curve.

Methods: A single-centre retrospective review of robotic-assisted rectal and rectosigmoid resections was performed. Baseline demographics and clinicopathologic outcomes were analyzed. Procedure subgroups included low anterior resection, abdominoperineal resection and low Hartmann procedure. Subgroups by surgeon learning curve were defined as the first and last 10 cases of the series.

Results: Sixty-seven patients with a mean age of 63.5 years (standard deviation [SD] ±9.3) and mean body mass index of 29.0 (SD ±6.2) were included. Median distance from anal sphincter was 5.0 cm (range 0-15). Thirty-day complication, readmission and mortality rates were 10.5%, 9.0% and 0%, respectively. No conversions occurred and complete/near complete total mesorectal excision rate was 98.5%. Operating time decreased between the first and last 10 cases ($p=0.011$) but did not differ by procedure type ($p=0.17$).

Discussion: Our study's clinicopathologic results are comparable to existing studies despite our group being robotic novices at the start of the series. Robotic operating time decreased significantly as surgeon experience increased.

Conclusion: Implementation of robotic rectal and rectosigmoid cancer resection in a Canadian centre is feasible with comparable clinicopathologic outcomes to other robotic centres.

2.2. Introduction

Robotic-assisted surgery is a novel minimally invasive approach in colorectal surgery[13,36]. Compared to the laparoscopic technique, the robotic platform offers three dimensional visualization with improved depth perception and greater degrees of instrument mobility[13,14]. These technical advantages are important when operating on rectal and rectosigmoid cancers in the confined space of the pelvis, where visualization and exposure are often challenging[3].

Although robotic rectal surgery has gained widespread use in the United States (US) and Europe, its implementation in Canada remains limited to select academic centres[19,20]. The biggest barrier to robotic uptake is high upfront costs, which is driven by significant equipment costs and longer operating time[34,37,45].

Due to limited implementation, there is minimal Canadian literature reporting robotic rectal cancer resection outcomes. Ramji et al. compared clinical and economic outcomes of robotic, laparoscopic, and open rectal cancer resection at the University Health Network, Toronto, Ontario[19]. This study found significantly lower rate of conversion to open surgery and lower estimated blood loss in the robotic cohort. However, the robotic approach was associated with significantly longer operating time and higher operating room costs. The study was limited by a small sample size of 26 patients in the robotic cohort and examined older data from 2011-2013. A more recent 2022 study by Patel et al. compared outcomes and costs associated with left-sided colorectal resection before and after robotic program implementation at the Kingston Health Sciences Centre in Kingston, Ontario[20]. This study showed improved clinical outcomes such as lower rate of conversion to open surgery and shorter length of stay. Although this study included a larger sample size of 129 patients in the robotic cohort, its primary goal was comparing time periods before and after robotic implementation rather than surgical approaches. In addition, it included left-sided resections for any indication. Thus, the study focus was not on rectal resection or cancer surgery, leaving ongoing gaps in the Canadian literature about updated outcomes after robotic-assisted rectal or rectosigmoid cancer resection.

Emerging healthcare programs such as robotic rectal cancer resection should be thoroughly evaluated in a publicly funded healthcare system given the importance of patient outcome maximization in resource-constrained systems[46]. One such component of healthcare program evaluation is clinical effectiveness, including clinicopathologic outcomes. At this time, long-term clinicopathologic outcomes are lacking in the literature due to the relatively recent introduction of robotic surgery. However, it remains feasible and valuable to study short-term clinicopathologic outcomes. Although literature on this subject in the setting of robotic rectal and rectosigmoid cancer surgery is available from other countries, it is important to collect Canadian data as our patient population and surgeon experience in robotic surgery differ from those of other countries. In the US, for example, 98% of colorectal fellowship programs surveyed in 2019 offer robotic training[47] whereas in Canada, this number is 0%. Differential training and volume are important because volume is often positively correlated with clinicopathologic outcomes[48–51].

Our primary objective was to report on updated short-term clinicopathologic outcomes after robotic-assisted rectal and rectosigmoid cancer resection using data from a quaternary Canadian centre. Our secondary objective was to compare operating time by type of rectal resection and by timing of surgery with respect to surgeons' robotic learning curve, defined arbitrarily in our series as the comparison between the first and last 10 cases. There is evidence that operating time differs by type of rectal resection[52] (e.g. low anterior resection vs. abdominoperineal resection) and by surgeon experience[53–55]. Operating time was examined as a secondary objective because it not only affects costs[56,57] but also affects short-term outcomes[58,59]. Costs were not included as part of this study because they are assessed in a separate cost-utility analysis performed by our group[60].

2.3. Methods

We performed a retrospective single-centre review of robotic-assisted rectal and rectosigmoid cancer resections performed at the University of Alberta Hospital (UAH) in Edmonton, Alberta, a quaternary care centre with a dedicated colorectal surgery service. The Edmonton robotic colorectal surgery program began in November 2018 and was the first robotic colorectal program in western Canada. A prospective database consisting of patients undergoing colorectal resection at the UAH was established at program inception and included patients undergoing colorectal resection for all indications and via all approaches, including the robotic approach. Patient information including name, medical record number, date of procedure, procedure performed, and surgical approach was collected. Patients were selected for the robotic approach if they did not have any contradictions to minimally invasive surgery (e.g. previous laparotomy suggestive of significant adhesions). The robot replaced laparoscopy as the approach of choice for MIS rectal and rectosigmoid resections once the robotic program was implemented.

For the present study, ethics approval was obtained from the Health Research Ethics Board of Alberta to use the prospective database to identify patients who underwent robotic-assisted rectal and rectosigmoid resection for cancer. A retrospective chart review was then performed to collect additional baseline and outcome data from Connect Care (Epic Systems Corporation, Wisconsin), the electronic medical records system employed at the UAH. This study is reported as per the Strengthening the Reporting of Observational Studies (STROBE) recommendations (Appendix 2.1).

2.3.1. Patient selection

We identified all patients undergoing elective robotic-assisted resection of rectal and rectosigmoid adenocarcinoma at the UAH from program inception on November 1, 2018 to September 30, 2021. Patients were included if they were 18 years or older at the time of surgery and if they had pathologic evidence of rectal or rectosigmoid adenocarcinoma, including malignant polyps. Procedures performed must be one of low anterior resection (LAR) with or without diverting loop ileostomy, abdominoperineal resection (APR) or low Hartmann procedure (HP). Patients were excluded if they underwent more extensive resection beyond what is routinely involved in an LAR, APR or HP. Examples of more extensive resection included concurrent liver metastatectomy or pelvic exenteration. Patients were also excluded if resection was performed in the emergency setting.

2.3.2. Technical approach

Robotic-assisted colorectal resection at the UAH is practiced via a hybrid laparoscopic-robotic model. The *da Vinci* robot (Intuitive Surgical Inc, Sunnyvale, CA) utilizing an Si surgical system is used to mobilize the left colon and isolate the superior hemorrhoidal vascular pedicle. The pedicle is ligated using a laparoscopic vessel sealing device. Following this, the robot is used to perform total mesorectal excision (TME). Bowel division at the distal resection margin is performed using a laparoscopic stapler. The specimen is then extracted via a Pfannenstiel incision. In LAR, the proximal colon is returned to the peritoneal cavity and an end-to-end colorectal anastomosis is performed using a circular stapler. If lysis of adhesions or mobilization of the splenic flexure is required, the laparoscopic technique would be employed given the single quadrant use of the da Vinci Si model.

Data from three surgeons certified in colorectal surgery by the Royal College of Physicians and Surgeons of Canada were included in our series. These surgeons were robotic novices at the start of the Edmonton robotic colorectal surgery program. They were skilled in laparoscopic colorectal resection but were not trained in robotic surgery during residency or fellowship, which were undertaken at Canadian institutions. Additional training was obtained by two of the three surgeons (Surgeons 1 and 2) while they were in practice. The third surgeon (Surgeon 3) obtained robotic training shortly before entering practice. Surgeons frequently scrubbed together for robotic cases to maximize each surgeon's robotic experience. All three surgeons undertook dry and wet lab skills training in the United States prior to being proctored in their first live patient cases.

2.3.3. Data collection

Collected data included baseline demographics, tumour characteristics and procedural characteristics. Baseline demographics included age, sex, body mass index (BMI) and Charlson Comorbidity Index (CCI). Tumour characteristics included tumour location (rectal vs. rectosigmoid), use of neoadjuvant therapy, distance from the anal sphincter, and pathologic T and N stages, as defined by the 8th edition of the American Joint Committee on Cancer (AJCC)'s TNM Staging System. Distance from the anal sphincter was based on pre-operative magnetic resonance imaging (MRI) of the pelvis.

In keeping with the primary objective, the primary outcomes of interest were divided into short-term clinical and short-term pathologic outcomes. Short-term outcomes were defined as those for which data would be available within 30 days postoperatively. Clinical outcomes included operating time, rate of conversion to open surgery, length of stay (LOS) in hospital and 30-day complication, readmission and mortality rates. Operating time was defined as time from skin incision to skin closure. Operating time was reported as a clinical outcome because there is evidence that prolonged operating time is associated with increased complications and morbidity, thus it could be considered a surrogate clinical outcome[58,59]. Readmission was defined as any postoperative complication requiring an additional inpatient stay within 30 days of the index operation. Pathologic outcomes included lymph node harvest, completeness of total mesorectal excision (TME) and margin positivity rate.

Subgroup analyses for operating time were performed in keeping with our secondary objective. Given LAR, APR and HP are distinct procedures and have evidence of differing operating times[52], operating time between procedures were compared to assess if there are any significant differences by procedure type in our cohort. The operating time of the first and last 10 cases in our series was compared to observe the difference in operating time as surgeon case volumes increased. We expect selection bias in the first 10 cases as this was the earliest cohort of patients undergoing the new robotic program, thus they were likely to be relatively healthy with favourable pelvic anatomy and tumour characteristics. Given the small cohort sizes and descriptive nature of this study, selection bias was accepted as a limitation when comparing the first and last 10 cases.

Data collection was performed by four individuals, consisting of a surgeon, a medical student and two research nurses. All data were collected from the electronic medical records system and managed using Research Electronic Data Capture (REDCap)[61,62], a secure electronic data capture tool hosted within the data centre of the Faculty of Medicine and Dentistry at the University of Alberta.

2.3.4. Statistical analysis

Data analysis was performed using Stata 15 (StataCorp, Texas). Results were represented as the mean when the distribution is normal and as the median when the distribution is not normal. The measure of spread is represented as standard deviation for means and range for medians. When data was missing for more than 3% of the sample, exploratory analyses were performed to explore the mechanism of the missing data. When data was missing at random, multiple imputation was used. To compare the differences in operating time by the three procedural subgroups of LAR, APR and HP, one-way analysis of variance (ANOVA) was used after the data was assessed for the normality and equal variance assumptions of ANOVA. To compare the difference in operating time between the first and last 10 cases in our series, the Welch's t-interval was used due to unequal variance. A p value of <0.05 was considered statistically significant. Differences between subgroups were not assessed statistically if any of the subgroups had a cohort size less than 30% of the overall cohort size.

2.4. Results

A total of 84 patients who underwent robotic-assisted rectal or rectosigmoid cancer resection were identified from the prospectively kept database. Of these, 67 met our study's inclusion and exclusion criteria. Baseline demographic results for the overall cohort are shown in Table 2.1. For the overall cohort, mean age was 63.5 years and 48 patients (71.6%) were male. The mean body mass index (BMI) of our cohort was 29. The median Charlson Comorbidity Index (CCI) was 4, with the largest proportions of patients scoring in the low to moderate ranges (35.8% with scores of 1-3 and 38.8% with scores of 4-5). Sixty-four of the 67 patients had rectal adenocarcinoma (95.5%) whereas the remaining 3 patients had rectosigmoid adenocarcinoma (4.5%). LAR was performed in 44 patients (65.7%), APR was performed in 18 patients (26.9%) and HP was performed in 5 patients (7.4%). Of the 64 with rectal adenocarcinoma, 40 patients (61.5%) received neoadjuvant long course chemoradiation, 9 patients (13.9%) received neoadjuvant short course radiation and 16 patients (24.6%) received no neoadjuvant treatment. Median tumour distance from the anal sphincter was 5.0 cm. The most common pathologic T stages were T2 (34.3%) and T3 (37.3%). The most common pathologic N stage was N0 (62.7%). The only variable with missing data was distance from anal sphincter, which was missing at random in 10 patients and managed using multiple imputation. Reasons for missing data included lack of pelvic MRI due to contraindication to MRI imaging (e.g. presence of cardiac pacemaker) and tumour not being visualized on MRI (e.g. excised malignant polyps).

Baseline characteristics by subgroups of procedure performed and by timing of surgery (first vs. last 10 cases in the series) are also presented in Table 2.1. Notable absolute differences include HP patients being older than the overall cohort as well as the LAR and APR groups (mean age of 74.0 years compared to 63.5 years overall, 61.2 years in the LAR group and 66.2 years in the APR group). HP patients were also more comorbid (median CCI of 8 compared to 4 in the overall group, 4 in the LAR group and 4.5 in the APR group). Although the HP group was small (n=5), patients who underwent HP were more often male and had a higher rate of neoadjuvant long course chemoradiation treatment (100% male compared to 71.6% overall, 70.5% in the LAR group and 68.4% in the APR group; 100% of HP patients underwent long course chemoradiation compared to 61.5% overall, 47.6% in the LAR group and 83.3% in the APR group). Another notable difference by procedure type was that patients who underwent APR had tumours that were located closer to the anal sphincter (0.45 cm vs. 5.0 cm overall, 6.1 cm in the LAR group and 5.5 cm in the HP group). However, this is within expectations given tumour proximity or tumour involvement of the sphincter is most often the indication for performing an APR. These differences are absolute rather than statistical given the small subgroup cohorts. With regards to spread of cases between the three surgeons, Surgeon 3 performed only 4.5% of all cases but performed 20% of the last 10 cases. This is because Surgeon 3 was the newest member of the colorectal service and joined the robotic team towards the end of our accrual period. Otherwise, baseline demographics and tumour characteristics of subgroups by procedure were similar to each other and to the overall cohort.

When stratified by the first and last 10 cases, patients differed by comorbidity and procedure type. The last 10 cases had a higher median CCI score than the first 10 cases (7 vs 4 points) and a higher proportion of APRs (five out of 10 cases compared to two out of 10 cases).

Table 2.2 shows the short-term clinical outcomes. The mean overall operating time was 303 minutes. Operating time by procedure showed that LARs had a mean operating time of 291 minutes, APRs had a mean operating time of 324 minutes and HPs had a mean operating time of 343 minutes. The difference in operating time by procedure was not statistically significant ($p = 0.17$). In contrast, the difference in mean operating time of 390 minutes in the first 10 cases and 270 minutes in the last 10 cases was statistically significant ($p = 0.011$). Other clinical outcomes in the overall cohort included an anastomotic leak rate of 1.5% and a median LOS of 5 days. There were no intraoperative complications and no conversions in any of the 67 cases. The 30-day complication rate was 10.5%. The 30-day readmission rate was 9.0%. There were no mortalities within 30 days.

With regards to short-term oncologic outcomes, a median of 15 lymph nodes were retrieved on pathologic examination (Table 2.3). Grading of TME quality showed that 70.8% of specimens were complete, 27.7% were nearly complete, and 1.5% were incomplete. There was one case of an involved surgical margin due to a positive circumferential resection margin (CRM).

2.5. Discussion

Most short-term clinicopathologic outcomes of robotic-assisted rectal and rectosigmoid cancer resection at a quaternary Canadian centre are comparable to existing Canadian and international studies. For certain parameters, however, outcomes are improved. Compared to the only existing Canadian study on robotic rectal cancer surgery by Ramji et al.[19], we had reduced operating time, conversion rate, anastomotic leak rate and 30-day readmission rate (Table 2.4). Our mean operating time was 303 minutes compared to 407 minutes. We had no conversions compared to a conversion rate of 12%. Our anastomotic leak rate was 1.5% compared to 8.0%. Our 30-day readmission rate was 9.0% compared to 24%. Our pathologic complete TME rate was also higher (70.8% vs 60%). The mean LOS, 30-day mortality rate, and number of lymph nodes harvested were similar (6.3 vs 7 days in Ramji et al., no 30-day mortality in either study, and a median number of 15 vs a mean of 16.7 nodes in Ramji et al.). No intraoperative complications occurred in our study or in Ramji et al. We did have one case of positive margins due to positive CRM compared to no cases with positive margins in Ramji et al. These findings are in the context of similar baseline characteristics in our study compared to those in the robotic cohort of Ramji et al.'s study (Table 2.5). Our cohort's mean age was 63.5 years compared to 62.1 years in Ramji et al. Most patients were male (72.6% in our study compared to 73% in Ramji et al.) and the mean BMI was similar (29.0 in our study vs 27.8 in Ramji et al.). The exception is the CCI score and the proportion of APRs performed. Our study had lower CCI scores (predominantly in the 1-3 and 4-5 ranges compared to the 4-5 and 6-7 ranges in Ramji et al.) and we performed more APRs (21% of all procedures vs 15% in Ramji et al.). The higher CCI scores in Ramji et al. may partially explain the longer operating time, higher conversion rate and higher 30-day readmission rate. However, these improved outcomes may be attributable to higher robotic case volumes in our study (67 vs. 23) and the fact that Ramji et al.'s cases were performed in an earlier era (2011-2013), at which time even laparoscopic bowel surgery was relatively novel. Surgeons in our group had more experience with robotic surgery given a higher robotic case count and may have had more mature minimally invasive skills due to laparoscopy being more widespread over time, both of which could have helped to improve clinical outcomes. It is difficult to comment on differences in tumor height as we reported on distance from the anal sphincter whereas Ramji et al. reported on distance from the anal verge. However, for gross correlation, our group had a median distance from anal sphincter of 5.0 cm whereas Ramji et al.'s group had a mean distance from anal verge of 8.6 cm. A comparison with the more contemporary Canadian study by Patel et al. is less applicable as Patel et al. included patients who underwent left-sided colonic resection and benign conditions. Considering these cohort heterogeneities, clinical outcomes with regards to operating time and length of stay remained similar (303 minutes vs 320 minutes in Patel et al., 5 days vs 4 days in Patel et al.). We had lower conversion rate (0% vs 7%), lower anastomotic leak rate (1.5% vs 5%) and lower 30-day readmission rate (9.0 vs 16%)

Our results are also comparable to the 2017 Robotic vs. Laparoscopic Resection for Rectal Cancer (ROLARR) trial. ROLARR is the largest randomized controlled trial (RCT) to date comparing robotic vs laparoscopic-assisted rectal cancer resection and had a robotic cohort size of 236 patients. Comparing our results to the robotic branch of the ROLARR trial, our intraoperative complication and conversion rates were lower (0% vs 15.3% and 0% vs 8.1%, respectively) and our LOS was shorter (6.3 vs 8 days). Our operating time and complete TME rates were similar (303 vs 299 minutes in ROLARR and 70.8% vs 75% in ROLARR, respectively). It is important to note that unlike our study, whereby surgeons performing the procedures were robotic novices at program inception, surgeons in ROLARR had a median 50 cases of experience in robotic-assisted procedures. However, the lower intraoperative complication and conversion rates in our study may be attributable to a smaller sample size which may not yet have accrued any intraoperative complications or conversions. The longer LOS in ROLARR could be attributable to the higher conversion rate and to clinical practice variation. Data from ROLARR pre-date our data collection by eight years, during which time Enhanced Recovery After Surgery (ERAS) programs have gained wider adoption and may have helped reduce LOS[63–65]. In addition, ROLARR results are based on procedures performed by 40 surgeons from 10 countries, some of whom may have clinical practices and preferences that contribute to a longer LOS. Finally, the ROLARR trial did have higher yield on lymph node harvest (23.2 vs 16.4 nodes), but both studies' mean nodal harvest exceed the minimum 12 nodes required for colorectal cancer staging.

Perhaps the most important short-term pathologic outcome in rectal cancer surgery is macroscopic completeness of the TME dissection, which is an important quality marker for rectal cancer dissection and was used to evaluate the oncologic success of laparoscopic surgery when it became more widespread[66]. Not only is the robotic complete TME rate in our study similar to that of ROLARR's, it remains robust when compared to laparoscopic and open complete TME rates. Landmark laparoscopic vs. open rectal cancer trials reporting on TME rates include the Comparison of Open versus laparoscopic surgery for mid or low REctal cancer After Neoadjuvant chemoradiotherapy (COREAN) trial[67], the COlorectal cancer Laparoscopic or Open Resection (COLOR II) trial[68], the American College of Surgeons Oncology Group Z6051 (ACOSOG Z6051) trial[69], and the Australasian Laparoscopic Cancer of the Rectum Randomized Clinical Trial (ALaCaRT)[70]. All four trials were RCTs comparing outcomes after open vs. laparoscopic rectal cancer resection. In several of these trials, the categories of complete and nearly complete TME were combined when reported. The combined complete/nearly complete TME rates in these trials ranged from 88-99% in the open cohorts and 92-97% in the laparoscopic cohorts[67–70]. In comparison, the combined rate in our study was 98.5%. Given that the robotic approach is novel in rectal cancer resection and that surgeons in our study were robotic novices at the beginning of this series, such a robust TME completion rate is suggestive that short-term pathologic outcomes could be assured even in new robotic rectal cancer programs. Possible reasons for this comparable complete/nearly complete TME rate include adequate training, consistent volume and the technical advantage of better visualization and degrees of movement offered by the robot.

With regards to difference in outcomes between subgroups, there were no statistically significant differences in operating time between different types of rectal resections. However, as surgeons progressed on the robotic learning curve, the operating time required to complete the procedure decreased significantly. Such a decrease in operating time persisted despite patients in the last 10 cases being more comorbid and proportionally undergoing more APRs, which trended towards a longer mean operating time compared to LARs. This correlation between increased experience and decreased operating time has also been shown in other studies involving robotic-assisted surgery, including in rectal dissection, radical cystectomy, and knee arthroplasty[53,71,72]. Reduction in mean operating time in the last 10 cases could have significant implications for new robotic colorectal surgery programs and their associated opportunity cost. Although robotic surgery is associated with high fixed costs[56,57,63,73], reduction in robotic operating time may give the surgeon the opportunity to complete more cases on the same day, thus reducing the opportunity cost of robotic surgery. Prospective robotic programs similar to ours may also see their operating times decrease, which may be a consideration in the decision for implementation. However, our results are based on small, non-matched cohorts in the first and last 10 cases and we did not report per-case costs in this study, thus the true implications of operating time reduction would be better addressed in a larger study with controlled cohorts that report on detailed costing.

Finally, a discussion on Canadian robotic surgery is incomplete without examining the overall longer operating time associated with robotic surgery in the literature[15,74]. This is both important in a resource-limited public healthcare system and in the era of the Coronavirus Disease 2019 (COVID-19) pandemic, which has caused significant interruptions to surgical care delivery in Canada[75–78] and abroad[79,80]. Additional operating time required to complete robotic procedures could theoretically be allocated to performing a greater number of the same procedures via laparoscopy or be allocated to other time-sensitive surgical care such as emergency or oncologic surgical care. On the other hand, proponents of robotic surgery during the pandemic have highlighted clinical benefits of the robotic approach including decreased length of stay, complication rates and risk of conversion to open procedures, which minimize healthcare usage[81,82]. In addition, the physical distance between the operating team and the patient during robotic surgery has been theorized to decrease viral transmission[81,82]. Although the place of robotic surgery in the COVID-19 era remains unclear, the appropriateness of its use likely varies depending on the healthcare jurisdiction and its evolving needs over time.

Limitations of our study include a relatively small sample size, the lack of a comparative cohort and limited generalizability. Although our existing clinicopathologic outcomes are comparable with those of other rectal cancer studies, these may change as our robotic volume continues to increase. For example, the existing 0% conversion rate and 30-day mortality rate may change when a greater number of robotic rectal cancer procedures have been performed. The absence of a comparative cohort is a result of robotics replacing laparoscopy once the robotic program was implemented, thus we do not have a laparoscopic cohort from the same time period. This limits our ability to make comparisons between approaches. The goal of the current study was to focus on our early robotic outcomes. However, we are in the process of conducting a propensity-matched retrospective cohort study using a historical laparoscopic cohort to address the lack of comparison. Being a single-institution study utilizing a *da Vinci* Si robot, our results may have limited generalizability elsewhere in Canada and in the world, especially for prospective centres looking to acquire the newer generation da *Vinci Xi* robot. However, our outcomes are comparable to multi-centre randomized trials as evidenced by our comparison with ROLARR. Also, other Canadian centres are still utilizing the da Vinci Si robot (e.g. resections in Patel et al.'s were a combination of cases done on the Si and Xi). Thus, there is validity to describing results of the Si given it is part of current practice. Future research will examine the cost-effectiveness of robotic colorectal surgery as compared to the laparoscopic approach, which will address cost concerns. Our cost-utility analysis on this subject is in progress.

2.6. Conclusion

We report on the updated Canadian outcomes in robotic-assisted rectal and rectosigmoid cancer resection using our centre's first 67 cases. Short-term clinicopathologic outcomes in this setting are comparable to prior published Canadian and international studies despite surgeons being robotic novices at the start of our series. This could be useful for other Canadian colorectal groups considering the adoption of robotic surgery in their oncology practice.

Declaration

None of the authors have any conflicts of interest or financial ties to disclose

Table 2.1. Baseline characteristics

Patient demographics	Overall	By procedure type			By timing of surgery	
		LAR	**APR**	**HP**	**First 10 cases**	**Last 10 cases**
	N = 67	**N = 44**	**N = 18**	**N = 5**	**N = 10**	**N = 10**
Age, mean (SD), years	63.5 (9.3)	61.2 (8.2)	66.2 (9.7)	74.0 (9.3)	65.0 (8.1)	68.8 (6.8)
Sex, male (%)	48 (71.6)	31 (70.5)	13 (68.4)	4 (100.0)	8 (80.0)	7 (70.0)
BMI mean, (SD)	29.0 (6.2)	29.1 (5.6)	28.8 (8.1)	28.7 (3.5)	28.5 (3.7)	26.8 (5.9)
CCI score						
Median (range)	4 (2-12)	4 (2-11)	4.5 (2-12)	8 (3-10)	4 (3-9)	7 (4-12)
1-3 – Low (%)	24 (35.8)	20 (45.5)	3 (16.7)	1 (20.0)	4 (40.0)	0
4-5 – Moderate (%)	26 (38.8)	17 (38.6)	8 (44.4)	1 (20.0)	4 (40.0)	4 (40.0)
6-7 – High (%)	4 (6.0)	1 (2.3)	3 (17.7)	0	0	1 (10.0)
≥ 8 – Very high (%)	13 (19.4)	6 (13.6)	4 (22.2)	3 (60.0)	2 (20.0)	5 (50.0)
Tumour characteristics						
Rectal adenocarcinoma (%)	64 (95.5)	41 (93.2)	18 (100.0)	5 (100.0)	9 (90.0)	10 (100.0)
Neoadjuvant long course chemoradiation (%)	40 (61.5)	20 (47.6)	15 (83.3)	5 (100.0)	4 (44.4)	6 (60.0)
Neoadjuvant short course radiation (%)	9 (13.9)	9 (21.4)	0	0	3 (33.3)	2 (20.0)
No neoadjuvant therapy (%)	16 (24.6)	13 (31.0)	3 (16.7)	0	2 (22.2)	2 (20.0)
Rectosigmoid adenocarcinoma (%)	3 (4.5)	3 (6.8)	0	0	1 (10.0)	0
Distance from sphincter, median (range), cm	5.0 (0-15)	6.1 (1.4-15)	0.45 (0-3)	5.5 (1.5-9)	6.0 (0-9.1)	3.0 (0-12.5)
Pathologic T stage						
Tis	1 (1.5)	0	0	0	0	1 (10.0)
T0	10 (14.9)	6 (13.4)	3 (16.7)	1 (20.0)	0	1 (10.0)
T1	6 (9.0)	5 (11.4)	1 (5.6)	0	1 (10.0)	0
T2	23 (34.3)	15 (34.1)	1 (5.6)	0	5 (50.0)	4 (40.0)
T3	25 (37.3)	16 (36.4)	8 (44.4)	4 (80.0)	4 (40.0)	4 (40.0)
T4	2 (3.0)	2 (4.6)	6 (27.8)	0	0	0

Pathologic N stage						
N0	42 (62.7)	26 (59.1)	14 (77.8)	2 (40.0)	9 (90.0)	4 (40.0)
N1	18 (26.9)	14 (31.8)	2 (10.6)	3 (60.0)	0	5 (50.0)
N2	7 (10.4)	4 (9.1)	2 (10.6)	0	1 (10.0)	1 (10.0)
Procedural characteristics						
LAR (%)	44 (65.7)	-	-	-	8 (80.0)	4 (40.0)
APR (%)	18 (26.9)	-	-	-	2 (20.0)	5 (50.0)
HP (%)	5 (7.4)	-	-	-	0	1 (10.0)
Surgeon performing procedure						
Surgeon 1 (%)	24 (35.8)	17 (38.6)	6 (33.3)	1 (20)	3 (30)	4 (40)
Surgeon 2 (%)	40 (59.7)	26 (59.1)	10 (55.6)	4 (80)	8 (80)	4 (40)
Surgeon 3 (%)	3 (4.5)	1 (2.3)	2 (11.1)	0	0	2 (20)

SD = standard deviation; BMI = body mass index; CCI = Charlson Comorbidity Index; LAR = low anterior resection; APR = abdominoperineal resection

Table 2.2. Clinical outcomes

Operating time, mean (SD), minutes		***p* value**
Overall	303 (79.3)	
LAR	291 (68.9)	0.17
APR	324 (102.2)	
HP	343 (51.5)	
First 10 cases	390 (118.7)	0.011
Last 10 cases	270 (27.5)	
Conversion rate (%)	0 (0)	
Anastomotic leak (%)	1 (1.5)	
Intraoperative complications (%)	0	
LOS, median (range), days	5 (1-34)	
30-day outcomes (%)		
30-day complications (%)	7 (10.5)	
30-day readmissions (%)	6 (9.0)	
30-day mortality (%)	0 (0)	

SD = standard deviation; LOS = length of stay

Table 2.3. Short-term pathologic outcomes

	N = 67
Lymph node harvest, median (range)	15 (5-37)
TME grading	
Complete (%)	46 (70.8)
Nearly complete (%)	18 (27.7)
Incomplete (%)	1 (1.5)
Positive margin (%)	1 (1.5)*

TME = total mesorectal excision
* One case of positive margin was due to positive circumferential resection margin.

Table 2.4. Clinicopathologic outcomes in comparison with other studies using robotic-assisted colorectal resection

	Li et al.	Other Canadian studies		ROLARR
		Ramji et al.	Patel et al.	
Clinical outcomes	**N = 67**	**N = 26**	**N = 129**	**N = 237**
Operating time, mean (SD), minutes	303 (79.3)	407 (97)	320 (-)	299 (88.7)
Conversion rate (%)	0	3 (12.0)	9 (7.0)	19/236 (8.1)
Anastomotic leak (%)	1 (1.5)	2 (8.0)	5/103 (5)	22/180 (12.2)
Intraoperative complications (%)	0	0	-	36/236 (15.3)
LOS, median (range), days	5 (1-34)	7 (-)	4 (-)	8.0 (5.9)‡
30-day outcomes (%)				
30-day complications (%)	7 (10.5)	-	-	78/236 (33.1)
30-day readmissions (%)	6 (9.0)	6 (24)	21 (16)	-
30-day mortality (%)	0	0	-	2/236 (0.8)
Pathologic outcomes				
Lymph node harvest, median (range)	15 (5-37)	16.7 (-)*	N/A†	23.2 (11.97)*
TME grading				
Complete (%)	46 (70.8)	15/25 (60)	N/A†	1278 (75.4)
Near complete (%)	18 (27.7)	-	N/A†	33 (14.0)
In complete (%)	1 (1.5)	-	N/A†	22 (9.3)
Positive CRM	1 (1.5)	0	N/A†	12/235 (5.1)

SD = standard deviation; LOS = length of stay; TME = total mesorectal excision; CRM = circumferential resection margin

* Ramji et al. and ROLARR reported lymph node harvest as mean (SD).

† Patel et al. was not a rectal-cancer specific study, thus no pathologic outcomes were reported.

‡ ROLARR reported LOS as mean (SD).

Table 2.5. Baseline characteristics in comparison with other studies using robotic-assisted colorectal resection

Patient demographics	Li et al.	Other Canadian studies		ROLARR
		Ramji et al.	Patel et al.	
	N = 67	N = 26	N = 129	N = 237
Age, mean (SD), years	63.5 (9.3)	62.0 (9.1)	61.7 (-)	64.4 (10.98)
Sex, male (%)	48 (71.6)	19 (73.0)	79 (61)	161 (67.9)
BMI mean, (SD)	29.0 (6.2)	27.8 (5.5)	29.3 (-)	N/A§
CCI score				
Median (range)	4 (2-12)	-	N/A‡	N/A‖
1-3 – Low (%)	24 (35.8)	3 (11)	N/A‡	N/A‖
4-5 – Moderate (%)	26 (38.8)	13 (48)	N/A‡	N/A‖
6-7 – High (%)	4 (6.0)	7 (26)	N/A‡	N/A‖
≥ 8 – Very high (%)	13 (19.4)	4 (15)	N/A‡	N/A‖
Tumour characteristics				
Rectal adenocarcinoma (%)	64 (95.5)	26 (100)	N/A¶	-
Neoadjuvant long course chemoradiation (%)	40 (61.5)	15 (58.0)	N/A¶	N/A# N/A#
Neoadjuvant short course radiation (%)	9 (13.9)	-	N/A¶	N/A#
No neoadjuvant therapy (%)	16 (24.6)	-	N/A¶	126 (53.2)
Rectosigmoid adenocarcinoma (%)	3 (4.5)	0	N/A¶	-
Distance from sphincter, median (range), cm	5.0 (0-15)	N/A*	N/A¶	N/A*
Pathologic T stage				
Tis	1 (1.5)	-	N/A¶	-
T0	10 (14.9)	5 (19.0)	N/A¶	22 (9.3)
T1	6 (9.0)	7 (27.0)	N/A¶	24 (10.2)
T2	23 (34.3)	4 (16.0)	N/A¶	64 (27.1)
T3	25 (37.3)	10 (38.0)	N/A¶	117 (49.6)
T4	2 (3.0)	0	N/A¶	5 (2.1)
Pathologic N stage				

N0	42 (62.7)	23 (88)	N/A[¶]	146 (61.9)
N1	18 (26.9)	N/A[†]	N/A[¶]	63 (26.7)
N2	7 (10.4)	N/A[†]	N/A[¶]	25 (10.6)
Procedural characteristics				
LAR (%)	44 (65.7)	22 (85.0)	63 (49)	152 (64.4)
APR (%)	18 (26.9)	4 (15.0)	22 (17)	52 (22.0)
HP (%)	5 (7.4)	-	-	-

SD = standard deviation; BMI = body mass index; CCI = Charlson Comorbidity Index; LAR = low anterior resection; APR = abdominoperineal resection; HP = low Hartmann procedure; N/A = not applicable; - denotes information not included in the comparative study

* Ramji et al. and the ROLARR trial reported distance from the anal verge rather than distance from anal sphincter, as in our study. Ramji et al. reported a distance from anal verge of 8.6 cm (SD 7.9 cm). ROLARR reported distance from anal verge in categories of 11-15 cm, 6-10 cm and 0-5 cm, with a respective 30.1%, 45.3% and 24.2% of patients in these categories.

† Ramji et al. reported nodal staging as node-negative or node-positive. Node-positive patients (12% of the robotic cohort) were not sub-categorized into N1 or N2.

‡ Patel et al. used the American Society of Anesthesiologists (ASA) classification rather than the CCI. The robotic cohort had an ASA score was 1 or 2 in 22% of patients and a score of 3 or 4 in 78%.

¶ Patel et al. was not a cancer-specific or rectal resection-specific study. The authors reported that 68% of the robotic cohort had a diagnosis of adenocarcinoma. However, tumour location (colon, rectosigmoid or rectal), tumour characteristics and use of neoadjuvant or adjuvant therapy were not reported.

§ The ROLARR trial did not report a mean BMI. Rather, BMI was categorized as underweight of normal (BMI 0-24.9, 39.2% of the robotic cohort), overweight (BMI 25.0-29.9, 38.0%), or obese (BMI ≥30, 22.8%).

|| ROLARR used the ASA classification, whereby the proportion of patients in ASA classes 1, 2, 3 and 4 were 16.5%, 63.3%, 19.4% and 0% respectively.

ROLARR reported neoadjuvant therapy as yes/no. “Yes” included both radiotion alone and chemoradiation; 46.8% of patients had either radiation or chemoradiation.

Appendix 2.1. STROBE Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	12-13
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	14-15
Objectives	3	State specific objectives, including any prespecified hypotheses	15
Methods			
Study design	4	Present key elements of study design early in the paper	15-16
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	15-18
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	16
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	17-18
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	17-18
Bias	9	Describe any efforts to address potential sources of bias	18
Study size	10	Explain how the study size was arrived at	16
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	17-18
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	18-19
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	19
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	19-20
Outcome data	15*	Report numbers of outcome events or summary measures over time	20

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	20
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	20
Discussion			
Key results	18	Summarise key results with reference to study objectives	21
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	24-25
Generalisability	21	Discuss the generalisability (external validity) of the study results	24
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

CHAPTER 3. Economic evaluations of robotic versus laparoscopic-assisted colorectal surgery: A systematic review

This chapter was submitted as **Li MY**, Daigle RJ, Clement F, Niven DJ (2022). Economic evaluations of robotic versus laparoscopic-assisted colorectal surgery: A systematic review. (Submitted to *Dis Colon Rectum*)

In this chapter we systematically review existing economic evaluations comparing RACS and LACS. Each study was critically appraised and their methodological differences were described.

3.1. Abstract

Background: Robotic surgery has been increasingly used in colorectal resection. However, its cost-effectiveness remains controversial.

Objective: To summarize the existing literature on the cost-effectiveness of robotic-assisted colorectal surgery compared to laparoscopic-assisted colorectal surgery.

Data sources: A search of MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, and EconLit was performed from January 1991 to October 2020.

Study selection: Included studies must be economic evaluations reporting on cost-effectiveness, cost-utility or cost-benefit.

Interventions: Robotic-assisted vs laparoscopic-assisted colorectal resection

Main outcome measures: This was a narrative synthesis reporting on economic outcomes such as cost-effectiveness, cost-utility or cost-benefit. Studies were compared based on study design and target anatomy of resection.

Results: Of 1108 citations, four cost-utility analyses met inclusion criteria. Two studies were conducted by a Spanish group and two were conducted by a US group. Each group authored a cost-utility analysis on proctectomy and another on colectomy. The Spanish studies found that robotic-assisted colorectal resection is cost-effective compared to laparoscopic-assisted colorectal resection. The Spanish studies were trial-based and used a healthcare system perspective, one-year time horizon, and a European willingness-to-pay threshold of €20,000-30,000/quality-adjusted life-year. The US studies found that the robotic-assisted approach was not cost-effective compared to the laparoscopic approach. The US studies were model-based and used both healthcare system and societal perspectives, a one-year time horizon, and a US-specific willingness-to-pay threshold of US$50,000-200,000/quality-adjusted life-year.

Limitations: There was significant interstudy heterogeneity in study design and healthcare jurisdictions, thus the existing studies are not directly comparable.

Conclusions: There is limited economic evidence regarding the cost-effectiveness of robotic-assisted colorectal surgery and existing studies draw differing conclusions. Further research is required to clarify the value of the robotic approach and guide usage of this technology.

3.2. Introduction

Diseases of the colon and rectum can be surgically resected in one of three general techniques: open colorectal surgery (OCS), laparoscopic-assisted colorectal surgery (LACS), or robotic-assisted colorectal surgery (RACS). The latter two approaches are considered minimally invasive because of the use of keyhole incisions. Whereas conventional laparoscopic surgery has no depth perception and is limited to 4 degrees of instrument movement, the more novel robotic platform offers 3D visualization and 7 degrees of wristed movement[13,14,83]. RACS is especially helpful for performing rectal dissection in the narrow, confined space of the pelvis[3]. Advantages of RACS include lower rates of intraoperative bleeding, decreased rate of conversion to open surgery[15–17,39,84].

The main disadvantage of RACS is its cost. Studies have shown that RACS costs are significantly higher than those of LACS and are driven by expensive robotic equipment and longer operating time[19,33–35,45,85]. However, most studies comparing RACS vs. LACS costs are costing studies without joint assessment of effectiveness. There are few economic evaluations to determine whether the benefits of RACS justify its price tag. Given the widespread use of RACS[86,87] and the scarcity of economic evaluations assessing its cost-effectiveness, this systematic review sought to examine existing evidence on the cost-effectiveness of RACS compared to LACS.

3.3. Materials And Methods

We conducted and reported this systematic review in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses[88] (PRISM) (Appendix 3.1). The study protocol was registered in the Prospective Register of Systematic Reviews (PROSPERO ID CRD42020215357). Protocol amendment was made to better define economic evaluations as full economic evaluations, which exclude partial evaluations such as costing studies.

3.3.1. Search Strategy

A systematic search of the literature was conducted in October 2020 and updated in February 2022 using the following electronic databases: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, and EconLit. The search was limited to studies published after January 1991, as this was the year when the first cases of minimally invasive colorectal resection were performed[89]. All languages were included. Databases were searched using three comprehensive themes: *colorectal surgery, robotics, economic outcomes.* The search strategy and associated keywords and truncations (Appendix 3.2) were reviewed by a librarian. Grey literature was not included in the search.

3.3.2. Study Selection

We included studies that described patients 18 years or older who underwent transabdominal colorectal resection. Studies must have used RACS as a treatment approach and compared it to the standard care minimally invasive approach, identified as LACS. OCS may be included if it was used as a comparator in addition to LACS. Studies must have been economic evaluations reporting on cost-effectiveness, cost-utility, or cost-benefit. Only full-text articles were considered for inclusion as abstracts and conference proceedings do not contain enough information to allow critical appraisal.

Studies were excluded if: (a) the patient population was younger than 18 years; (b) patients underwent transanal colorectal resection; (c) no colorectal resection was undertaken (e.g. ventral rectopexy for rectal prolapse without sigmoidectomy); (d) surgeries other than colorectal resection was included; e) the laparoscopic approach was not included as a comparator; (f) cost and effectiveness measures were reported separately without being assessed in the context of each other; or (g) the study was not primary research (e.g. systematic reviews or meta-analyses).

The Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) was used for study selection. Two reviewers (MYL and RJD) screened titles and abstracts separately. Full text was reviewed for titles or abstracts that potentially met inclusion criteria. Studies were included in the final review if all inclusion criteria and none of the exclusion criteria were met. Disagreements between reviewers were resolved by consensus or by consultation with a third reviewer (DJN). Agreement between reviewers was examined by calculating Cohen’s kappa.

3.3.3. Data Extraction and Quality Assessment

Data extraction was performed independently and in duplicate using Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA, USA). The extracted data included: 1) study characteristics such as year of publication, country of origin, and study design; 2) procedure characteristics such as target anatomy of resection, operative indication, and the robotic model employed; and 3) method and results of the economic evaluation. Methods extracted included measurement and valuation of costs and effectiveness. Results extracted included the incremental cost-effectiveness ratio (ICER) and the willingness-to-pay threshold (WTP) to which it was compared. The ICER is the ratio of the difference in costs between two interventions to the difference in effectiveness[90]. In cost-utility analyses (CUAs), effectiveness is measured in quality-adjusted life years (QALYs), a function of health state preference and time spent in that health state. Health state preference is represented as a utility value between negative infinity and one, where one is associated with perfect health, zero is associated with death, and negative values are associated with states worse than death[90]. The ICER of a CUA is compared to the WTP, which is a country-specific measure of what society or the decision-maker is willing to pay for a QALY. If the ICER is lower than the WTP, an intervention is considered cost-effective[90].

In addition to the ICER and WTP, other elements critical to the interpretation of the economic evaluation were also collected. These include the time horizon, perspective, presence of discounting and types of sensitivity analyses. When the study is model-based, model inputs for costs and effectiveness were extracted. Extraction variables that were not presented in the main text or supplemental material were considered missing or not performed.

Quality assessment was performed using the Consensus on Health Economic Criteria (CHEC) list, a 20-item list to appraise economic evaluations[91]. The CHEC list focuses on areas such as clear study reporting, appropriate measurement and valuation of costs and effectiveness and adequacy of the time horizon, perspective and sensitivity analyses chosen. Quality assessment was performed independently by two reviewers (MYL and RJD) and conflicts were resolved by consulting a third reviewer with expertise in appraising economic evaluations (FC).

3.3.4. Outcomes and Data Analysis

Our primary analysis examined the cost-effectiveness of RACS vs. LACS when the target anatomy of resection included both the colon and rectum. In anticipation that the cost-effectiveness of RACS may vary between colectomy vs proctectomy given the advantages of

RACS in the pelvis, we also examined outcomes by operative site. Results were synthesized using a narrative summary. Meta-analysis was not undertaken as significant heterogeneity was expected between studies with regards to different healthcare jurisdictions and their influence on the measurement and valuation of cost and effectiveness.

3.4. Results

3.4.1. Study Selection and Characteristics

Our search yielded 1,108 citations, of which 693 were unique (Figure 3.1). Full text was obtained for 118 studies, of which four were included in our systematic review. One excluded study which appeared to meet initial screening criteria was Young et al.[92]'s cost analysis of robotic, laparoscopic, and open pelvic procedures utilizing decision analytic modelling to simulate clinical workflow. This was excluded because it was a costing study with no assessment of effectiveness. In addition, it included procedures which were not colorectal resections (e.g. urological procedures), which was an exclusion criteria. Interrater agreement was excellent for abstract and full-text screening (K = 0.97 and K = 0.90, respectively). All four economic evaluations were CUAs, two of which were trial-based while the other two were model-based.

3.4.2. Trial-based Cost-utility Analyses

The two trial-based analyses by Quijano et al. and Ferri et al.[43,93] both originated from Spain and were performed by the same research group who recruited patients undergoing colorectal surgery at the same centre (Table 3.1). Quijano et al. compared RACS and LACS for rectal cancer whereas Ferri et al. compared the two approaches in patients undergoing right hemicolectomy for neoplasms, including adenocarcinomas and endoscopically unresectable adenomas. In both studies, RACS incurred higher costs and led to higher QALYs at one year. This resulted in an ICER of €1,555.90/QALY in rectal cancer resection and €11,691.81/QALY in right hemicolectomy (Table 3.2). Since Spain does not have a specific WTP threshold in healthcare, a threshold of €20,000-30,000 established by the United Kingdom's National Institute for Health and Care Excellence (NICE) was used. As both ICERs were below the adopted WTP, the analyses concluded that RACS was cost-effective compared to LACS in proctectomy and right hemicolectomy for neoplastic disease.

Both studies included the costs of the index hospital stay and index operation. Quijano et al. included costs of outpatient visits and readmissions within 90 days whereas Ferri et al.'s readmission data was limited to 30 days. Neither study included equipment acquisition or maintenance costs. QALYs were used to quantify effectiveness and were calculated using the Health Utilities Index 2 (HUI 2) in both studies. The HUI 2 was derived from eight subscales of the Short Form 36 (SF-36) questionnaire. The SF-36 was administered to trial patients at three months postoperatively in Quijano et al. and at one, three, six and 12 months in Ferri et al.

Probabilistic analysis using 5000 Monte Carlo simulations was performed to propagate uncertainty in parameter values affecting cost and effectiveness estimations. At WTP thresholds of €20,000 and €30,000, Quijano et al. found a respective 95.54% and 97.18% probability that RACS was cost-effective in rectal cancer resection compared to LACS. Ferri et al. found these probabilities to be 78.78% and 95.04% for right hemicolectomy. Both studies used a healthcare system perspective, one year time horizon, and performed one-way sensitivity analyses. These analyses showed that the results were most sensitive to hospitalization and operating room (OR) costs. Quijano et al. adjusted costs to 2018 euros for rectal resection whereas Ferri et al. did not specify the valuation year.

3.4.3. Model-based Cost-utility Analyses

The two model-based analyses were conducted by Simianu et al., a multi-institutional team of researchers from the United States. They included both LACS and OCS as comparators to RACS and utilized a decision tree model that considered the possibilities of conversion to open surgery and postoperative complications. If conversion occurred, the costs and effectiveness of the open approach were adopted. Complications were mutually exclusive and may be either ileus, surgical site infection or incisional hernia. Simianu et al.'s first study examined patients undergoing proctectomy for any indication and will be referred to as Simianu, Curran et al.[44] Their second study examined patients undergoing colectomy for any indication and will be referred to as Simianu, Gaertner et al.[85] (Table 3.1).

Model inputs for costs and effectiveness included those related to quality of life (QOL), costs and clinical outcomes (Table 3). Both models used a time horizon of one year and a US-specific WTP threshold of US$50,000-200,000/QALY. Unlike the trial-based studies, both societal and healthcare system perspectives were undertaken. In addition, equipment and maintenance costs were included. These costs were removed in the societal perspective as a sensitivity analysis to examine their effect on the ICER.

Both studies concluded that RACS was not cost-effective compared to LACS (Table 3.2). In the proctectomy model, the RACS ICER was $751,056/QALY from the societal perspective and $1,485,139/QALY from the healthcare system perspective, both of which exceeded the WTP threshold of US$50,000-200,000/QALY. The probabilities of RACS and LACS being the cost-effective approach were similar, at approximately 40% from the societal perspective and 35% from the healthcare system perspective. However, this probability was slightly higher for LACS and remained so when WTP was varied from US$50,000 to 200,000/QALY, consistent with the conclusion that LACS is cost-effective compared to RACS.

In the colectomy model, the RACS ICER was $2,322,715/QALY from the societal perspective and $4,174,848/QALY from the healthcare system perspective. As in proctectomy, these ICERs exceeded the WTP of US$50,000-200,000/QALY. In contrast to the proctectomy study, the probability that RACS is the cost-effectiveness approach was much lower than that of LACS regardless of the WTP threshold. These probabilities ranged from 30%–35% for RACS depending on perspective, compared to 55% for LACS under both perspectives.

In sensitivity analyses, equipment and maintenance costs did not influence the cost-effectiveness assessment of RACS in either study. However, results were sensitive to robotic QOL, OR costs, length of stay, and early return to work. Both studies adjusted costs to 2017 US dollars and explained discounting was not necessary given the time horizon of one year. However, there was no indication that either study performed model validation to ensure that the model was internally free of errors and externally correlated with findings from trials or similar models (Table 3.3). OCS was not included in the final comparison because it was dominated, a process whereby a comparator is eliminated as a cost-effective alternative because it results in lower effectiveness and higher cost.

3.4.4. Quality Assessment

The trial-based cost-utility analyses by Quijano et al. and Ferri et al. scored 14 and 13 out of 19 points on the CHEC list, respectively (Figure 3.2). The total possible score was modified to 19 because item 5 of the CHEC list assesses the economic model so it did not apply to the trial-based analyses. Points were deducted in both studies due to inappropriate time horizons, omission of equipment costs, lack of consideration for oncologic outcomes and lack of discussion regarding ethical and distributional issues related to RACS. The time horizon of one year was not long enough to capture all relevant costs and effectiveness (item 6). For example, bowel, bladder and sexual dysfunction after rectal resection could be permanent so a one-year horizon is unable to capture costs and reduction in QOL associated with these morbidities. Similarly, costs and decrease in QOL associated with complications occurring beyond one year (e.g. adhesive bowel obstruction and incisional hernia) would not be included. Lack of consideration for equipment costs represents incomplete inclusion of relevant costs (item 8), especially since equipment costs contribute significantly to RACS expenditure. Lack of consideration for oncologic outcome in both studies' effectiveness measures represents incomplete inclusion of relevant outcomes (item 11), especially since both studies' populations are predominantly patients with cancer. Finally, the CHEC list requires that economic evaluations discuss ethical and distributional issues relating to the interventions compared (item 20), which were not mentioned in these analyses.

Items specific to each study that failed to meet CHEC criteria include inappropriate discounting for a time horizon of one year (item 15) in Quijano et al., inadequate valuation of costs (item 10) due to an unclear valuation year in Ferri et al., and lack of discussion on the generalizability of the study findings to other settings and patient groups (item 18) in Ferri et al.

The model-based studies scored 16 out of 20 points. Neither study addressed model validation, generalizability, or ethical and distributional issues (items 5, 18, and 20). Similar to the trial-based studies, their time horizon of one year was too short to capture all relevant costs and effectiveness (item 6).

3.5. Discussion

We present a systematic review of the economic evaluations of RACS compared to LACS. While many costing studies exist in the literature, only four studies analyzed cost and effectiveness jointly and could be considered full economic evaluations. The two trial-based studies found RACS to be cost-effective compared to LACS whereas the two model-based studies found the contrary. Interpretation of this lack of consensus must consider the significant interstudy heterogeneity arising from differences in methodology and healthcare jurisdictions.

3.5.1. Comparison between trial-based and model-based CUAs

Notable differences in study methodologies include: 1) differential likelihood of including RACS-specific clinical outcomes, 2) differential eras from which effectiveness estimates were derived, 3) differential types of costs included by the two research groups, and 4) differential surgeon experience with RACS.

As the most novel surgical approach, RACS-specific clinical outcome data is more limited in the literature than those related to LACS or OCS. When there is no RACS-specific data in the literature, model-based studies must make assumptions about RACS inputs. In the two studies by Simianu et al., there were no RACS-specific utility values to describe RACS QOL or RACS-specific days off work (Table 3.3). To make a model-based analysis possible, the authors assumed them to be equal to those in LACS in most instances and used imputation to derive a utility score for RACS in the proctectomy study. Since both model-based studies' sensitivity analyses showed that the models were sensitive to RACS QOL and early return to work, using assumptions that approximate RACS outcomes to those of LACS may have diminished the models' abilities to capture effectiveness differences between the two, thus impacting the studies' conclusions on cost-effectiveness.

Although all four studies were published in the same year, effectiveness estimates used in the trial-based studies were more recent than those in the model-based studies. The trial-based studies published their trial data in 2020 by way of including them in the CUAs discussed in this review. In contrast, the model-based studies used older literature (Table 3.3). This included a 2004 RCT[94] for days off work in Simianu, Curran et al. and studies from 2005 and 2012 for postoperative ileus and surgical site infection rates in Simianu, Gaertner et al.[95,96]. Given that clinical practice such as enhanced recovery programs evolve over time, older studies may not accurately reflect contemporary reduction in days off work. Similarly, as surgical experience with RACS increases over time, dated complication rates may not reflect current outcomes. Yet, both colectomy and proctectomy models were sensitive to days off work and QOL, the latter of which is impacted by complication rates. Differential eras from which effectiveness estimates were derived may make the two pairs of studies less comparable and contribute to their different cost-effectiveness conclusions.

Surgeon experience may also vary widely between trial-based and model-based studies. In Quijano et al., surgeons had baseline experience with RACS (40 RACS cases performed at the authors' centre prior to data collection) whereas the experience was mixed in Ferri et al. (five surgeons had RACS experience whereas three did not). In Simianu, Curran et al., some effectiveness inputs were based on studies where surgeons had robotic experience (30 cases/surgeon in Kim et al.[97], at least 10 cases/surgeon in ROLARR[33]) while other inputs were based on large databases such as the National Surgical Quality Improvement Program (NSQIP), where it is impossible to discern surgeon experience. Similarly in Simianu, Gaertner et al., many clinical outcome inputs were based on databases where surgeon experience is unclear. Given the known impact of surgeon experience, volume, and operating time on RACS outcomes and costs[34,53,98], it is difficult to compare the trial and model-based studies without explicit knowledge of these important determinants.

Robotic capital equipment and maintenance costs are substantial, and the ways in which they are accounted for may impact the results. The trial-based studies did not include these costs in their analysis whereas the model-based studies did. Even though the model-based studies did not find that robotic acquisition and maintenance costs influenced the assessment of cost-effectiveness, the differential inclusion of equipment and maintenance costs across the four studies is yet another dissimilarity that may account for the differences in results.

Finally, it is important to recognize that the findings of economic evaluations often have limited generalizability to other healthcare jurisdictions. Thus, cost-effectiveness analyses performed in different jurisdictions cannot be directly compared. For example, the Spanish studies used costs specific to their healthcare jurisdiction, adopted WTP thresholds that are more appropriate to a European setting and valued costs in 2018 euros. In contrast, the US studies used costs applicable to the US, adopted US-specific WTP thresholds and valued costs in 2017 US dollars. These system considerations are unique to the decision setting of the economic evaluation and result in limited generalizability between jurisdictions even when the same technology is under study.

Comparison to Cost-effectiveness of Robotic Technology in Other Surgical Contexts

Similar to our findings in the colorectal surgery literature, economic evaluations of robotic-assisted surgery in other surgical disciplines are inconclusive[99–104]. Full economic evaluations comparing robotic vs. laparoscopic/open technology have been performed in urology[105–109], hepatobiliary surgery[110,111], orthopedic surgery[72,112–116] and gynecology[117,118]. Radical prostatectomy is the most extensively studied robotic-assisted procedure. While some studies have found robotic prostatectomy to be cost-effective[106,119,120], others have not[108,121]. A limited number of economic evaluations in robotic distal pancreatectomy[110,111] and hip/knee arthroplasties[72,112,114,115] draw similarly inconsistent conclusions. As in our study, inconsistencies often arise from methodological differences such as differential inclusion of costs. Some studies did not include equipment costs[111] while others assumed that they were shared by different specialties or spread across high volumes[115,116,119,122], which would lower the robotic incremental costs. Based on two existing evaluations of robotic hysterectomy[118,119], the robotic approach is not cost-effective compared to laparoscopic or open approaches.

3.5.2. Cost-effectiveness of RACS and its Implications

The cost-effectiveness of RACS compared to LACS is unclear given the limited number of economic evaluations identified and their contradictory conclusions. Until more definitive evidence is available, the choice between RACS and LACS will be best informed by system considerations, patient preference for the surgical approach used, and clinical factors such as pelvic anatomy, body habitus, and tumour characteristics. The question of whether the cost-effectiveness of RACS vs. LACS differs between proctectomy and colectomy is also unclear. Both the Spanish and US studies seem to suggest that RACS is more likely to be cost-effective in proctectomy given a lower proctectomy ICER in the trial-based studies and a RACS probability of being cost-effective that nearly approaches that of LACS in the model-based studies.

However, it cannot be definitively stated that RACS is “more” cost-effective in proctectomy since the number of studies and their generalizability are limited. Future studies should include relevant costs such as equipment acquisition and maintenance as well as relevant effectiveness measures such as oncologic outcomes when the target population includes patients with cancer.

The strengths of our study include a comprehensive search strategy and a detailed review of the four economic evaluations. However, our results are limited by the fact that the studies retrieved originated from American and European data, whose unique healthcare systems likely affect the results of the studies and may not be applicable to other healthcare settings. The review process is not exhaustive in its review of all published literature. However, we included all major clinical and economic databases in our search and encountered significant overlap in search results findings, which likely indicates that we have screened most published material relevant to our search.

3.6. Conclusion

There is limited economic evidence regarding the cost-effectiveness of RACS. Existing economic evaluations draw differing conclusions and vary in design, source of effectiveness data, surgeon volume, and types of costs included. The cost-effectiveness of RACS compared to LACS remains unknown.

Declaration and other information

None of the authors have any conflicts of interest or financial ties to disclose. This review was not funded or sponsored.

The MEDLINE search is available in Appendeix 3.1. Template data collections forms are not publicly available but could be requested from the corresponding author.

Appendix 3.1. PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	36
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	37
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	39
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	39
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	40
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	39
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	39-40
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	40
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	40
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	40-41
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	40-41
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	41
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A*
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A*

Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A*
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	41-42
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A*
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A*
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A*
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A*
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	42
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	42
Study characteristics	17	Cite each included study and present its characteristics.	42-44
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	44-45
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	42-44
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A*
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A*
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A*
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A*
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A*
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A*
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	45-48
	23b	Discuss any limitations of the evidence included in the review.	48-49

Section and Topic	Item #	Checklist item	Location where item is reported
	23c	Discuss any limitations of the review processes used.	49
	23d	Discuss implications of the results for practice, policy, and future research.	48-49
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	39
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	39
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	39
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	49
Competing interests	26	Declare any competing interests of review authors.	49
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	49

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

* No meta-analysis was undertaken due to significant inter-study heterogeneity, thus no measurement of effect/statistical synthesis was performed.

Appendix 3.2. Detailed search strategy - OVID MEDLINE

#	Searches
1	colorectal.mp. or exp Colorectal Surgery/
2	exp Colon, Sigmoid/
3	exp Proctectomy/ or exp Rectum/
4	colorectal.tw,kf.
5	rectal.tw,kf.
6	rectum.tw,kf.
7	rectosigmoid.tw,kf.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	exp Robotic Surgical Procedures/ or exp Surgery, Computer-Assisted/
10	da vinci.tw,kf.
11	telerobot*.tw,kf.
12	robot*.tw,kf.
13	davinci.tw,kf.
14	9 or 10 or 11 or 12 or 13
15	exp "Costs and Cost Analysis"/
16	exp Cost-Benefit Analysis/
17	exp Hospital Costs/ or exp Health Care Costs/
18	economic evaluation.tw,kf.
19	cost*.tw,kf.
20	economics.fs.
21	cost utility.mp. or exp Quality-Adjusted Life Years/
22	health technology assessment.mp. or exp Technology Assessment, Biomedical/
23	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	8 and 14 and 23

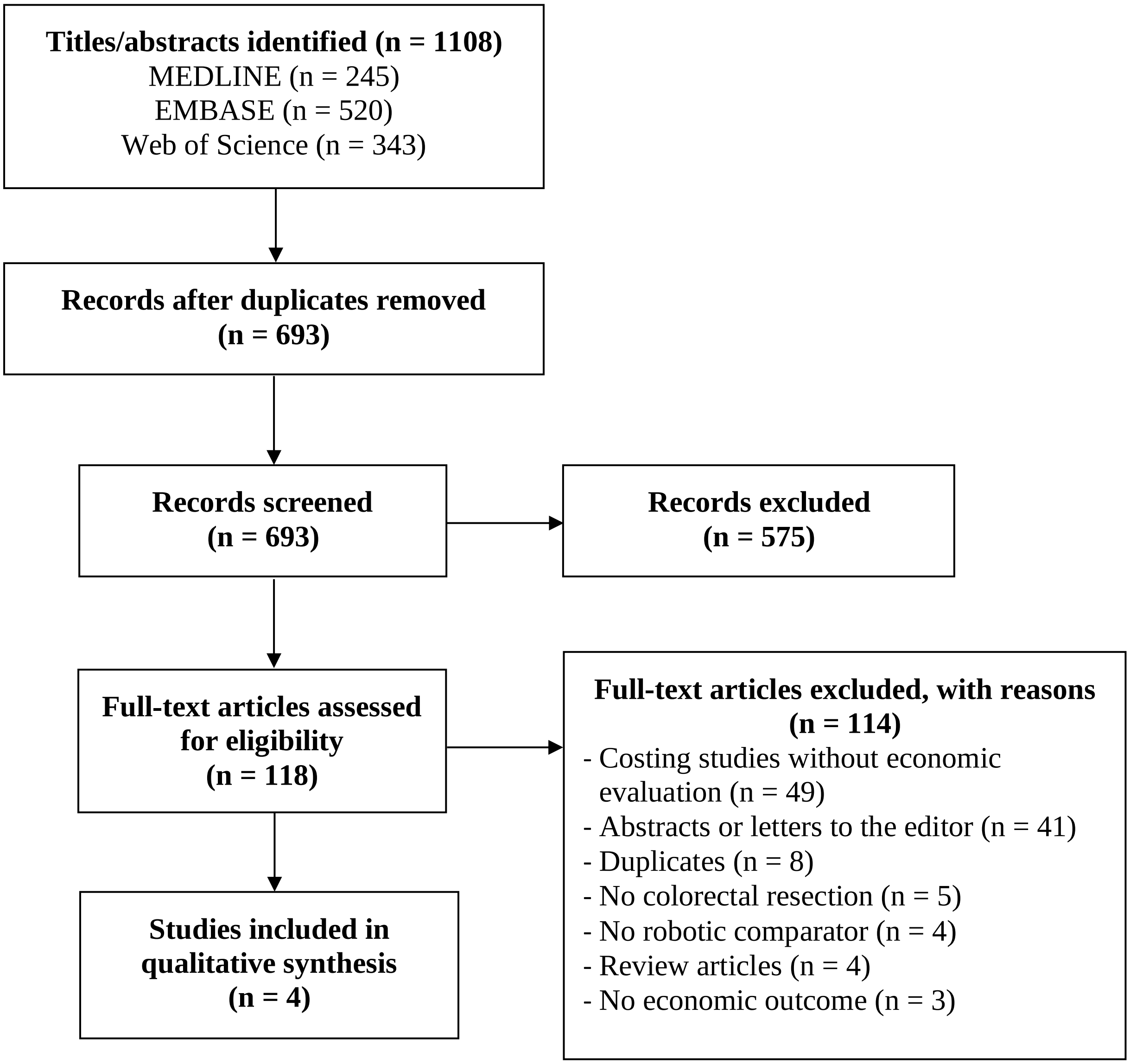

Figure 3.1. PRISMA flow diagram. Transparent and concise representation of screened records. The diagram identifies the number of records screened, included, excluded and documents reasons for exclusion. The PRISMA flow diagram is the preferred reporting system to depict phases of a systematic review.

Table 3.1. Study characteristics

Analytic approach	**Trial-based studies**		**Model-based studies**	
Author	**Quijano et al.**	**Ferri et al.**	**Simianu, Curran et al.**	**Simianu, Gaertner et al.**
Year of publication	2020	2020	2020	2020
Country	Spain	Spain	USA	USA
Study design	CUA	CUA	CUA	CUA
Clinical study/model type	Retrospective cohort	Retrospective cohort	Decision tree	Decision tree
Total sample size (RACS)	185 (81)	70 (35)	N/A	N/A
Target anatomy	Rectum	Right colon	Rectum	Colon
Indication	Neoplasm	Neoplasm	Any	Any
Robotic model used	Xi and Si	Xi and Si	N/A	N/A
Comparator	LACS	LACS	LACS and OCS	LACS and OCS

CUA = cost-utility analysis; **RACS** = robotic-assisted colorectal surgery; **LACS** = laparoscopic-assisted colorectal surgery; **OCS** = open colorectal surgery; **N/A** = not applicable

Table 3.2. Details of economic evaluations by analytic approach

Analytic approach	**Trial-based studies**		**Model-based studies**	
Author	**Quijano et al.**	**Ferri et al.**	**Simianu, Curran et al.**	**Simianu, Gaertner et al.**
Target anatomy	Rectum	Colon	Rectum	Colon
Types of costs included	**Direct in healthcare**: Index hospital stay costs (ward, ICU, OR, pharmaceutical, PACU, laboratory, radiology and pathology). 90-day outpatient visits and readmission costs. OR costs included OR time and disposable instruments.	**Direct in healthcare:** Index hospital stay costs (ward, ICU, OR, pharmaceutical, PACU, laboratory, radiology and pathology). 30-day readmission costs. OR costs included OR time and disposable instruments.	**Direct in healthcare:** Capital investment costs* Disposable instrument costs Equipment maintenance costs OR time per minute costs Cost of conversion Hospital stay costs **Indirect healthcare:** Cost of hernia repair Cost of caregiver Cost per day off work *Capital investment costs were only included in the healthcare sector perspective.	Same as for Simianu, Curran et al.
Cost measurement and valuation	**Measurement**: Costs obtained from cost diaries. **Valuation**: Euros (2018 exchange rate).	**Measurement**: Cost obtained from cost diaries. **Valuation**: Euros (valuation year unclear). Did not adjust for inflation.	**Measurement**: N/A **Valuation**: 2017 US Dollars. Charges were adjusted to costs using charge-to-cost ratios when cost data was not available.	**Measurement**: N/A **Valuation**: 2017 US Dollars. Charges were adjusted to costs using charge-to-cost ratios from the 2014 Healthcare Cost and Utilization Project Nationwide Inpatient Sample file when cost data was not available.

Effectiveness measurement and valuation	**Measurement**: Indirect utility assessment using the SF-36 questionnaire (administered to patients at 3 months after surgery). **Valuation**: QALY was calculated from the HUI 2, which was derived from 8 subscales of the SF-36. **QALY values from trial:** RACS: 0.85 LACS: 0.65	**Measurement**: Indirect utility assessment using the SF-36 questionnaire (administered to patients at 1, 3 6, months and 1 year) after surgery. **Valuation**: QALY was calculated from the HUI 2, which was derived from 8 subscales of the SF-36. **QALY values from trial:** RACS: 0.83 LACS: 0.72	**Measurement:** Utilities for QOL for RACS and LACS were estimated from 2018 RCT data comparing RACS to LACS by Kim et al[97]. QOL from OCS was empirically estimated based on the difference in QOL between LACS and OCS from the 2012 QOL analysis of long-term follow-up data of the 2002 COST trial[123]. Baseline QOL and QOL after recovery were assumed to be 0.75. Difference in QOL between minimally invasive surgery and OCS was assumed to last 2 weeks. Surgical complications were assumed to be associated with a lower QOL (exact value was unspecified), which would last 3 days if ileus or 2 days if SSI. **Valuation**: QALY was used to represent utility. **Base case QALY values:** RACS: 0.64 LACS: 0.63 OCS: 0.58	**Measurement:** Utilities for QOL for LACS and OCS were based on a 2012 QOL analysis of long-term follow-up data of the 2002 COST trial[123]. QOL from RACS was assumed to be the same as LACS because there are no published studies on RACS QOL after colectomy. Baseline QOL and QOL after recovery was assumed to be 0.9. Difference in QOL between minimally invasive surgery and OCS was assumed to last 2 weeks. Surgical complications were assumed to be associated with a QOL of 0.7, which would last 3 days if ileus or 2 days if SSI. **Valuation**: QALY was used to represent utility. **Base case QALY values:** RACS: 0.77 LACS: 0.77 OCS: 0.74
WTP threshold	€20,000 - €30,000/QALY	€20,000 - €30,000/QALY	\$50,000 - \$200,000/QALY	\$50,000 - \$200,000/QALY
ICER	€1,555.90/QALY gained with RACS compared to LACS	€11,691.81/QALY gained with RACS compared to LACS	**Societal:** \$751,056/QALY	**Societal:** \$ 2,322,715/QALY

	Incremental QALY = 0.195 95.54% probability that RACS is cost-effective at €20,000. 97.18% probability that RACS is cost-effective at €30,000.	Incremental QALY = 0.105 78.78% probability that RACS is cost-effective at €20,000. 95.04% probability that RACS is cost-effective at €30,000.	Probability of being most cost-effective at WTP of $50,000/QALY: RACS: 38% LACS: 41% OCS: 21% **Healthcare:** $ 1, 485,139/QALY Incremental QALY = 0.00066	Probability of being most cost-effective at WTP of $50,000/QALY: RACS: 39% LACS: 54% OCS: 7% **Healthcare:** $4, 174,848/QALY Incremental QALY = 0.00032
Time horizon	1 year	1 year	1 year	1 year
Perspective	Healthcare sector	Healthcare sector	Societal and healthcare sector	Societal and healthcare sector
Discounting	Discount rate of 3% per year was applied to costs and QALYs	Not performed due to time horizon of 1 year	Not performed due to time horizon of 1 year	Not performed due to time horizon of 1 year
Sensitivity analyses	Multivariate and stochastic sensitivity analyses	Multivariate and stochastic sensitivity analyses	Probabilistic and one-way sensitivity analyses	Probabilistic and one-way sensitivity analyses
Sensitivity analysis findings	The model was most sensitive to robotic hospitalization costs and OR costs followed by laparoscopic hospitalization costs and OR costs.	The model was most sensitive to laparoscopic hospitalization costs, robotic OR costs, robotic hospitalization costs and laparoscopic utility.	The model was most sensitive to robotic OR costs (OR time/minute, duration, disposable instrument usage), LOS and earlier return to work. RACS could be more cost-effective than LACS with small changes: Reducing disposable costs by $400 or shortening OR time by 20 minutes. Capital equipment costs did not influence the cost-effectiveness assessment when cost-effectiveness between the societal and healthcare sector perspectives were compared.	The model was most sensitive to robotic disposable costs, OR time, LOS and earlier return to work. RACS could be more cost-effective than LACS if the following occurred: Lowering robotic disposable costs by 30%, reducing OR time by 20%, reducing RACS LOS by 1 day shorter than LACS LOS, or returning to work 3 days sooner in RACS than LACS. Capital equipment costs did not influence the cost-effectiveness assessment when cost-effectiveness

				between the societal and healthcare sector perspectives were compared.
Conclusions	Compared to LACS, RACS is a cost-effective procedure in the surgical treatment of rectal cancer at WTP thresholds of €20,000 - €30,000/QALY.	Compared to LACS, RACS is a cost-effective procedure in the setting of right hemicolectomy at WTP thresholds of €20,000 - €30,000/QALY.	In proctectomy, LACS is most likely to be the cost-effective approach, followed by RACS and OCS at a WTP threshold of $50, 000/QALY. However, RACS was the cost-effective approach nearly as often as LACS and could surpass LACS with small decreases in cost or LOS.	In colectomy, LACS is most likely to be the cost-effective approach, followed by RACS and OCS at a WTP threshold of $50, 000/QALY. RACS would only surpass LACS if there were significant changes in costs, LOS, time off work and hernia rates; it remains unclear whether RACS can achieve improvements of this magnitude.

ICU = intensive care unit; **OR** = operating room; **PACU** = post-anesthetic recovery unit; **N/A** = not applicable; **SF-36** = Short Form 36; **QALY** = quality-adjusted life year; **HUI** = Health utilities index; **QOL** = quality of life; **RACS** = robotic-assisted colorectal surgery; **LACS** = laparoscopic-assisted colorectal surgery; **OCS** = open colorectal surgery; **RCT** = randomized controlled trial; **COST** = Clinical Outcomes of Surgical Therapy; **SSI** = surgical site infection; **WTP** = willingness-to-pay; **ICER** = incremental cost-effectiveness ratio; **LOS** = length of stay

Table 3.3. Model inputs and validation of model-based studies

Model-based study	Simianu, Curran et al.	Simianu, Gaertner et al.
Target anatomy	Rectum	Colon
Model used	Decision-analytic model using decision tree	Decision-analytic model using decision tree
Model validation	Structurally valid. No internal or external validation performed.	Structurally valid. No internal or external validation performed.
Source of RACS effectiveness in model	**QOL:** RACS/LACS: 2018 RCT[97] (n=163) OCS: empiric **Clinical outcomes:** RCS/LACS conversion rate, OR time, LOS: 2017 ROLARR RCT[33] (n=471) OCS OR time, LOS: 2016-2017 NSQIP data, empiric Days off work RACS/LACS/OCS: 2004 RCT[94] (n=403) SSI rate RACS/LACS: ROLARR SSI rate OCS: empiric Ileus rate RACS/LACS: 2016-2017 NSQIP data, empiric Ileus rate OCS: empiric Hernia rate RACS/LACS: 2017 SR MA[124], 2018 population-based cohort study[125] Hernia rate OCS: 2008 SR[126]	**QOL**: RACS/LACS/OCS: 2012 QOL analysis of long-term follow-up data of the 2002 COST trial[123] (n=449) **Clinical outcomes:** RACS/LACS conversion rate, OR time, LOS: retrospective cohort studies from 2014-2018[84,127–131], 2014 SR MA[57] OCS OR time, LOS: 2005 SR MA[95] Days off work RACS, LACS, OCS: 2015 Kaiser Family Foundation[132] SSI rate and ileus rate RACS, LACS, OCS: 2005 SR MA[95], 2012 CEA on LACS vs OCS[96] Hernia rate RACS, LACS, OCS: 2017 US Bureau of Labour Statistics[133]
Costing source	RACS capital investment, disposables, maintenance: Intuitive Surgical LACS/OCS capital investment, disposables, maintenance: estimate from authors' institution	Same as for Simianu, Curran et al.

	Equipment lifespan (RACS, LACS, OCS): author estimate Cost of OR time per minute and hospital cost per day: 2016 physician leadership cover story[134], 2015 Kaiser Family Foundation[132] Cost of caregiver and cost per day off work: 2017 US Bureau of Labour Statistics[133], 2012 CEA on LACS vs OCS[96]	

QOL = quality of life; **RACS** = robotic-assisted colorectal surgery; **LACS** = laparoscopic-assisted colorectal surgery; **OCS** = open colorectal surgery; **RCT** = randomized controlled trial; **OR** = operating room; **LOS** = length of stay; **SSI** = surgical site infection; **ROLARR** = Robotic vs. Laparoscopic Resection for Rectal Cancer; **NSQIP** = National Surgical Quality Improvement Program; **SR MA** = systematic review and meta-analysis; **COST** = Clinical Outcomes of Surgical Therapy; **CEA** = cost-effectiveness analysis

CHEC-extended items	Quijano et al.	Ferri et al.	Simianu, Curran et al.	Simianu, Gaertner et al.
1. Clear description of the study population	Met criteria	Met criteria	Met criteria	Met criteria
2. Clear description of competing alternatives	Met criteria	Met criteria	Met criteria	Met criteria
3. Well-defined research question posed in answerable form	Met criteria	Met criteria	Met criteria	Met criteria
4. Economic study design appropriate to the stated objective	Met criteria	Met criteria	Met criteria	Met criteria
5. Appropriate reporting of structural assumptions and validation methods (if model-based study)	Not applicable	Not applicable	Did not meet criteria	Did not meet criteria
6. Appropriate time horizon to include relevant costs and consequences	Did not meet criteria	Did not meet criteria	Did not meet criteria	Did not meet criteria
7. Appropriate perspective	Met criteria	Met criteria	Met criteria	Met criteria
8. Important and relevant costs for each alternative are identified	Did not meet criteria	Did not meet criteria	Met criteria	Met criteria
9. Appropriate measurement of costs in physical units	Met criteria	Met criteria	Met criteria	Met criteria
10. Appropriate valuation of costs	Met criteria	Did not meet criteria	Met criteria	Met criteria
11. Important and relevant outcomes for each alternative are identified	Did not meet criteria	Did not meet criteria	Met criteria	Met criteria
12. Appropriate measurement of outcomes	Met criteria	Met criteria	Met criteria	Met criteria
13. Appropriate valuation of outcomes	Met criteria	Met criteria	Met criteria	Met criteria
14. Appropriate incremental analysis of costs and outcomes of alternatives is performed	Met criteria	Met criteria	Met criteria	Met criteria
15. Future costs and outcomes are discounted appropriately	Did not meet criteria	Met criteria	Met criteria	Met criteria
16. Important variables of uncertain value are appropriately subjected to sensitivity analysis	Met criteria	Met criteria	Met criteria	Met criteria
17. Conclusions follow from the data reported	Met criteria	Met criteria	Met criteria	Met criteria
18. Study discusses the generalizability of the results to other settings and patient groups	Met criteria	Did not meet criteria	Did not meet criteria	Did not meet criteria
19. Potential conflict of interest is indicated	Met criteria	Met criteria	Met criteria	Met criteria
20. Ethical and distributional issues are discussed appropriately	Did not meet criteria	Did not meet criteria	Did not meet criteria	Did not meet criteria

Met criteria
Did not meet criteria
Not applicable

Figure 3.2. Quality assessment using the Consensus on Health Economic Criteria (CHEC) list. The trial-based studies by Quijano et al. and Ferri et al. scored 14 and 13 out of 19 points respectively. Both studies had inadequate time horizons of one year, omitted equipment costs, did not consider oncologic outcomes, and did not discuss regarding ethical and distributional

issues related to RACS. Quijano et al. performed discounting inappropriately. Ferri et al. did not specify valuation year or discuss study generalizability.

The model-based studies scored 16 out of 20 points. Neither study addressed model validation, generalizability, or ethical and distributional issues. Both had an inadequate time horizon of one year.

CHAPTER 4. Robotic vs laparoscopic-assisted rectal cancer resection: A cost-utility analysis

This chapter will be submitted as **Li MY**, Dykstra MA, Snelgrove R, Wang H, Dixon E, Rennert-May E, Crump T (2022). Robotic vs laparoscopic-assisted rectal cancer resection: A cost-utility analysis. (Pending submission to *Ann Surg*).

We describe a model-based cost-utility analysis used to assess the value of RACS vs LACS rectal cancer resection in an Alberta setting using a decision tree. Our model adds to the scarce literature of economic evaluations on this subject and improves upon existing studies by adopting a lifetime time horizon and adding the diversity of a Canadian perspective.

4.1. Abstract

Objective: To assess the cost-effectiveness of implementing a new robotic vs. laparoscopic-assisted program for rectal cancer resection in a Canadian healthcare setting.

Background: Robotic surgery has been increasingly used in rectal cancer resection. However, its cost-effectiveness remains controversial and there is a paucity of economic evaluations to guide decision-making in robotic program implementation.

Methods: A model-based cost-utility analysis using a decision tree was performed. A lifetime time horizon, healthcare system perspective and annual discount rate of 1.5% were adopted. The outcome was the incremental cost-effectiveness ratio (ICER), which was compared to a cost-effectiveness threshold of CAN $100,000/quality-adjusted life year. Probabilistic and one-way sensitivity analyses were performed. Three scenario analyses considered changes in outcome when operating time and length of stay from the Robotic vs. Laparoscopic Resection for Rectal Cancer (ROLARR) trial were used, when robotic volume was reduced, and when costs of the *da Vinci* Xi robot were used.

Results: Robot-assisted rectal cancer resection was cost-effective compared to the laparoscopic approach at an ICER of CAD $17,500/QALY. Results were most sensitive to length of stay, operating time and complication rate. The robotic approach remained cost-effective with inputs from ROLARR and costs from the *da Vinci* Xi. However, when robotic volume decreased by 78% by assuming the robot was no longer shared between specialties, the robotic approach was no longer cost-effective.

Conclusions: Implementation of a new robotic program has a higher probability of being cost-effective than a laparoscopic program in the setting of Canadian rectal cancer care, a cost-

effectiveness threshold of CAD $100,000/QALY and high robotic volume. When implementing a robotic program, centres should consider length of stay, operating time and minimization of complications.

Keywords: robotic surgery, laparoscopic surgery, rectal cancer resection, cost-utility analysis, cost-effectiveness

4.2. Introduction

Surgery for rectal cancer can be performed open or minimally invasively. Compared to open surgery, minimally invasive surgery (MIS) results in decreased pain, wound infection, bleeding and length of hospital stay[5,6]. These clinical benefits have led to the widespread use of MIS, with the open technique increasingly reserved for patients who are not candidates for MIS or for when an attempt at MIS is aborted due to bulky tumours, poor visualization and/or lack of working space[135,136].

The two main types of MIS are robotic-assisted colorectal surgery (RACS) and laparoscopic-assisted colorectal surgery (LACS). LACS is more established and considered the standard MIS approach. However, RACS offers improved 3D visualization and greater degrees of instrument mobility[13,14], which are technically advantageous for resecting rectal cancers in the confined space of the pelvis[3]. Clinically, RACS is associated with decreased length of hospital stay, reduced blood loss and lower rate of conversion[15–17]. Despite its relative novelty, RACS has been shown to maintain the same short-term oncologic outcomes as LACS[137,138].

However, the implementation of RACS in rectal cancer resection remains controversial due to high costs[139,140]. The market-dominating *da Vinci* robotic system (Intuitive Surgical Inc, Sunnyvale, CA) has been reported to cost 2.5 million US dollars and requires expensive robotic consumable instruments[36,37,141,142]. Longer robotic operating time due to robotic set-up and surgeon learning curve is another cost driver. It is unclear if the greater clinical effectiveness of RACS would render it cost-effective compared to LACS.

There are two cost-utility analyses comparing the cost-effectiveness of RACS vs LACS rectal resection. The Spanish study[43] by Quijano et al. was rectal cancer-specific and concluded that RACS is cost-effective compared to LACS. The United States (US) study[44] by Simianu et al. included all indications for proctectomy and concluded that RACS is cost-ineffective. Both studies utilized a time horizon of one year, which may be insufficient for capturing long-term cost and effectiveness consequences of RACS rectal resection, such as permanent bowel, bladder and sexual dysfunction. Also, conclusions of economic evaluations may be less applicable outside their decision settings due to the influence of healthcare jurisdiction on costs and effectiveness[143]. Therefore, there is not only a paucity of economic evaluations comparing RACS to LACS rectal cancer resection, but existing studies provide different conclusions, use potentially inadequate time horizons and represent limited healthcare jurisdictions.

We aim to assess the cost-effectiveness of RACS compared to LACS rectal cancer resection in a Canadian healthcare setting using a lifetime time horizon. This allows value assessment of RACS in a healthcare setting not previously studied and allows comprehensive inclusion of relevant costs and effectiveness. The practical relevance of our study is to guide decision-making with regards to robotic funding in Canadian RACS rectal cancer resection and to provide another perspective to RACS cost-effectiveness to an international audience, some of whose RACS utility rates far exceed that of Canada's[20,37].

4.3. Methods

4.3.1. Decision model and inputs

Our target population consisted of patients 18 years or older with stage III rectal cancer undergoing low anterior resection (LAR) with diverting loop ileostomy (DLI). Stage III is the most commonly described stage in studies investigating RACS rectal cancer resection[19,33,144] while LAR with DLI was the most commonly performed operation in this patient population[69]. LAR with DLI also captures potential stoma-related complications and subsequent bowel dysfunction once the stoma is reversed.

The setting and perspective were that of the publicly funded Canadian healthcare system. The location was the province of Alberta, where a RACS program was established in 2018. The decision problem consisted of the cost-utility of implementing a new RACS vs LACS program for rectal cancer resection. The base case considers the Alberta RACS program, which utilizes a *da Vinci* Si robot whose costs and console time are shared with other surgical subspecialties. The comparators were RACS vs LACS, the latter of which was considered standard of care because it is the more established MIS approach to rectal cancer[15,145,146]. The primary outcome was the incremental cost-effectiveness ratio (ICER), represented as the ratio of incremental cost to incremental quality-adjusted life years (QALYs) between the alternative surgical options. A lifetime time horizon was adopted and an annual discount rate of 1.5% was applied to costs and effectiveness as per the Guidelines for the Economic Evaluation of Health Technologies: Canada, 4th edition[28].

Effectiveness was derived from utility measurements in the literature and valued as QALYs (Table 4.1). A utility is a measure of preference that individuals have for a particular health state[23,147,148]. It is valued between negative infinity and one, where one represents perfect health, zero represents death and negative values represent states worse than death. QALY is a function of utility and time spent in the health state. Given multiple sources were used to derive utility values, utilities associated with complications were transformed into dis-utilities to standardize values across studies.

Costs were valued in 2021 Canadian dollars (CAD) and included those associated with the equipment, index operation, index inpatient stay, early complications and late complications (Table 4.1). Any CAD costs incurred before 2021 were converted to a reference period of June 2021 using the Canadian Consumer Price Index, Health and Personal Care category[149]. Costs incurred in US dollars (USD) were converted to CAD using the currency conversion rate from June 1st, 2021. A cost-effectiveness threshold of CAD $100,000 /QALY was used as this is a widely accepted threshold for cancer care in Canada[150]. Costs of the index operation and of hospital stays (index or due to complications) were calculated by multiplying the time units used by the cost of a time unit in these clinical areas. Time units were based on 46 RACS and 26 LACS rectal cancer cases from an Edmonton, Alberta database. Costs per time unit was based on 15 RACS patients from the same database. Cost per case amortizes equipment costs over nine years, as this is the average lifespan of the *da Vinci* robot[151].

We developed a decision analytic model in the form of a decision tree (Figure 4.1). This included the two MIS comparators and considered the possibility of subsequent conversion to open surgery, as there is evidence of differential morbidity and costs associated with conversion[152,153]. Relevant complications were included and categorized as either early or late. Early complications were defined as those occurring within 30 days post-operatively and late complications describe those occurring after 30 days postoperatively. These were chosen to be consistent with how complications are described in the clinical literature[19,20,33]. Complications were considered relevant if they are common and/or there is evidence to suggest differential costs and utilities associated with RACS vs LACS. Permanent complications such as bowel, bladder and sexual dysfunction were included to fully capture costs and effectiveness consequences over a lifetime. Each branch of the decision tree is associated with a probability derived from relevant literature. A detailed description of model inputs for probabilities, effectiveness and costs is found in Appendix 4.1.

Key model assumptions are as follows: 1) converted procedures will have the same utility as open procedures but will incur both MIS and open equipment costs; 2) death may occur as a result of early complications but not of late complications; 3) utility decrement from bowel, bladder, sexual dysfunction and rectovaginal/rectovesical fistulas will be permanent. Cancer recurrence is not a decision branch but is presumed to be accounted for as part of the median life expectancy used in the model. A complete list of model assumptions and their rationale is found in Appendix 4.2.

The model was conceptualized in consultation with Canadian colorectal surgeons practicing in Alberta and health economists with expertise in the Canadian healthcare system. In addition, the US-based cost-utility analysis comparing RACS vs LACS rectal resection was consulted, as it is the only existing economic model on this subject[44]. The model was built in and analyzed using Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA). The model is not publicly available but could be requested from the corresponding author.

4.3.2. Sensitivity analysis

Three scenario analyses were performed to better inform our decision problem. Scenario 1 considered length of stay (LOS) and OR time from the RObotic vs. LAparoscopic Resection for Rectal Cancer (ROLARR) trial. Scenario 2 assumed that all RACS equipment costs would be borne by the colorectal surgery program. Scenario 3 assumed the costs of the *da Vinci* Xi robot.

The rationale for using LOS and OR time from ROLARR is owing to the relatively small sample sizes of 46 RACS and 26 LACS cases in the Edmonton database. The 2017 ROLARR trial by Jayne et al. is the largest randomized controlled trial to date comparing RACS vs. LACS clinical outcomes in rectal cancer. Although ROLARR may be less generalizable to the Canadian setting because it involved mostly European patients and surgeons, its sample size was much larger (n=237 in RACS and n=234 in LACS) and 67% of each group underwent LAR. Thus, data from ROLARR could be considered high quality, recent and applicable to our target population. ROLARR also reported different LACS OR time and RACS LOS than that used in our base case (longer LACS OR time of 261 vs 226 minutes and longer RACS LOS of 8.0 vs 6.8 days), making its data appropriate for a scenario analysis.

Scenario 2 assumed all robotic equipment costs were borne by the colorectal surgery program. This was a valuable scenario analysis because the base case considered *da Vinci* Si equipment costs that were proportional to the colorectal service's use of the robot. Given the Alberta RACS program shares the robot between different specialties, colorectal surgery performed 50 out of 228 robotic cases in 2019. However, since the decision problem examines the cost-utility of implementing new RACS vs LACS programs, it is possible that a colorectal service would acquire a robot and be solely responsible for its costs. In this scenario, the colorectal volume would remain constant since the incidence of rectal cancer should remain the same. Scenario 2 was designed to illustrate the effect on cost-effectiveness if operating volume is lowered, such as in low volume centres or when the robot cannot be shared (e.g. scheduling conflicts or lack of surgeons with robotic training).

Scenario 3 examines the cost-effectiveness of RACS vs LACS when the robotic model is the *da Vinci* Xi, which is the most recent *da Vinci* operating system and would be the most likely model acquired by a newly implemented program. The Xi capital equipment costs are higher but there are certain cost savings in consumable instruments due to extended lifespan in this generation[151,154]. Scenario 3 was designed to be informative for institutions looking to purchase the up-to-date model on the robotic market.

Probabilistic analysis for the base case and each scenario analysis was performed using 5,000 Monte Carlo simulations. Results from the probabilistic analyses are presented as a cost-effectiveness acceptability curve (CEAC) and represented on the cost-effectiveness plane using an ICER scatterplot. A tornado diagram[155] was generated by varying input parameters by +/-10% to assess the parameters that the model results are most sensitive to. Standard deviations used to calculate gamma distributions are listed in Appendix 4.3. All QALYs were valued equally but an applicable equity concern is the fact that in the current Canadian healthcare system, only patients with rectal cancer residing in/near major academic centres have access to RACS. Patients who belong to smaller health regions have inequitable access to robotic care.

This cost-utility analysis was reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS) criteria[156] (Appendix 4.4). Ethics approval for the Edmonton colorectal cancer surgery database was obtained from the Health Research Ethics Board of Alberta.

4.4. Results

4.4.1. Reference Case

In the base case analysis, RACS cost CAD $30,427 per case of LAR with DLI whereas LACS cost CAD $29,626 per case, resulting in an incremental cost of CAD $801 per case. RACS led to an estimated QALY of 4.69 compared to 4.64 in LACS, resulting in an incremental QALY of 0.046 (Table 4.2). These incremental costs and effects generated an ICER of CAD $17,500/QALY.

4.4.2. Sensitivity Analysis

The 10 most influential parameters were identified in one-way sensitivity analyses and presented in the tornado diagram (Figure 4.2). The model was most sensitive to changes in LOS, complication rates (especially bowel dysfunction) and OR time. LACS and RACS LOS were the top two parameters the model was sensitive to.

Probabilistic analysis demonstrated that the probability of RACS being cost-effective at CAD $100,000/QALY is 79% compared to 21% for LACS (Figure 4.3). The scatterplot shows that most simulations were associated with an increase in cost and in QALY when RACS was compared to LACS (Figure 4.4). However, a significant portion of simulations were in the cost-saving quadrant of the cost-effectiveness plane, whereby RACS was associated with an increase in QALY and decrease in cost. There was a moderate amount of variation in ICERs (Figure 4.4).

4.4.3. Scenario 1: ROLARR operating time and length of stay

When OR time and LOS from the more robust ROLARR trial was used, RACS cost per case was CAD $32,690 while LACS cost per case was CAD $29,925. The incremental cost was CAD $2,765. The incremental QALY remained the same at 0.046 (Appendix 4.5, Table S3). The resulting ICER was CAD $60,412/QALY. The probability of RACS being cost-effective at a threshold of CAN $100,000/QALY decreased to 63%, while this probability for LACS increased to 37% (Appendix 4.5, Figure S1). A smaller proportion of ICERs from the 5000 simulations were found in the cost-saving plane but the ICER scatterplot is overall similar to that of the base case (Appendix 4.5, Figure S2).

4.4.4. Scenario 2: New colorectal surgery program bearing all RACS equipment costs

When RACS volume remained the same but all upfront RACS costs were borne by the colorectal surgery program, the cost per case of RACS LAR with DLI increased to CAD $38,574 per case. The incremental cost per case increased to CAD $8,948 and the incremental QALY was unchanged, resulting in an ICER of CAD $195,480/QALY (Appendix 4.6, Table S4). Probabilistic analysis showed that with this increased cost burden on RACS, the probability of RACS being cost-effective at a threshold of CAN $100,000/QALY decreased to 25%, compared to 75% for LACS (Appendix 4.6, Figure S3). The ICER scatterplot is concentrated around higher incremental cost levels, as would be expected given the scenario (Appendix 4.6, Figure S4).

4.4.5. Scenario 3: Costs of the da Vinci Xi

When costs of the *da Vinci* Xi were used to populate RACS capital equipment, maintenance, consumable and disposable costs, RACS costs per case increased to CAD $31,597. The incremental cost is $1,971 and the incremental QALY was unchanged from the base case (Appendix 4.7, Table S5). The resultant ICER was CAD $43,056 and probabilistic analysis showed a 72.4% probability of RACS being cost-effective at a threshold of CAN $100,000/QALY compared to 27.6% for LACS (Appendix 4.7, Figure S4). The ICER scatterplot showed a smaller amount of variation but is overall similar to the base case (Appendix 4.7, Figure S5).

4.4.6. Model Validation

Face validation was assessed via expert consultation with colorectal surgeons in Alberta who perform MIS rectal cancer resection. These surgeons were not involved in the Edmonton RACS program and have no financial interests in the technologies evaluated in this analysis. Internal validation was performed by verifying equations and cross-referencing results between different types of analyses (base case vs scenario analyses, deterministic vs probabilistic). Expertise from experienced health economists was sought to resolve technical errors. External validation was performed by comparing the results of our evaluation with the only existing economic model on RACS proctectomy by Simianu et al.[44].

4.5. Discussion

The results of our cost-utility analysis show that when a cost-effectiveness threshold of CAN $100,000/QALY is used and relevant health utilities are captured over a lifetime horizon, implementing a new RACS program for LAR with DLI in a Canadian setting is cost-effective compared to a similar program using LACS. Consistent with other cost-utility analyses on robotic vs laparoscopic rectal surgery[43,44], LOS and OR time are some of the parameters the results are most sensitive to. The three scenario analyses serve to overcome some of the limitations of the base case. Since OR time and LOS affect cost, basing these inputs on a small Alberta sample may make findings more generalizable to our setting but reduce precision. Our first scenario analysis improves model output precision by using ROLARR's higher quality data and bigger sample size. The ICER increased when estimates from ROLARR were used, likely because the reduction in LOS associated with RACS was less pronounced than in our base case (reduction of 0.2 days in ROLARR compared to 1.6 days in the Edmonton RACS program). The diminished LOS reduction would have also diminished RACS's capacity for cost savings, which was further amplified in the ICER results considering that the model is most sensitive to LOS estimates. Nonetheless, the ICER using ROLARR OR time and LOS remained cost-effective at a threshold of CAD $100,000/QALY. This scenario suggests that in centres where RACS LOS and LACS OR time are longer than in the Alberta setting (6.8 days and 226 minutes), RACS may remain cost-effective if these parameters are similar to that in ROLAAR (8.0 days and 261 minutes).

The results of our second scenario analysis echo findings from economic evaluations of robotic technology in other surgical fields[115,116,119,122]: the probability of the robotic approach being cost-effective diminishes when robotic operating volume is decreased. Since greater robotic volume means equipment cost is shared across more cases, lower volume reduces the ability to cost share. This increased per case costs result in increased incremental cost between RACS and LACS. Our results suggest that RACS rectal cancer resection should be performed at high-volume centres to contain costs, with the added benefit that higher volume robotic surgeons may progress more quickly on their learning curve and reduce OR time, which lowers costs. Higher volume could be achieved via consolidating referrals or sharing the robot between specialties.

Our third scenario analysis shows that when the more expensive *da Vinci* Xi is the robotic model of a new rectal cancer surgery program, RACS remained cost-effective. The ICER increased from CAD $17,500/QALY in the base case to CAD $43,056 in the Xi scenario with an attendant decrease in the probability of RACS being the cost-effective approach. However, the Xi ICER remained below the CAD $100,000/QALY cost-effectiveness threshold, which suggests that cost-effectiveness of RACS in LAR with DLI could withstand a certain increase in equipment costs as a result of technological updates.

Our model has made improvements based on the two existing cost-utility analyses on this subject. Simianu et al. performed the only model-based cost-utility analysis on RACS vs LACS proctectomy using a decision tree. They found that that RACS was not cost-effective compared to LACS but differ from our study by their indication for surgery (all indications were included), time horizon (1 year), jurisdiction (US-based) and postoperative complications (only two early complications and one late complication were included in the group's decision tree). Our model considered a lifetime horizon that would better capture the utility decrement of permanent complications. In addition, we considered six early and six late complications. This wider inclusion of relevant complications would better reflect the complexity of postoperative course after rectal cancer surgery and better capture incremental costs and effectiveness between RACS and LACS. For these reasons, it is possible that Simianu et al. were less able to detect incremental changes between RACS and LACS, leading to the finding of cost-ineffectiveness when RACS was compared to LACS at thresholds of USD $50,000-20,000/QALY.

Quijano et al.[43] performed the only rectal cancer-specific cost-utility analysis comparing RACS vs LACS. They took a trial-based approach using a non-randomized cohort of 81 RACS and 104 LACS cases. The time horizon was relatively short at one year and effectiveness was only measured at three months postoperatively, which is relatively early considering the consequences of late complications and permanent dysfunction may not be apparent at three months, especially in patients who are diverted. Although the authors concluded that RACS was cost-effective compared to LACS at a threshold of €20,000 - €30,000/QALY, RACS capital equipment and maintenance cost were omitted. A model-based approach in our study facilitates inclusion of a lifetime time horizon, which would have been difficult to include as part of a trial. Multiple changes in effectiveness during this time horizon were considered rather than a single value. Lastly, capital equipment and maintenance costs are substantial in RACS. Our inclusion of these costs makes our results more meaningful to those interested in all relevant costs of RACS and to programs that will be responsible for robot purchase and maintenance.

Given our findings, we feel that it is reasonable to consider greater implementation of robotic rectal cancer surgery programs in Canada assuming high volume use of the robot. Possible cost-saving measures include reducing RACS LOS, OR time and complications as well as increasing robotic volume to offset robotic costs. Where budgetary constraints prohibit the establishment of a rectal cancer robotic program, the value of existing laparoscopic programs can be enhanced by reducing LACS LOS, LACS OR time, and optimizing postoperative care to reduce LACS complications and LOS in hospital.

We did not perform a budget impact analysis or value of information analysis. The former may be salient in the practical adoption of RACS by decision-makers as RACS upfront costs may be prohibitive. The latter could help inform the value of conducting further research to resolve some of the uncertainty surrounding parameter estimates, such as the lack of approach-specific inputs and of standardized utility values.

4.5.1. Limitations

Although we used the highest-level evidence available in the literature, some inputs may not be generalizable to our target population while others may be of limited quality. For example, none of the source studies for probability inputs included Canadian patients (Table 4.1) while other approach-specific probabilities were not available, leading to the need for assumptions. Also, the quality of source studies for utility values is variable given significant heterogeneity in methods of measurement and lack of standardization between studies with respect to illness context and source population[157–160] (discussed in detail in Appendix 4.1).

Given the variability in costs and health state preference between jurisdictions, our study may be less generalizable to non-Canadian jurisdictions. However, model inputs were derived from literature originating in US, Europe and Asia, thus retaining some relevance to other regions. Our work helps to populate the scarce literature on RACS vs LACS cost-effectiveness in rectal cancer with the possibility of serving as a reference for decision-making in other jurisdictions or for groups from wishing to pursue similar studies.

4.6. Conclusion

For patients with stage III rectal cancer needing LAR with DLI in Canada, findings from this cost-utility analysis suggest that implementing a new robotic program has a higher probability of being cost-effective than a laparoscopic program, using a cost-effectiveness threshold of CAD $100,000/QALY and assuming an annual volume of at least 200 cases. When implementing a robotic program, centres should consider length of stay, operating time and minimization of complications.

Declarations

This work was not funded or sponsored in any form. The authors have no conflicts of interest.

Table 4.1. Model inputs

Variable	Approach	Mean	Probabilistic distribution	Source
Probability/rate				
Conversion	RACS	0.075	Beta	[15]
	LACS	0.129	Beta	[15]
Early complications (within 30 days)	RACS	0.272	Beta	[15]
	Converted	0.371	Beta	[68]
	LACS	0.267	Beta	[15]
30-day mortality	RACS	0.006	Beta	[15]
	Converted	0.006	Beta	Assumed same as LACS given rates similar in study by Garfinkle et al.[161]
	LACS	0.006	Beta	[15]
Ileus	RACS	0.149	Beta	[161]
	Converted	0.204	Beta	[161]
	LACS	0.146	Beta	[161]
Wound infection	RACS	0.067	Beta	[15]
	Converted	0.076	Beta	[161]
	LACS	0.071	Beta	[15]
Intraabdominal abscess	RACS	0.071	Beta	[161]
	Converted	0.047	Beta	[161]
	LACS	0.056	Beta	[161]
Stoma complications	RACS	0.045	Beta	[97]
	Converted	0.027	Beta	Assumed same as LACS given rates similar in study by Colombo et al.[162]
	LACS	0.027	Beta	[97]
Anastomotic leak	RACS	0.026	Beta	[161]
	Converted	0.014	Beta	[161]

	LACS	0.023	Beta	[161]
Late complication	RACS	0.370	Beta	[163]
	Converted	0.370	Beta	[163]
	LACS	0.370	Beta	[163]
Bowel dysfunction	RACS	0.609	Beta	[164]
	Converted	0.651	Beta	Assumed same as LACS given evidence of such in Nocera et al.[165]
	LACS	0.651	Beta	[164]
Sexual dysfunction	RACS	0.062	Beta	Assumed same as LACS
	Converted	0.104	Beta	[166]
	LACS	0.062	Beta	[166]
Bladder dysfunction	RACS	0.080	Beta	[167]
	Converted	0.080	Beta	Assumed same as LACS given evidence of such in Lim et al.[168]
	LACS	0.080	Beta	[167]
Incisional hernia	RACS	0.058	Beta	[169]
	Converted	0.187	Beta	[170]
	LACS	0.170	Beta	[170]
Small bowel obstruction	RACS	0.125	Beta	Assumed same as LACS
	Converted	0.119	Beta	[170]
	LACS	0.125	Beta	[170]
Rectovaginal/rectovesical fistula	RACS	0.016	Beta	[171]
	Converted	0.016	Beta	[171]
	LACS	0.016	Beta	[171]
Costs (2021 CAD $)				
Equipment cost/case, over 9 years of use	RACS	$ 1,233.67	-	Minogue Medical[172]

	Converted	$	11.87	-	Estimates from authors' institution
	LACS	$	36.92	-	Estimates from authors' institution
Annual service costs	RACS	$	1,114.47	-	Minogue Medical[172]
	Converted	$	50	-	Assume same as LACS
	LACS	$	50	-	Estimates from authors' institution
Instrument costs (consumables and disposables)	RACS	$	2,914.54	-	Minogue Medical[172] and estimates from authors' institution
	Converted	$	685.96	-	Estimates from authors' institution
	LACS	$	1,067.66	-	Estimates from authors' institution
Operating room cost	RACS	$	7,471.13	-	See source of cost per minute and of OR time below
	Converted	$	7,208.57	-	See source of cost per minute and of OR time below
	LACS	$	5,709.22	-	See source of cost per minute and of OR time below
Cost per minute of operating time	-	$	25.27	-	Alberta Health Services costing data of the rectal cancer cases in the Edmonton RACS database
Operating time (minutes)	RACS		296	Normal	Edmonton RACS database
	Converted		285	Normal	[19]
	LACS		226	Normal	Edmonton RACS database
Inpatient stay costs	RACS	$	14,313.26	-	See source of ward cost per day and of length of stay below
	Converted	$	26,127.38	-	See source of ward cost per day and of length of stay below
	LACS	$	17,691.97	-	See source of ward cost per day and of length of stay below
Ward cost per day	-	$	2,090.19	-	AHS micro-costing data of LAR with DLI in the Edmonton RACS database
Length of stay (LOS) (days)	RACS		6.85	Gamma	Edmonton RACS database
	Converted		12.5	Gamma	[19]

	LACS		8.3	Gamma	Edmonton RACS database
Death cost (3 nights of ICU care)	-	$	14,798.61	-	AHS Calgary Zone 2013-2014 rates, Surgical Intensive Care[173]
Ileus cost	-	$	10,450.95	-	Ward cost per day x 5 days
Wound infection cost	-	$	6,770.57	-	Ward cost per day x 3 days + CAN $500 empiric home care costs (outpatient)
Abscess cost	-	$	10,450.95	-	Ward cost per day x 5 days
Stoma complication cost	-	$	10,450.95	-	Ward cost per day x 5 days
Anastomotic leak cost	-	$	14,760.33	-	Alberta Interactive Data Application by Case Mix Group code, unplanned open colorectal without colostomy, Edmonton Zone 2018-2019 rates[174]
"Other" early complication cost	-	$	6,270.57	-	Ward cost per day x 3 days
Bowel dysfunction cost	-	$	250.21	-	Alberta Medical Association (AMA) fee navigator[175]
Sexual dysfunction cost	-	$	250.21	-	AMA fee navigator[175]
Bladder dysfunction cost	-	$	250.21	-	AMA fee navigator[175]
Incisional hernia cost	-	$	5,425.86	-	Canadian Institute for Health Information (CIHI) Patient Cost Estimator: 2018-2019 cost for CMG code 229 (non-complex hernia repair), age group 60-79.[176]
Small bowel obstruction cost	-	$	10,450.95	-	Ward cost per day x 5 days
Rectovaginal/rectovesical fistula cost	-	$	217.87	-	AMA fee navigator[175]
Utility*					
Death	-		0.00	-	-
Ileus	-		0.65	Gamma	[177]
Wound infection	-		0.70	Gamma	[178]
Abscess	-		0.64	Gamma	[177]
Stoma complication	-		0.73	Gamma	[178]
Anastomotic leak	-		0.64	Gamma	[177]

Early "other"	-	0.73	Gamma	[177]
No complications at all	-	0.86	Gamma	[179]
Bowel dysfunction	-	0.59	Gamma	[178]
Sexual dysfunction	-	0.86	Gamma	[180]
Bladder dysfunction	-	0.74	Gamma	[180]
Incisional hernia	-	0.77	Gamma	[181]
Small bowel obstruction	-	0.65	Gamma	[177]
Rectovaginal/rectovesical fistula	-	0.68	Gamma	[177]
Life expectancy (years)				
All other health states	-	6.33	Normal	[182]

* All utilities associated with complications were transformed into dis-utilities. Dis-utilities were subtracted from the utility for the health state of "No complications at all" in order to standardize utility values from different sources in the literature.

RACS = robotic-assisted colorectal surgery; LACS = laparoscopic-assisted colorectal surgery

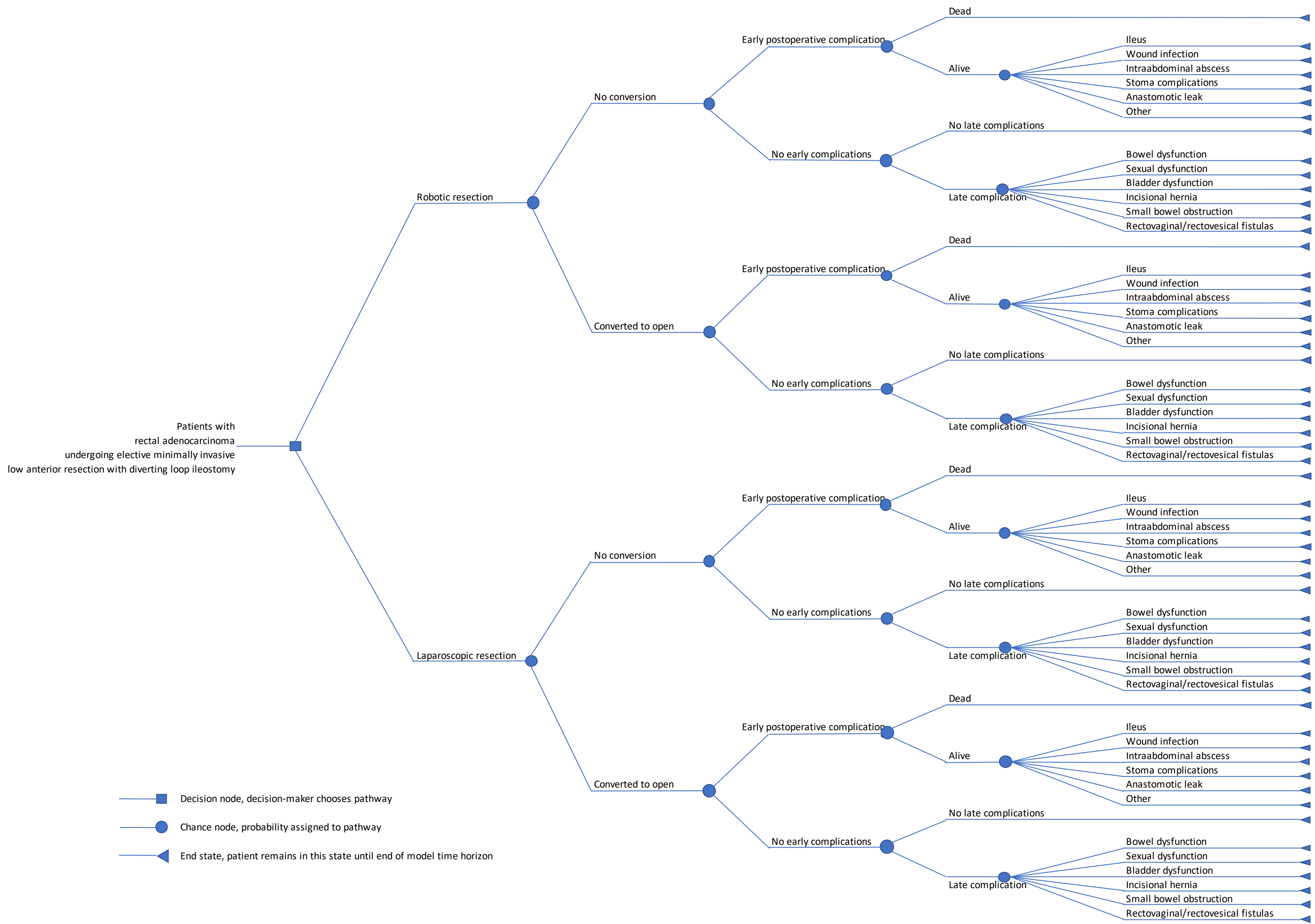

Figure 4.1. Decision tree describing the comparators of RACS vs LACS and subsequent risk of conversion and complications.

RACS = robotic-assisted colorectal surgery; LACS = laparoscopic-assisted colorectal surgery

Table 4.2. Base case disaggregated results

	Total cost (CAN$)	Total effectiveness (QALY)	ICER
RACS	30,427	4.69	17,500
LACS	29,626	4.64	-
Incremental	801	0.046	-

RACS = robotic-assisted colorectal surgery; LACS = laparoscopic-assisted colorectal surgery

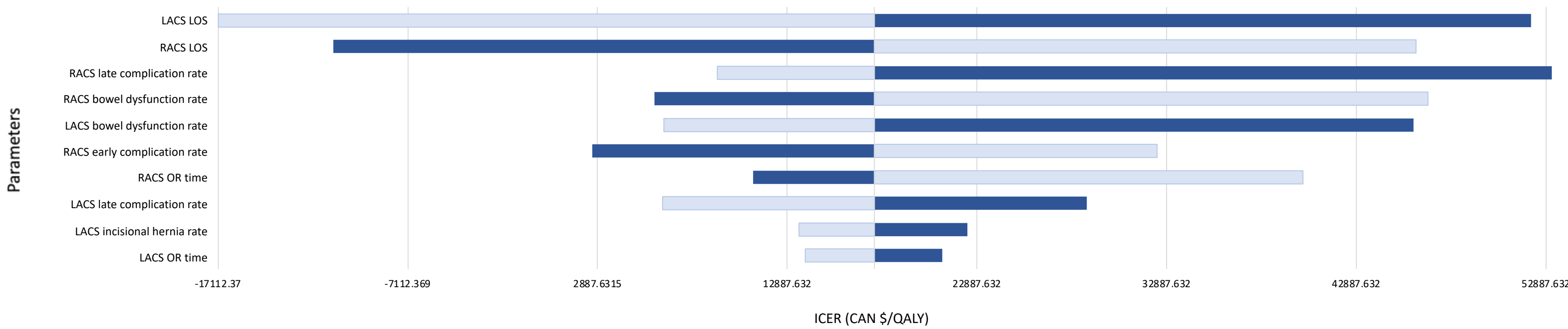

Figure 4.2. Tornado diagram of one-way sensitivity analyses of changes in ICER of RACS vs LACS when parameters affecting cost (y-axis) are varied. Light blue represents high end of costs, dark blue represents lower end of costs.

RACS = robotic-assisted colorectal surgery; LACS = laparoscopic-assisted colorectal surgery; LOS = length of stay; OR = operating room

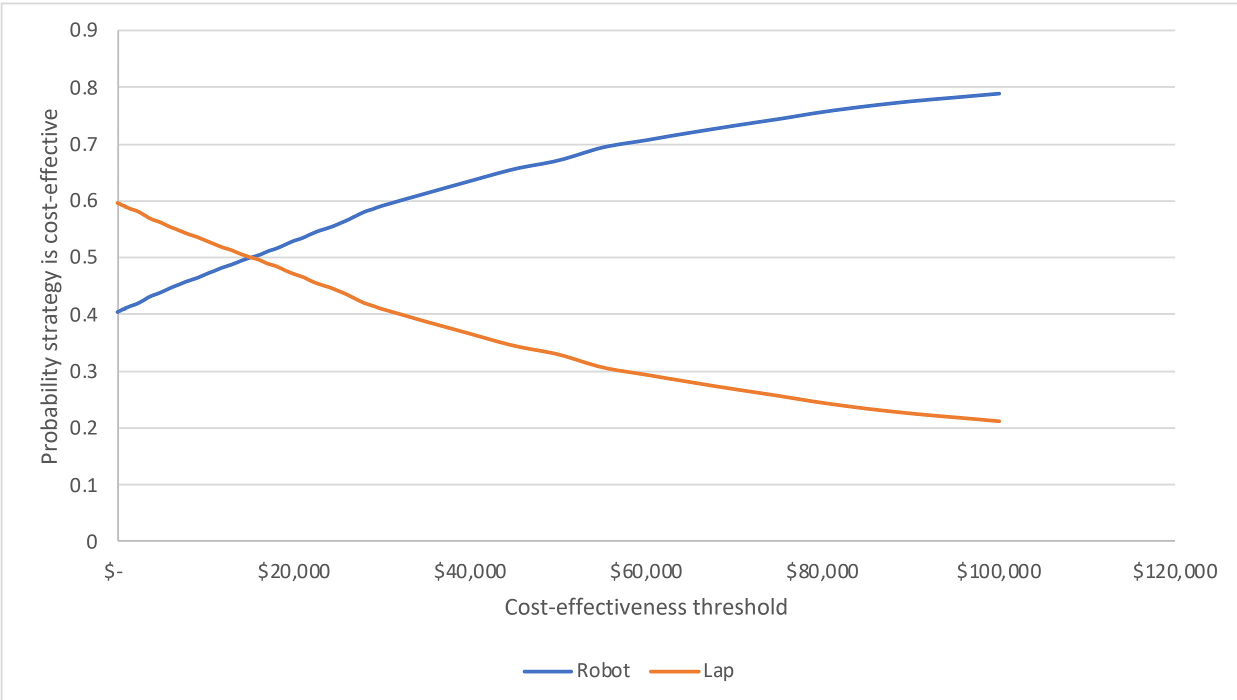

Figure 4.3. Cost-effectiveness acceptability curve for RACS vs LACS LAR with DLI. The probability of RACS being cost-effective at CAD $100,000/QALY is 79% compared to 21% for LACS.

Robot = robotic-assisted colorectal surgery (aka RACS)
Lap = laparoscopic-assisted colorectal surgery (aka LACS)
LAR = low anterior resection
DLI = diverting loop ileostomy
QALY = quality-adjusted life year

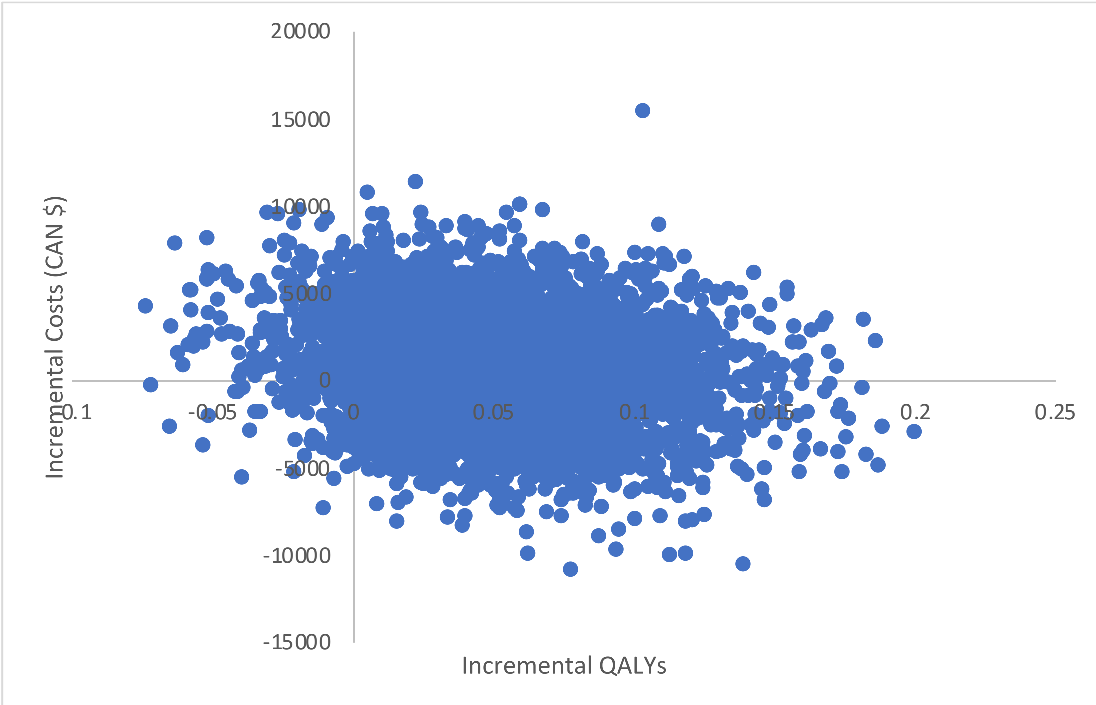

Figure 4.4. ICER scatterplot on a cost-effectiveness plane. Most simulations were associated with an increase in cost and in QALY when RACS was compared to LACS. However, a significant portion of simulations were in the cost-saving quadrant of the cost-effectiveness plane, whereby RACS was associated with an increase in QALY and decrease in cost.

ICER = incremental cost-effectiveness ratio
QALY = quality-adjusted life year
RACS = robotic-assisted colorectal surgery
LACS = laparoscopic-assisted colorectal surgery

Robotic vs laparoscopic-assisted rectal cancer resection: A cost-utility analysis

Supplemental content - Appendices

Appendix 4.1. Detailed description of model inputs

Probabilities

Model inputs for probabilities were derived from the highest-level evidence where available, consisting of systematic reviews, meta-analyses[15,166,167], randomized controlled trials (RCTs)[33,68,164,170] and large multicentre cohort studies on rectal cancer[161,171] (Table 4.1). Literature search for probability values was conducted in May 2021 using PubMed, Google and by hand-searching references of relevant articles. Keywords included rectal resection, proctectomy, the specific surgical approach and the complication in question. Despite a comprehensive literature review, certain approach-specific probabilities were not available. Rates for 30-day mortality, stoma complications, bowel dysfunction and bladder dysfunction after conversion were not found. However, there is evidence that no difference exists between the laparoscopic and open approaches[161,162,165,168]. Thus, the converted rates were assumed to be the same as the LACS rates. RACS rates for small bowel obstruction were not available, thus it was assumed to be the same as the LACS rate. Late complication rates defined as after 30 days postoperatively were not available for any of the three potential approaches (RACS, LACS and converted), thus a single late complication rate from a study comparing patients with ostomies vs. anastomoses[163] was used for all three approaches. This study did not specify the approach used in their cohort. The late complication rate in the group with permanent ostomies was used to be conservative (higher rate of late complications in ostomates[163]). Finally, the rate of rectovaginal fistula was used for the rectovaginal/rectovesical fistula decision branch. Although rectovaginal fistulas only apply to female patients, rectovesical fistulas are sufficiently rare that fistulization after LAR would be more conservatively represented by rectovaginal fistulas (higher fistulization rate in women[183–186]. To assess uncertainty in model inputs, all values for event probabilities were transformed into probabilistic variables using a beta distribution[187]. This beta distribution was calculated from the event and non-event rates, which were found in the original study providing the model input.

Effectiveness

Effectiveness was derived as utilities from various observational studies and valued in QALYs (Table 4.1). Literature search for relevant utility values was conducted in the same time period as the probability inputs and used the same search engines. Keywords included quality of life, utility, EQ-5D, rectal cancer, rectal resection/proctectomy and the health state in question. Utility for the health state of no complications was derived from van der Brink et al.'s 2004 cost-utility analysis comparing cost-effectiveness of neoadjuvant radiation and total mesorectal excision (TME) compared to TME alone. The utility was measured using the EuroQol-5 Dimension (EQ-5D) scale at more than 9 months after surgery. Utility for wound infection, stoma complications and bowel dysfunction were derived from Wilson et al.'s 2006 observational study consisting of 201 patients with rectal cancer[178]. EQ-5D was used to measure utilities at 6 weeks postoperatively. Utilities for sexual and bladder dysfunction were sourced from Volk et al.'s 2004 cross-sectional study assessing preferences for outcomes after prostate cancer treatment[180]. These preferences were elicited from patients presenting for general medical care who have not had prior prostate cancer treatment. A time-tradeoff method was used. Utility for incisional hernia was derived from Rognoni et al.'s 2020 study of 75 hernia registry patients[181] and measured using EQ-5D prior to surgical repair. All other utilities were taken from Stevenson et al.'s 2014 retrospective cohort study consisting of 119 patients with bladder cancer[177]. Measurement methods used in this study were heterogenous[188] and included the EQ-5D, the Health and Limitations Index and expert elicitation. However, all utility values were presented on a scale of 0 to 1. To standardize heterogenous methodology and patient populations, all utilities following complications were converted to a disutility[189] which was subtracted from the baseline utility of no complications from van der Brink et al[179]. This ensured that all health states had the same baseline but varied by the disutility caused by the complication in question. The exception was the utility of death, which is given a reference value of zero in the literature[147,148]. Utility values were made probabilistic using the gamma distribution[187], which is calculated using the standard deviation (SD). SD from Rognoni et al. was used for incisional hernia but empiric SDs were used for all other utilities as none of the other studies provided SDs. Empiric SDs used in our model is found in Appendix 4.3.

To calculate QALYs, each post-intervention state was assigned a duration. For all terminal health states other than death, a median overall survival of 76 months was used. This is based on Cheung et al.'s 2009 cohort study on outcomes after stage II and III rectal cancer[182], where patients who received adjuvant chemotherapy within three months had a median overall survival of 76 months. A normal distribution was used to derive the probabilistic value of median overall survival[187]. The SD required for this distribution was empirically decided as one year since an SD was not provided by Cheung et al. An empiric maximum life expectancy of 20 years after resection was used.

Costs

Cost estimates were derived from the robotic medical device company servicing Alberta, Minogue Medical, from Alberta Health Services (AHS), from the Alberta Medical Association and from the Canadian Institute for Health Information (CIHI) (Table 4.1). Costs of operating room (OR) time were calculated by multiplying OR time in minutes by the mean cost of a minute of OR time. Costs of the index admission and any non-operative re-admissions were calculated by multiplying the mean length of stay (LOS) in days by the cost of a day on the surgical ward.

Mean OR time and LOS for RACS and LACS were estimated using a RACS database based in Edmonton, Alberta. This database was established at the Alberta RACS program's inception and include cases of RACS and LACS LAR with DLI. OR time and LOS for RACS and LACS were calculated using 46 RACS and 26 LACS cases, respectively. OR time and LOS for converted cases were derived from the open rectal cancer cohort of a 2016 Canadian study comparing RACS, LACS and open rectal cancer resection[19]. However, converted surgeries typically take longer to complete than open surgery due to time required for the MIS attempt followed by abortion and conversion. Thus, the open OR time from Ramji et al. was multiplied by a factor of 1.33 to represent a 30% increase in OR time when an MIS case is converted. This factor was empirically decided by study authors after consulting a review of 15 studies reporting on operating time of converted procedures and laparoscopic procedures[153].

The per minute cost of OR time and per day cost of LOS were derived from micro-costing data of 15 robotic rectal cancer cases from the Edmonton database. Since OR time, LOS and cost per time unit directly impact costs of the index operation and inpatient stay, these inputs were made probabilistic to propagate uncertainty in these parameters. A normal distribution was used for OR time because it was able to generate values close to the mean whereas the gamma distribution resulted in unrealistic OR durations such as 3000 minutes/case. A gamma distribution for LOS was performed using standard errors (SEs). RACS and LACS SEs were taken from the Edmonton RACS database and calculated using Stata 15 (StataCorp, Texas). SE for converted procedures was empirically derived because Ramji et al. did not provide SEs or

SDs. Other cost parameters such as equipment purchase cost had no uncertainty, thus no probabilistic distributions were assigned. The overall per case cost of a LAR with DLI considers equipment amortization over nine years, as this is the average lifespan of the da Vinci robot.

Appendix 4.2. Model assumptions

Table S1. Detailed list of model assumptions

Operative procedure
Converted procedures are assumed to be midline incisions, since the incidence of incisional hernia in muscle-splitting incisions (e.g. Pfannenstiel) are much lower and more simliar to minimally invasive incisional hernia rates. (Harr et al. 2016)
When a procedure does not remain totally laparoscopic or robotic, it will be assumed to be converted to open via midline incision. Other options e.g. laparoscopic-assisted using smaller incision than typical open case to do lower rectal dissection will not be considered in base case. These "partially" open cases will incur similar costs as "fully" open but may have lower morbidity because the size of the incision may be smaller.
Costs of the open portion of a converted case are assumed to be the same as in open cases.
When conversions are made, cost of procedure includes equipment and service costs of both the minimally invasive and open approaches since both types of instruments would have been used. In addition, if converted from robotic approach, the cost of robot consummables will also be included because these instruments are opened from the beginning of a case. In contrast, disposable costs of the laparoscopic approach will not be included because these costs are related to the anastomosis (staplers), which will only be done using an open approach in converted cases.
OR time of converted procedures will be 1.33 times that of open procedures; the arbitrary addition of 30% of base open time accounts for the fact that it takes time to for the surgeon to "struggle" minimally invasively, abort and re-orient once the procedure is converted.
Outcomes of converted procedures are the same as open procedures.

Complications overall
Early complications are mutually exclusive whereas patients may have multiple late complications simultaneously.
Except for death within 30 days postoperatively, no patients required ICU stay, which has different costs than ward stays.
Those who died postoperatively incur the costs of 3 nights of ICU stay (assume relatively brief because early deaths are due to cardiovascular complications e.g. massive PE, or delayed diagnosis of sepsis, all of which are rapidly progressive to death).
If patients did not have any postoperative complications within 30 days of surgery, they will survive any complications thereafter.
Death as an early postoperative complication is assumed to occur within 30 days postop and will accrue no QALYs given negligible time spent in the postoperative health state.
All patients will receive a temporary diverting ileostomy reversed within 1 year, thus they will be at risk of early stoma complications but not late stoma complications given the option of early reversal.

Early complications
Ileus results in costs of 5 additional LOS days and its utility lasts 7 days, following which quality of life returns to the routine postoperative state (no immediate complications) for 3 weeks then to baseline (aka no complications).
Assume wound infections require 3 additional LOS days followed by home care for 2 weeks. Home care costs CAN $500 (assuming nursing salary of $40/hour for 10 hours over 2 weeks, and $100 of wound supplies). Utility of wound infections last 4 weeks then quality of life returns to baseline (aka no complications).
Abscess results in costs of 5 additional LOS days. Utility of abscess lasts 1 month following which quality of life returns to baseline.
Early stoma complications are high output stoma that resolve with conservative management (does not need re-operation), thus incur costs of 5 additional LOS days. Stoma complication utility lasts 1 month following which utility returns to baseline (aka no complications).

Assume leaks are managed operatively because the model assumes everyone was diverted, so a leak that occurs despite diversion must be clinically significant and require operative exploration/washout with attendant costs. Utility reduction lasts 1 month following which utility returns to baseline (aka no complications).
Assume "other" early complications require on average 3 days of additional LOS during index admission. Utility reduction lasts 1 week and returns to baseline. Utility value is the same as that of urinary tract infections.

Late complications
Bowel, bladder and sexual dysfunction are life-long thus disutilities from these complications will last the entire time horizon.
Utility of bowel dysfunction is equated to that of major LARS (low anterior resection syndrome); utility of bladder dysfunction is equated to that of incontinence; utility of sexual dysfunction is equated to that of impotence.
Assume complications of bowel, sexual and bladder dysfunction will result in the cost of 4 physician visits at general surgery rates as per the Alberta physician fee guide (accessed June 2021) and will be managed conservatively (1 initial consultation and 3 follow-ups).
Incisional hernia will result in an elective repair; utility reduction lasts 1 year following which patients receive repair with no complications in year 2 and utility returns to baseline (year 2 costs will be the discounted costs of elective repair; year 2 utility will be the discounted baseline utility, aka utility of no complications).
Small bowel obstruction (SBO) will result in an admission to hospital with conservative management only, lasting 5 days of admission (no Alberta-specific SBO costing data available). Reduction in utility lasts 2 weeks, following which utility returns to baseline. Only 1 episode of SBO per patient will occur in this model (no recurrences). SBO will occur in year 2 so year 2 costs will be that of discounted SBO costs only. Year 1 utility is baseline and year 2 utility includes the discounted SBO utility.
Rectovaginal/rectovesical fistulas require 3 physician visits at general surgery rates but no other costs. Reduction in utility will be permanent. Physician visits will occur in year 2, thus year 2 costs will be that of discounted physician visit fees. Assume probability, utility and costs of rectovaginal fistulas because rectovesical fistulas are very rare (literature comprised largely of case reports) thus negligible.

Surveillance, recurrence and survival
Surveillance program and costs of surveillance will be identical in all patients in the model, therefore are not included.
Risk of recurrence and mortality will not differ between laparoscopic and robotic patients as there are no evidence that short-term oncologic outcomes are different.
Recurrence affects survival, thus risk of recurrence will be considered accounted for in the estimation of life expectancy and was not modelled into the tree for simplicity and to avoid "bushiness" of the decision tree.

Appendix 4.3. List of empiric standard deviations

Table S2. List of empiric standard deviations (SD) used

Utility variable	Mean utility	Distribution used	Source	Empiric SD	Sample size from study
Within 1 month postop	0.77	Gamma	[179]	0.12	1530
Ileus	0.65	Gamma	[177]	0.05	119
Wound infection	0.699	Gamma	[178]	0.1	31
Abscess	0.64	Gamma	[177]	0.01	119
Stoma complication	0.73	Gamma	[178]	0.2	82
Anastomotic leak	0.64	Gamma	[177]	0.01	119
Early "other"	0.73	Gamma	[177]	0.05	119
No complications at all	0.86	Gamma	[179]	0.01	1530
Bowel dysfunction	0.585	Gamma	[178]	0.2	196
Sexual dysfunction	0.86	Gamma	[180]	0.5	168
Bladder dysfunction	0.74	Gamma	[180]	0.2	168
Incisional hernia	0.768	Gamma	[181]	N/A*	75
Small bowel obstruction	0.65	Gamma	[177]	0.01	119
Rectovaginal/ rectovesical fistula	0.68	Gamma	[177`]	0.2	119

* Rognoni et al. reported a standard error for the mean utility value of incisional hernia thus no empiric standard deviation (SD) assumption was required.

Appendix 4.4. CHEERS 2022 Checklist

Topic	No.	Item	Location where item is reported
Title			
	1	Identify the study as an economic evaluation and specify the interventions being compared.	64
Abstract			
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	65-66
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	67-68
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	N/A*
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	68
Setting and location	6	Provide relevant contextual information that may influence findings.	68
Comparators	7	Describe the interventions or strategies being compared and why chosen.	68
Perspective	8	State the perspective(s) adopted by the study and why chosen.	68
Time horizon	9	State the time horizon for the study and why appropriate.	68
Discount rate	10	Report the discount rate(s) and reason chosen.	68

Topic	No.	Item	Location where item is reported
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	68
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	69
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	69-71
Measurement and valuation of resources and costs	14	Describe how costs were valued.	69
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	69
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	69-70
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	70-71
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	70-71
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	71
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	71
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	N/A**
Results			

Topic	No.	Item	Location where item is reported
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	78-82, 89-92, 95
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	72-73
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	72-73
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	N/A**
Discussion			
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	74-76
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	77
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	77

From: Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report

of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022;25. doi:10.1016/j.jval.2021.10.008

* A health economic analysis plan was less applicable as this was not a trial-based analysis. In addition, many of the elements suggested in a health economic analysis plan overlap with those required in CHEERS 2022[190]. Therefore, a health economic analysis plan was not developed separately.

** Patient and stakeholders were not involved in the design of this analysis.

Appendix 4.5. Results of scenario analysis 1, ROLARR LOS and OR time

Table S3. Scenario 1 disaggregated results

	Total cost (CAN$)	Total effectiveness (QALY)	ICER (CAN$/QALY)
Robotic	32,690	4.69	60,412
Laparoscopic	29,925	4.64	-
Incremental	2,765	0.046	-

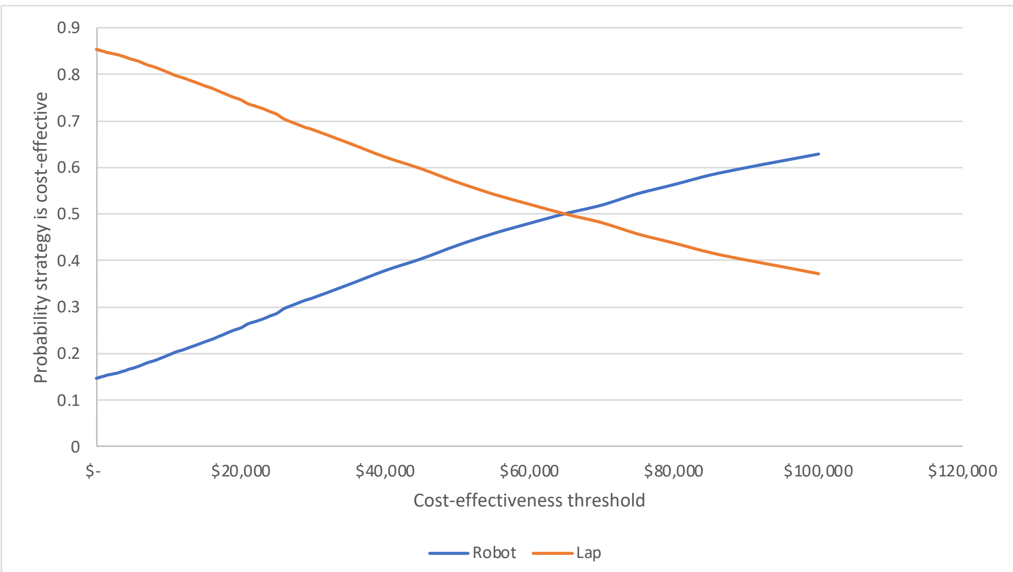

Figure S1. Scenario 1 CEAC

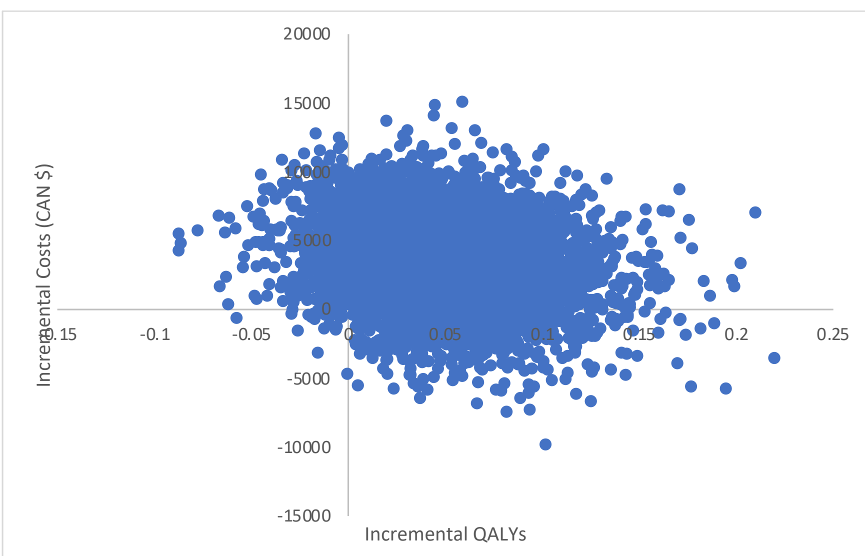

Figure S2. Scenario 1 ICER scatterplot

Appendix 4.6. Results of scenario analysis 2, colorectal program bearing all upfront RACS costs

Table S4. Scenario 2 disaggregated results

	Total cost (CAN$)	Total effectiveness (QALY)	ICER (CAN$/QALY)
Robotic	38,574	4.69	195,498
Laparoscopic	29,626	4.64	-
Incremental	8,943	0.046	-

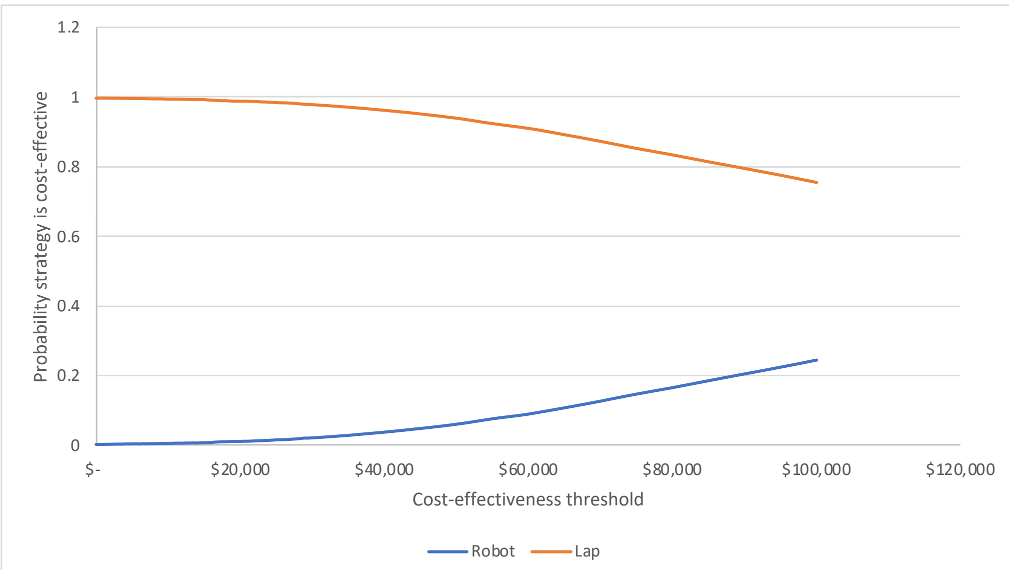

Figure S3. Scenario 2 CEAC

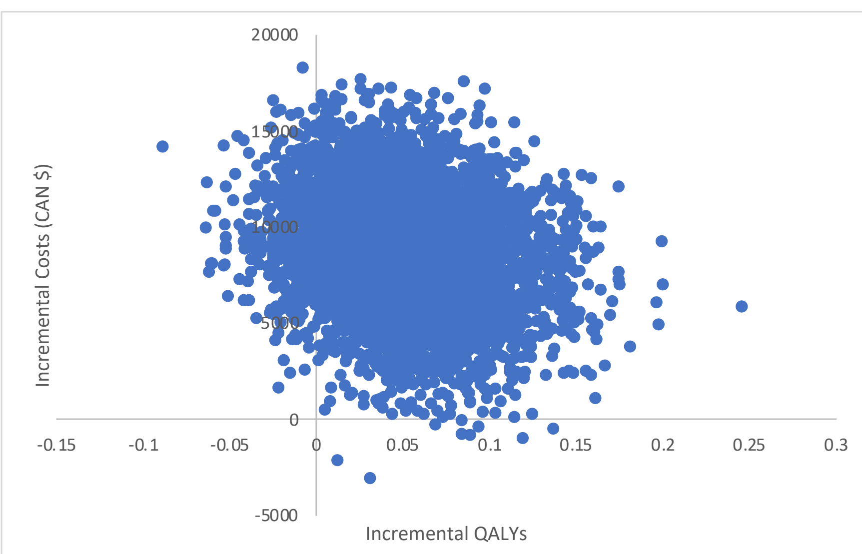

Figure S4. Scenario 2 ICER scatterplot

Appendix 4.7. Results of scenario analysis 3, da Vinci Xi costs

Table S5. Scenario 3 disaggregated results

	Total cost (CAN$)	Total effectiveness (QALY)	ICER (CAN$/QALY)
Robotic	31,597	4.69	43,056
Laparoscopic	29,626	4.64	-
Incremental	1,971	0.046	-

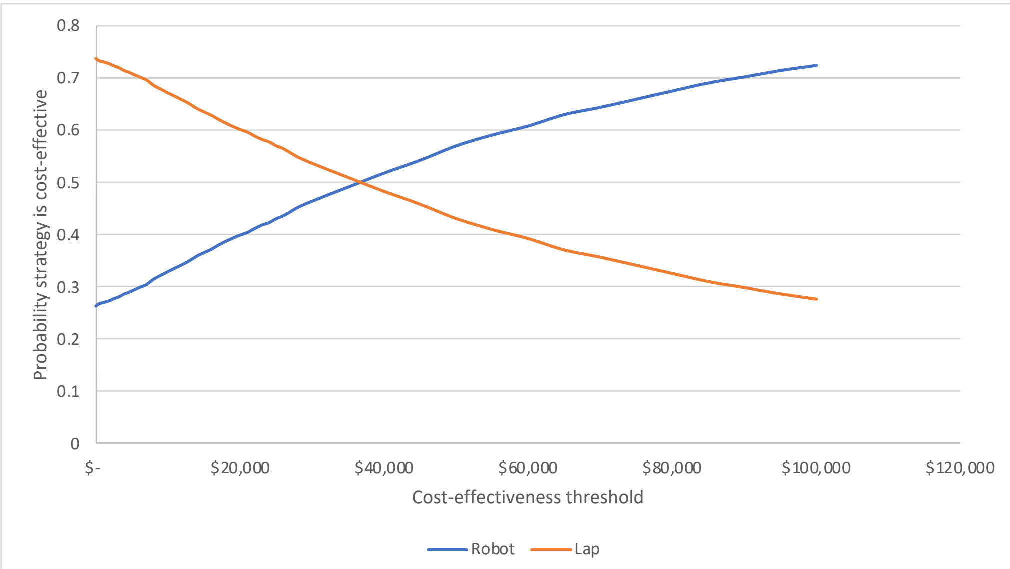

Figure S4. Scenario 3 CEAC

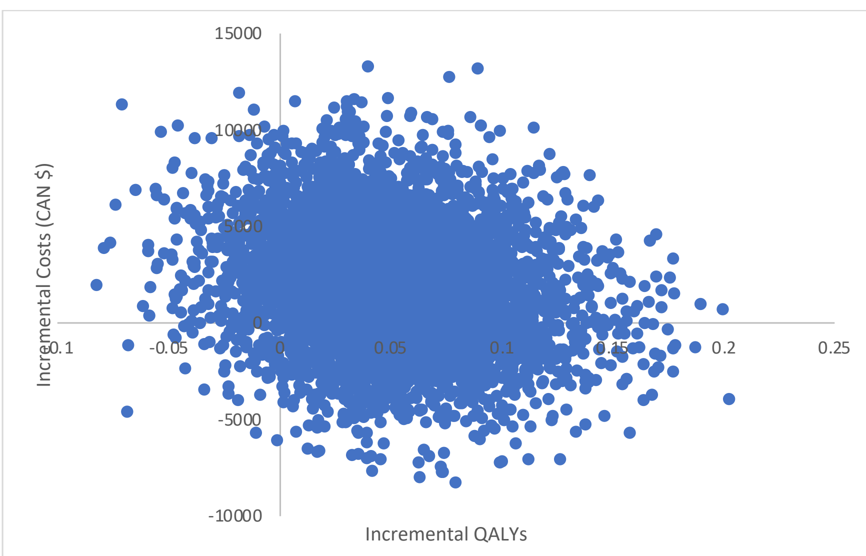

Figure S5. Scenario 3 ICER scatterplot

CHAPTER 5. Synthesis and Overriding Conclusions

5.1. Synthesis of Findings

As technology advances, newer interventions in surgical care have emerged. Although the driver to innovation is often increasing clinical benefits, such interventions may also come at a higher cost. However, the measurement of clinical effectiveness and cost in isolation is unable to assess the true value of a new intervention. Thus, economic evaluations are paramount in health technology assessment and to help stakeholders make decisions regarding adoption and funding of new technologies.

In Chapter 1, we outline three objectives central to our work. In Chapter 2, we report on short-term clinicopathologic outcomes and surgeon learning curve to explore Canadian outcomes associated with RACS rectal and rectosigmoid cancer resection. In Chapter 3, we systematically review existing literature on RACS vs LACS cost-effectiveness to guide our subsequent economic evaluation. In Chapter 4, we perform a cost-utility analysis comparing RACS vs LACS rectal cancer resection to improve upon limited existing literature.

5.1.1. Clinicopathologic outcomes and surgeon learning curve in an Alberta RACS program

Using data from Alberta's first RACS rectal cancer program, we were able to study the first 67 cases of RACS rectal and rectosigmoid cancer resection performed in western Canada. Despite surgeons being robotic novices at the start of this series, the 30-day clinical outcomes are comparable to previous Canadian data and to ROLARR, the largest existing international RCT. With regards to oncologic quality of resection, the short-term pathologic outcomes are also comparable to these previous studies. In addition, mean operating time decreased significantly from the first 10 cases to the last 10 cases despite increased comorbidities and a larger proportion of APRs in the last 10 cases. For other Canadian centres looking to adopt RACS, these findings suggest RACS rectal and rectosigmoid cancer resection is safe and feasible. Given the cost concerns with the robotic approach, the significant decrease in operating time suggests that cost reduction is realistic over time as surgeons become more facile with this approach.

5.1.2. Review of literature on economic evaluations examining RACS vs LACS cost-effectiveness

Economic evaluation is becoming increasingly prevalent in health technology assessment. However, evaluations of RACS vs LACS cost-effectiveness remain limited. To study current evidence and summarize existing findings, we systematically reviewed the literature and found four cost-utility analyses comparing RACS and LACS. Two studies were trial-based and performed by a Spanish group, while the other two studies were model-based and produced by a US group. The Spanish studies found RACS to be cost-effective compared to LACS whereas the US studies did not. Significant inter-study heterogeneity such as differing methodology and data sources may have contributed to these different conclusions. Although the cost-effectiveness of RACS compared to LACS is unclear given the limited number of economic evaluations identified and their contradictory conclusions, this review identified the need for additional economic evaluations and highlighted the nuances of interpretation to clinical audiences.

5.1.3. The cost-utility of RACS vs LACS in rectal cancer resection

Having identified a paucity of economic evaluations comparing RACS vs LACS and a lack of any such evaluations in a Canadian context, we performed a model-based cost-utility analysis focusing on rectal cancer resection. Compared to existing literature, we utilized a comprehensive lifetime time horizon and built a more inclusive decision tree to model complications after rectal cancer resection. We found that RACS is cost-effective compared to LACS at a cost-effectiveness threshold of CAN $100,000/QALY and remained so when inputs from a larger trial such as ROLARR was used and when the higher costs of the *da Vinci* Xi was adopted. However, RACS was no longer cost-effective compared to LACS when robotic volumes decreased to one quarter of our base case volume. Such findings suggest that implementation of RACS rectal cancer programs should be considered in the Canadian setting assuming high robotic volumes, which help to contain costs.

5.2. Significance of research findings

Given that RACS and LACS achieve similar oncologic outcomes in rectal cancer but that RACS may provide better clinical outcomes, RACS has the potential to replace LACS as the minimally invasive surgical approach of choice. The significance of our study is that it not only informs the cost-effectiveness of RACS vs LACS in rectal cancer but supports this finding with Canadian outcome data and a thorough review of the economic literature to date.

Our research demonstrates that RACS rectal cancer resection is cost-effective compared to LACS at a Canadian cost-effectiveness threshold when modeled after an existing RACS program in Edmonton, Alberta. This provides valuable information to Canadian decision-makers because we included costs and clinical parameters specific to our healthcare setting. Also, we thoroughly considered costs that the healthcare system would be responsible for. For example, most robots used in Canadian colorectal surgery were purchased by hospital foundations through private donations and did not require public healthcare funding in its start-up costs. However, if RACS implementation were to be more widely expanded, this is not a sustainable funding model. Our analysis included the significant upfront costs for maximal informativeness and relevancy to decision-makers considering wider RACS implementation in Canada.

On an international level, our cost-utility analysis constitutes the second-ever rectal cancer-specific economic evaluation on RACS vs LACS. As more economic evaluations on this subject emerge, our decision model and methodology have the potential to guide future evaluations, as previous analyses have guided ours. Although our results may be less applicable to non-Canadian jurisdictions, they may nonetheless serve as a reference for decision-making elsewhere in the world.

Our findings of comparable clinicopathologic outcomes between Canadian and international RACS rectal and rectosigmoid cancer resection further support wider Canadian implementation of robotic technology. The feasibility and safety demonstrated by established programs is a strong example of the viability of RACS in our healthcare setting. Our outcome results also serve as a benchmark for future Canadian programs looking to improve parameters such as complication rates, length of hospital stay and operating time.

Lastly, the significance of our systematic review is two-fold. Firstly, it is the only systematic review summarizing economic evaluations on RACS vs LACS, thus offering a foray into current evidence on cost-effectiveness between these interventions. Secondly, it was able to show a paucity of studies for a technology that is increasingly popularized, thus indicating a clear gap in knowledge to be filled by future research. By way of evaluating existing studies, it also provides an educational opportunity to clinical audiences with regards to critical appraisal of economic evaluations.

5.3. Research implications

If wider RACS implementation is adopted by decision-makers, several implications should be considered. On a patient level, wider adoption means more equitable access to robotic surgical care, as existing Canadian robotic programs are limited to major academic centres[191]. On a surgeon level, the colorectal surgery practice landscape would change in terms of surgeon robotic re-training during practice and patient counselling. Surgical education will also change as the next generation of Canadian general and colorectal surgeons gain robotic experience during training. Such exposure is not currently available in Canada[192]. Early exposure to RACS could result in shorter OR time and improved outcomes, which may in turn affect future cost-effectiveness, funding decisions and overall quality of rectal cancer care[44,193,194]. On a decision-maker level, our findings have the potential to affect resource allocation. Since our cost-utility analysis shows there is a probability of cost savings in RACS compared to LACS rectal resection, any additional costs saved may be re-invested to improve robotic programs or re-directed to other areas of need in healthcare[195].

5.4. Challenges and limitations

No body of work is without limitations and ours is no exception. Many of our limitations have been addressed in the manuscript chapters. However, one limitation that deserves further elaboration is perhaps the lack of a comparative group in Chapter 2, our study on short-term clinicopathologic outcomes after robotic rectosigmoid and rectal resection.

Our original plan was to compare this study's robotic cohort with a propensity-matched laparoscopic cohort undergoing rectosigmoid and rectal cancer resection. However, a laparoscopic cohort from the same period as the robotic cohort was not available due to the robotic approach replacing laparoscopy for elective MIS procedures. We thus attempted to use a historical cohort by querying data from the Alberta provincial ERAS database, which tracks elective MIS colorectal resections starting in 2014 and could help us identify eligible MIS patients on whom we would perform retrospective chart review to collect baseline and outcome information. While working with the ERAS database, we discovered that there were errors in procedure coding in this database. Low anterior resection, which is an appropriate oncologic resection for rectosigmoid and rectal cancers, was often coded as anterior resection, which means removal of the sigmoid colon. This meant we had no easy way of identifying eligible patients unless we reviewed charts for all patients coded as “anterior resection” and “low anterior resection” by the ERAS database. This would have been a data collection process that required significant time investment. At the same time, we realized that there were not enough historical laparoscopic procedures from the UAH to perform propensity matching. We had pre-emptively done propensity matching with the help of a statistician based on what was coded as “anterior resection” and “low anterior resection” in the ERAS database. However, even when caliper-based matching was used to maximize comparisons, there were not enough laparoscopic matches for the number of robotic cases we had. We suspect the reasons for this inadequate number are two-fold: 1) prior to 2017, there was only one MIS-trained colorectal surgeon at UAH performing laparoscopic colorectal surgery, compared to multiple non-MIS trained surgeons who preferred the open approach. Thus, laparoscopy represented a small proportion of rectal cancer cases performed; 2) many of the laparoscopic cases found in the UAH ERAS database were converted, whereby the pelvic dissection was performed open.

We therefore looked to acquiring data from other sites in Edmonton that performed laparoscopic colorectal resections. The site that had a large enough laparoscopic cohort and that would be likely to provide the number of laparoscopic matches we needed was the Misericordia Hospital. The logistical challenge at this point was that the Misericordia Hospital is governed under Covenant Health instead of Alberta Health Services (which governs the UAH). This means that any chart review using Misericordia Hospital data will require separate ethics, operational and administrative approvals. Once this was done, the large volume of chart reviews necessary to identify the correct patients would still apply due to ERAS mis-coding.

The additional time required for this process was not compatible with the timeline of this thesis. We still intend to follow through with the above process to obtain a laparoscopic comparative cohort and allow our findings in robotic outcomes to be more informative. However, the data is anticipated to be available after the completion of this thesis project. The complex interaction between databases, surgeon practice patterns, ethics and operational logistics, health authorities, and research timelines is a representative example of real-life challenges and barriers in scientific work.

5.5. Gaps in research and future directions

Areas of uncertainty remain with regards to RACS outcomes and cost-effectiveness. Although observational studies comparing RACS vs LACS would be a useful starting point in the limited Canadian literature, more randomized controlled trials comparing the clinical benefits of these approaches are needed on an international level. Although ROLARR has been informative, its findings of no statistically significant difference between RACS and LACS continue to be contested by meta-analyses summarizing the evidence.

More economic evaluations on RACS vs LACS cost-effectiveness are also needed. Although our cost-utility analysis adds to the literature, there is limited generalizability of economic evaluations to jurisdictions beyond that described in the decision problem. Therefore, more studies from different jurisdictions are required to best determine the value of RACS compared to LACS.

If more model-based economic evaluations were to be performed, better model inputs are required. This applies especially to higher quality, standardized utility values. Studies eliciting health state preference are difficult to perform given the inherent heterogeneity in study population, illness context and measurement methods[196,197]. This leads to difficulty standardizing values when more than one source in the literature is used. Ideally, jurisdiction-specific utility values should be studied for different health states. These values should also be updated as valuations could change over time depending on changes in society's perception and prioritization of health and wellness.

5.6. Final Comments

New technologies in healthcare must be assessed for both costs and effectiveness and decision-making should occur in joint consideration of both. This means that robust clinical outcome data is necessary for the new intervention and its comparator. As well, full economic evaluations are paramount as they are the only type of analysis able to jointly evaluate costs and effectiveness. The research we have completed are starting points for such assessments but nonetheless suggest a cost-effectiveness benefit to RACS compared to LACS. We hope our findings inform subsequent research and that the summative evidence over time will positively influence healthcare delivery.

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