INDOCYANINE GREEN ANGIOGRAPHY (ICGA) AND NOVADAQ SPY IMAGING SYSTEM IN COLORECTAL SURGERIES IN BRITISH COLUMBIA

Evaluation of safety, effectiveness and cost-effectiveness of performing intraoperative Indocyanine Green Angiography (ICGA) for anastomosis assessment in colorectal surgeries (open or laparoscopic) in British Columbia, and budget impact.

HEALTH TECHNOLOGY ASSESSMENT REPORT

A report for the BC Health Technology Review Office, on behalf of health authorities and the Ministry of Health. Vancouver. July 2017.

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The views expressed herein are those of the authors and do not necessarily represent the views or official policy of the Government of British Columbia, British Columbia health authorities, or any other agency.

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List of Abbreviations

ASA	American Society of Anesthesiology physical status
AV	Anal verge
BC	British Columbia
BCCSSS	BC Clinical and Support Services Society
BMI	Body mass index
CADTH	Canadian Agency for Drugs and Technologies in Health
CEAC	Cost-effectiveness acceptability curve
CRT	Chemoradiotherapy
CT	Computed tomography
DAD	Discharge Abstract Database
FDA	United States Food and Drug Administration
HTA	Health technology assessment
HTR	Health Technology Review
ICD	International Classification of Diseases
ICER	Incremental cost-effectiveness ratio
ICG	Indocyanine green
ICGA	Indocyanine Green Angiography
IHCC	Individual hospital capital cost
ISR	Intersphincteric resection
LAR	Lower anterior resection
LFA	Laser fluorescence angiography
MSP	Medical Services Plan
NIR	Near infrared
NIRF	Near infrared fluorescence
NNT	Number needed to treat
NSAID	Nonsteroidal anti-inflammatory drug
OR	Odds ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	Quality-adjusted life years
RCT	Randomized controlled trials
RIW	Resource intensity weights
RN	Registered Nurse
RR	Risk ratio
SD	Standard deviation
SLN	Sentinel lymph node
WTP	Willingness-to-pay

Executive Summary

Indocyanine green angiography (ICGA) is a tool for intraoperative perfusion assessment, useful in many different surgeries, with a number of different devices on the market.

The purpose of this HTA is to summarize the available evidence on ICGA for anastomosis assessment in colorectal surgeries (open or laparoscopic) in British Columbia (BC) and to perform a cost-effectiveness and budget impact analysis of ICGA versus the standard of care in BC.

Across Canada, ICGA has been applied in a few hospitals in neurosurgery, reconstructive surgeries (breast, fingers, and lower extremities), colorectal surgeries, hernia repairs and lymphedema surgeries with no known written policy or guidance. No MSP fee to perform ICGA has been reported, and some instances of ICG dye shortage have been an issue in some sites.

In colorectal resection surgeries, ICGA is a tool for anastomotic assessment with the main goal of preventing leakage. Anastomotic leak is a serious postoperative adverse event that can increase mortality, morbidity, health care resource utilization and worsen quality of life of patients, with long term implications. Currently, there are no guidelines for anastomosis assessment and it is mostly based on visual clinical judgment.

No literature on the patient experience of using ICGA was found. Research on patient experiences after colorectal surgery due to colorectal cancer report the core outcome sets for those patients include oncologic outcomes, operative outcomes, and quality of life. Patients reported gaps in the information provided before surgery about surgical outcomes and negative health effects of the surgery. Surgeons believe ICGA could also be useful for research purposes and they support the training of new cohorts of surgeons.

In the current evidence on the clinical effectiveness of ICGA (four comparative nonrandomized studies and one single-arm study), anastomotic leakage was the most commonly reported outcome. The pooled estimated from those studies suggested that ICGA significantly reduced the risk of anastomotic leakage (risk ratio 0.55 [95% CI 0.35, 0.86], absolute risk reduction of 4%, and number needed to treat was 25). Evidence for other outcomes was poor. Due to the low quality of evidence, high risk of selection bias and lack of blinding it was not

possible to rule out confounding factors. There is no evidence available to compare the Spy imaging systems to the other near-infrared fluorescence detection devices.

In a cost-effectiveness analysis tailored for British Columbia, the best available evidence suggests that the use of intraoperative ICGA in colorectal surgeries for bowel perfusion assessment is likely cost-saving or cost-effective at conventional willingness-to-pay levels compared with the current standard of care (visual clinical judgment) in most estimated scenarios and across most hospitals in the Province. The estimates were most sensitive to four factors: leak rates for the local surgery teams, the effect of the technology in lowering leak rates, the incremental cost of leaks, and the capital cost per surgery (directly affected by the hospital-specific volume of surgery). There is a moderate degree of uncertainty in the model since the effectiveness estimates were generated from observational studies.

In the budget impact evaluation, the BC health care system should expect a progressive increase in the number of primary colorectal surgeries due to population growth and aging. Policy changes that lead to decreased complications from these surgeries can substantially reduce costs and mortality. Implementing intraoperative ICGA can be cost-saving assuming the reallocation of resources from complications avoided. If implemented in high-volume hospitals, the technology can reduce mortality by 32 percent, and the incremental costs with the new technology ($85.9 million over 20 years) can be offset. Implementing ICGA in every hospital in BC would have a higher incremental cost for the new technology ($144.9 million), which could still be offset by complications avoided. Due to efficiency aspects, the average capital cost of ICGA can range from $172 to $2,316 per surgery.

The main challenges for implementation are the capital costs and logistics for machine placement, cost of disposables, need for adequate infrastructure and logistics in the operating rooms, adequate supply of contrast, and potential adoption beyond colorectal surgeries. Adoption under controlled trial circumstances or monitored environment is recommended to confirm the cost-effectiveness.

Chapter 1 Background and Problem

1.1 Purpose of this health technology assessment (HTA)

The purpose of this HTA is to summarize the available evidence on indocyanine green angiography (ICGA) for anastomosis assessment in colorectal surgeries (open or laparoscopic) in British Columbia (BC) and to perform a cost-effectiveness and budget impact analysis of ICGA versus the standard of care in BC.

The report includes evidence on key stakeholders' perspectives, the efficacy, and safety of ICGA performed by the Spy Elite system or other devices, and the cost-effectiveness and budget impact of ICGA with Spy imaging system compared to clinical judgment/visual assessment.

The report also includes a summary of the volume of evidence about the intraoperative use of ICGA in other non-ophthalmologic procedures.

1.2 Policy question and research objectives

ICGA can be performed with different brands of devices. Some BC sites have been using Novadaq's Spy imaging system, routinely or on a trial basis, in indications other than neurosurgery.

At Fraser Health Authority, hospital foundations have purchased three devices for use in mastectomy and breast reconstruction surgery. Vancouver Coastal Health Authority and Vancouver Island Health Authority have expressed interest in acquiring similar devices. Surgeons at Vancouver Coastal Health and Fraser Health also have expressed interest in expanding the use of ICGA to other reconstructive surgeries and to colorectal surgeries. Cardiac surgeons and the endoscopy teams in Vancouver did not have a strong interest in adding ICGA into their practice.

Novadaq indicates that their intraoperative ICGA system (Spy) can be used in gastrointestinal surgeries, breast reconstructions, neurosurgeries, other reconstructive surgeries and sentinel lymph node (SLN) mapping. In the United States, the Spy imaging system is licensed for the surgeries listed above except SLN mapping (still off-label).

The government of BC has committed to support the province's technology sector through an array of actions under the 2016 BCTECH Strategy. This policy is relevant to our report because Novadaq, the manufacturer of the Spy Elite system, is located in Greater Vancouver.

The BC Ministry of Health aims to evaluate the impact of expanding the use of Spy imaging system into colorectal surgeries. Approximately 4,800 colorectal surgeries are performed in BC per year, mostly in patients who are 50 years of age and older. As such, the present HTA focuses on colorectal surgeries and their associated outcomes.

1.2.1 Primary policy question or decision problem to be answered by this HTA

- Is ICGA clinically effective for routine anastomosis assessment in colorectal surgeries to reduce complications? If yes, is the Spy imaging system cost-effective and what would be the budget implications of implementing this technology?

1.2.2 Primary research questions

- What is the burden of anastomosis complications for patients undergoing colorectal surgeries in BC?
- What are the patterns of care and service delivery capabilities in BC related to colorectal surgeries?
- How safe and effective is intraoperative ICGA compared to clinical judgment/visual assessment in colorectal surgeries?

- What is the evidence on the effectiveness of the Spy imaging systems in intraoperative ICGA compared to other devices?
- How cost-effective is intraoperative ICGA using the Spy imaging systems compared to clinical judgment/visual assessment in colorectal surgeries?
- What is the budget impact of providing intraoperative ICGA using the Spy imaging systems?

1.3 Background information

1.3.1 Description of condition, severity, and burden

An estimated 4,859 colorectal resections and colostomies were performed in BC in the fiscal year 2014/15 (1). Among these patients, based on the International Classification of Diseases (ICD) codes, colorectal neoplasm accounted for 67% of the cases; diverticulitis (17%) was the second most common cause. Most of the patients were 50 years and older (Table 1). The number of surgeries performed in each health authority can be found in Table 2.

In colorectal resection surgeries, the surgeon assesses anastomotic integrity by ensuring the intestinal lumen is patent and there is no mechanical disruption, bowel ischemia, or bleeding at the site. Anastomotic leak is a devastating complication that has a strong negative impact on immediate postoperative mortality and morbidity, overall survival, and the chance of a long, disease-free life (2). It is also associated with longer hospital stay and increased health care costs and resource utilization (3).

Table 1. Distribution of colorectal surgeries in BC by age group, 2014/2015

Age	%
< 20	0.45%
20–29	1.65%

30–39	2.96%
40–49	6.85%
50–59	16.86%
60–69	27.82%
70–79	26.84%
80 +	16.57%

Data source: DAD, 2014/15.

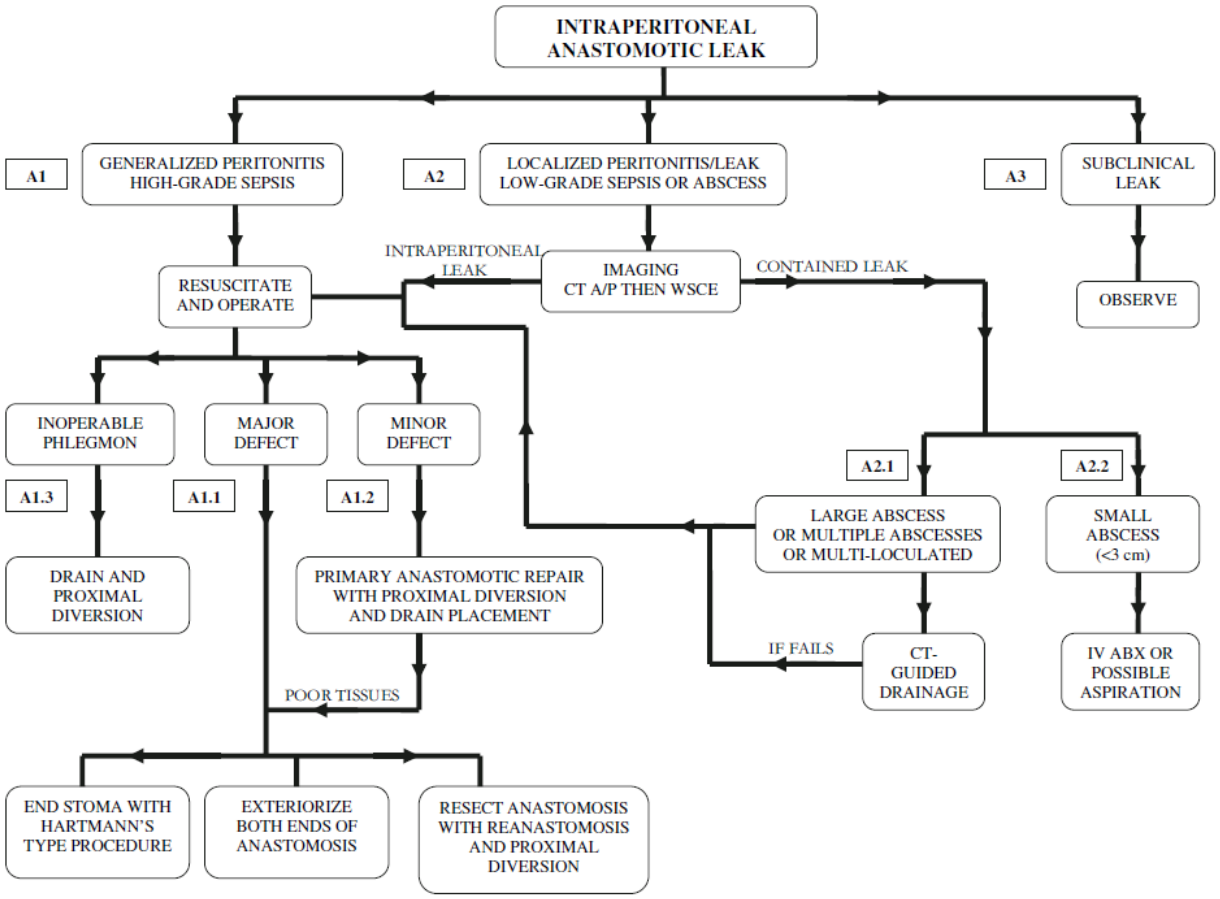
Table 2. Distribution of colorectal surgeries in BC by Health Authority, 2014/2015

Health Authority	Number of Surgeries	%
001 Interior	955	19.65%
002 Fraser	1392	28.65%
003 Vancouver Coastal	1313	27.02%
004 Vancouver Island	957	19.70%
005 Northern	242	4.98%
	4859	

Data source: DAD, 2014/15.

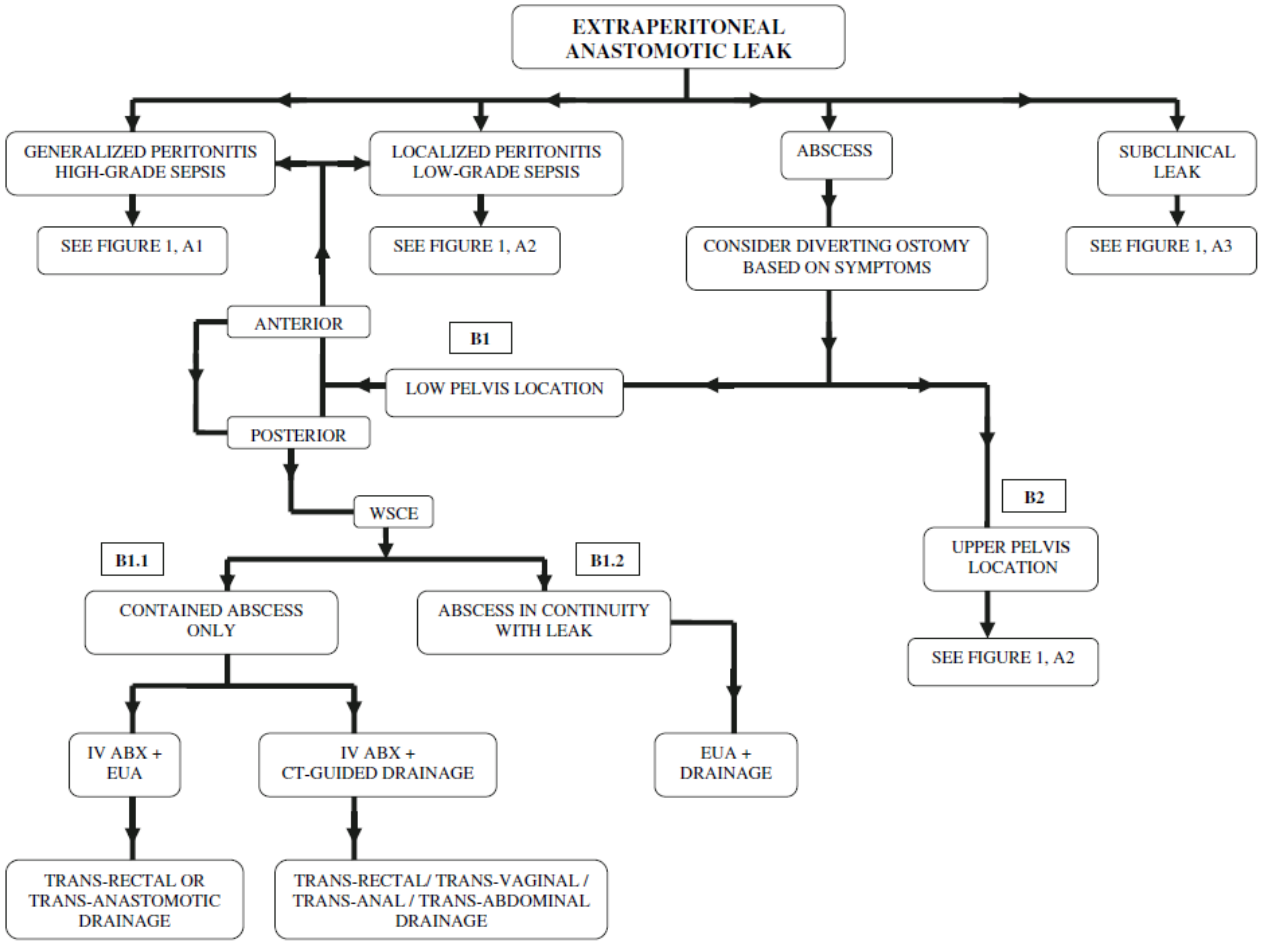
There is no clear definition for anastomotic leak, nor for their classification (e.g., subclinical/clinical, intraperitoneal/extraperitoneal) (3). In an attempt to standardize the management of anastomotic leaks, the International Anastomotic Leak Study Group published an algorithm based on intraperitoneal leaks (Figure 1), extraperitoneal leaks (Figure 2), and leaks in the presence of fecal diversion (Figure 3) (3, 4).

Figure 1. Recommendations for management of intraperitoneal anastomotic leak.



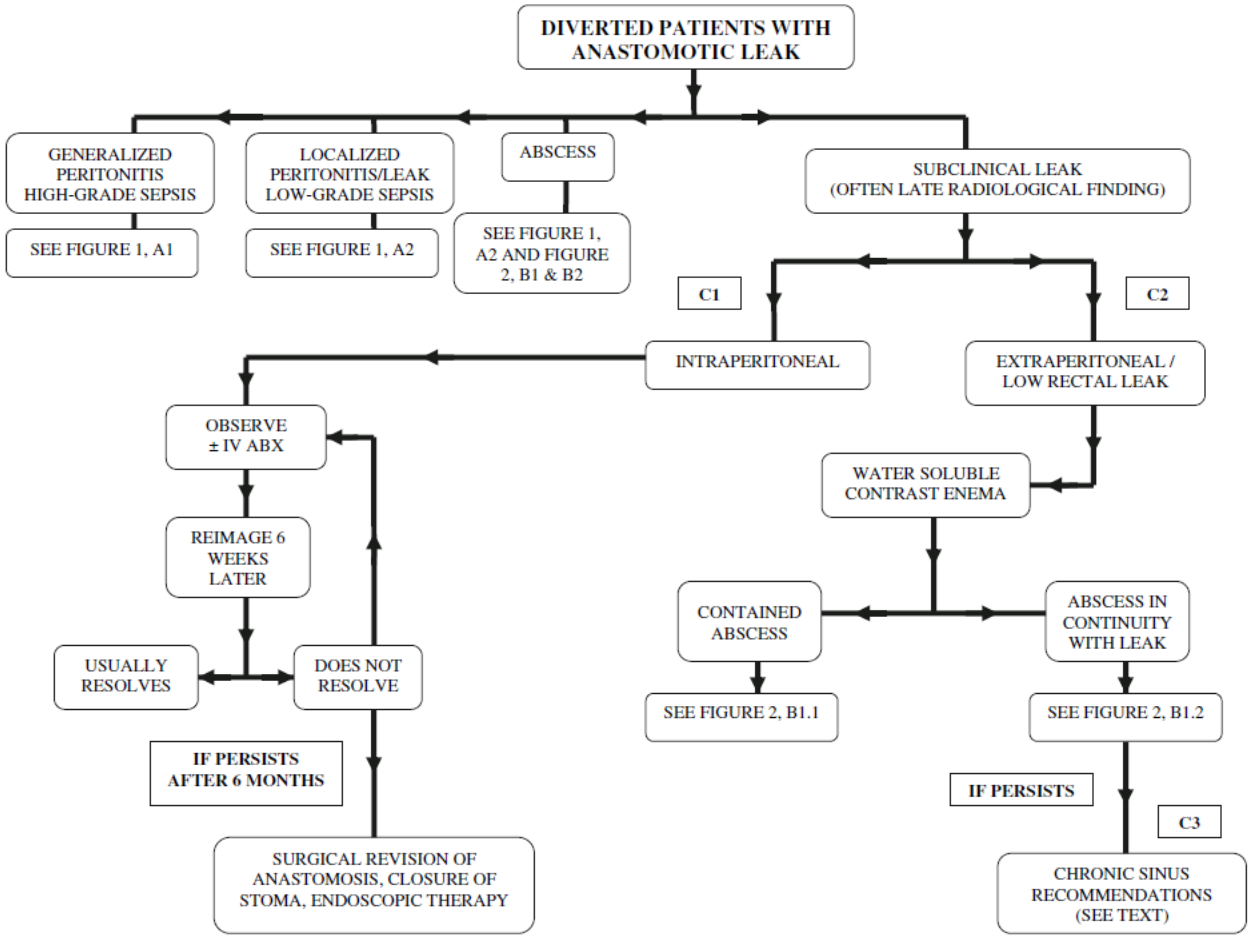
Note: A/P = abdomen and pelvis; CT = computerized tomography; IV ABX = intravenous antibiotics; WSCE = water-soluble contrast enema.

Figure 2. Recommendations for management of extraperitoneal anastomotic leak.



Note: EUA = examination under anesthesia; IV ABX = intravenous antibiotics; WSCE = water-soluble contrast enema.

Figure 3. Recommendations for management of intraperitoneal anastomotic leak in a patient who is already diverted (with a stoma).



Note: IV ABX=intravenous antibiotics.

Sepsis remains the main cause of morbidity and mortality associated with leak (5, 6). Early administration of antimicrobials is a hallmark for the medical management and stabilization of all patients with anastomotic leak to prevent sepsis (3). Patients with severe sepsis are at risk of developing septic shock, which has a high mortality rate. Timely and appropriate intervention is therefore imperative if a patient develops sepsis. Initial management should include the “sepsis six” care bundle: administer high-flow oxygen, take blood cultures, measure lactate and full blood count, measure urine output, administer broad-spectrum

antibiotics, and conduct an intravenous fluid challenge. Septic shock often requires treatment in the intensive care unit.(6)

Several intraoperative factors might influence the integrity of anastomoses, such as blood perfusion, treatment with steroids or COX-2 selective nonsteroidal anti-inflammatory drugs (NSAIDs), and technical failure. Perfusion is thought to be the most important factor (7).

In a 2012 Danish study, the leakage rate in colorectal surgeries was 15.6 percent (7). In a systematic review, cancer patients who experienced anastomotic leak had significantly higher risk of mortality and the risk of local cancer recurrence significantly increased from 10.1 percent to 17.5 percent (7). In BC, there is no official database for leakage rate in colorectal surgeries and the associated consequences. However, a sample analysis of 4,901 patients submitted to those surgeries showed that sepsis occurred in 3.6 percent of patients.

1.3.2 Available options

Selection of an optimal site for anastomosis is based on clinical judgment of indicators such as the color of the bowel wall, bleeding edges of resected margins, and palpable pulsations of mesenteric arteries (2). Currently, the most common methods to assess and quantify the perfusion of gastrointestinal anastomoses intraoperatively include visual evaluation under white light and testing of pulsatile bleeding in a vessel near the anastomosis (7). Other methods of anastomosis assessment include patency tests (air or fluid leakage), endoscopic visualization techniques, and microperfusion techniques (Doppler ultrasound, flowmetry, tonometry, fluorescence imaging, etc.) (2). The accuracy of clinical judgment depends heavily on the skill and experience of the surgeons, which can be subjective and highly variable.

Fluorescence imaging technologies such as ICGA can be a useful tool for perfusion assessment. Using ICGA rather than clinical judgment in intraoperative anastomosis assessment allows surgeons to more accurately identify the optimal site for anastomosis and perform corrections immediately (8). Indocyanine green (ICG) has been approved for intravenous use since 1956 (9). It is commonly used in retinal angiography, liver clearance test, and cardiac output monitoring. ICG has a short serum half-life and is eliminated by the liver. Due to the short half-life, it can be re-administered within a short time (10). ICGA can be a simple, more practical and economical alternative to other intraoperative monitoring technologies such as X-ray, CT, MRI, and PET.

1.3.3 Definition of technologies under assessment

ICGA is a relatively new technique based on the fluorescent property of ICG when exposed to near-infrared light. Other than colorectal surgery, ICGA has also been used in breast reconstruction. Evidence shows promising results in breast reconstruction but the quality of evidence is still poor, as concluded in a published review (11). This review included only one comparative study that showed ICGA reduced necrosis in autologous breast reconstruction (14% vs 22%) and prosthetic breast reconstruction (13% vs 23%). ICG is given as an intravenous bolus and does not leave the blood. The fluorescence intensity is correlated with tissue perfusion; bright fluorescence indicates good perfusion (7).

Special camera filters are needed to visualize and record the ICG fluorescence. Several ICG fluorescence imaging devices are available on the market (Table 3). Although the architecture can differ among devices, the core components are similar. These include the light source for exciting ICG, optical filters for separating emitted fluorescent signals from strong

back-scattered excitation light and ambient light signals, and an area detector for sensing the emitted fluorescent signals (Figure 4) (9).

The Spy imaging system and its robot-assisted surgery counterpart, Firefly™, use laser diodes as the light source. Laser diodes emit a focused beam of light that produces the greatest sensitivity by minimizing the back-scattered infrared light. The light source excites the ICG in the blood, and a detector picks up the fluorescence and presents it on a monitor (Figure 5).

The Spy imaging system uses ICG and laser technology to image blood supply at the microvascular level so that surgeons can assess perfusion in real time. A surgeon using the technology has equated it to "having X-ray vision." It also offers objective analysis toolkit software that predicts the potential for necrotic complications.

Figure 6 and Figure 7 are images produced by the Spy Elite system and show the alternatives for surgeons in different indications. For instance, in colorectal surgery, on the left is a visual assessment based on clinical judgment of the anastomosis perfusion, and on the right, visual assessment based on the images.

BC is particularly interested in the Spy imaging system manufactured by Novadaq and its variations (Spy Elite for open surgeries, Pinpoint for laparoscopic surgeries).

A refurbished Spy imaging system costs approximately $[redacted]; a brand-new system costs up to $[redacted] (2016 quote). Disposables for ICGA testing cost around $[redacted] per surgery. The device can easily be moved between operating rooms, but not between hospitals. The device is not complicated to use, but surgeons and surgical nurses do need some training.

Table 3. Summary of various ICG imaging devices

Device	Excitation source			Fluorescence collection				WD (cm)	FOV (cm^2)
	Source type	Wave-length	Fluence rate ($mWcm^{-2}$)	Camera type	Dynamic rate (bits)	Integration time (ms)	Collection wave-length		
FDPM imager	Laser	785 nm	<1.9	Intensified CCD	16	50-800	825-835 nm	<76.2	<900
Mini-FLARE™	LED	760 nm	7.7	CCD	12	0.1-800	800-848 nm	10-32	12x9
SPY	Laser	806 nm	31 (narrow) 4 (wide)	CCD	8	Real time	Centered at 830 nm	30	7.6x5 19x12.7
Photodynamic eye	LED	760 nm	4.0	CCD	8	NS	>820 nm	20	10x6.7
HyperEye Medical system	LED	760-780 nm	NS	CCD	NS	NS	800-850 nm	NS	NS
FLUOBEAM®	Laser	750 nm	5.0	CCD	8	1-1000	>800 nm	15-25	2.2x1.5 to 20x14
IC-View	Laser	780 nm	Incident power NS	CCD	NS	NS	NS	NS	NS
Visual Navigator	LED	740 nm	Incident power NS	CCD	NS	NS	Centered at 820 nm	NS	NS
The prototype surgical navigation system	LED	760 nm	Incident power NS	Electron multiplying CCD	16	Real time	810-870 nm	60	7.9x7.9 to 12.5x12.5
Leica FL800	Xenon	700-800 nm	NS	CCD	NS	NS	820-860 nm	NS	NS
INFRARED™ 800	Xenon	700-800 nm	NS	CCD	NS	NS	820-900 nm	NS	NS
FIREFLY™ for da Vinci®	Laser	806 nm	NS	CCD	NS	NS	NS	NS	NS
Laparoscopic near-infrared fluorescence system	Xenon	NS	NS	CCD	NS	NS	NS	NS	NS
Stryker InfraVision™	LED	NS	NS	NS	NS	NS	NS	NS	NS
IRIDIUM™	Laser	805 nm	NS	PHD	NS	Real time	825-850 nm	20-45	NS
ViTOM® II ICG	Xenon	805nm	NS	NS	NS	Real time	835nm	20-30	NS

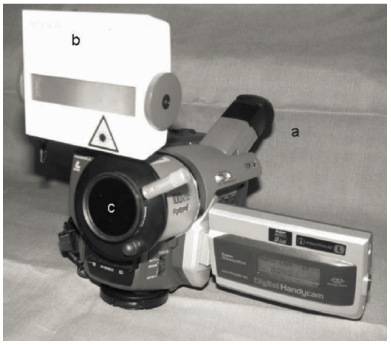
Source: adapted from Zhu et al. 2015 (9)

Note: CCD = charge-coupled devices; FOV = field of view; LED = light-emitting diode; NS = not specified; WD = working distance.

Note: Device manufacturers: FDPM imager (University of Texas Health Science Center at Houston, TX); FIREFLY for robotic surgery (Novadaq Technologies Inc., Toronto, ON, Canada); FLUOBEAM (Fluoptics, Grenoble, France); HyperEye (Mizuho Medical Co., Ltd, Tokyo, Japan); IC-View (Pulsion Medical Systems SE, Feldkirchen, Germany); INFRARED 800 (Zeiss™; Karl Zeiss Inc., Jena, Germany); IRIDIUM (Visionsense, Philadelphia, PA, USA); Laparoscopic near-infrared fluorescence system (Olympus, Tokyo, Japan); Leica FL800 (Leica Microsystems Inc., Buffalo Grove, IL); Mini FLARE (Israel Beth Deaconess Medical Center, Boston, MA); Photodynamic eye (PDE; Hamamatsu Photonics Co., Hamamatsu, Japan); Spy (Novadaq Technologies Inc.); Stryker InfraVision (Stryker, Kalamazoo, MI, USA); The prototype surgical navigation system (Chinese Academy of Sciences, Beijing, China); Visual Navigator (SH System, Seoul, Republic of Korea), and ViTCOM II ICG (Karl Storz ,Tuttlingen, Germany).

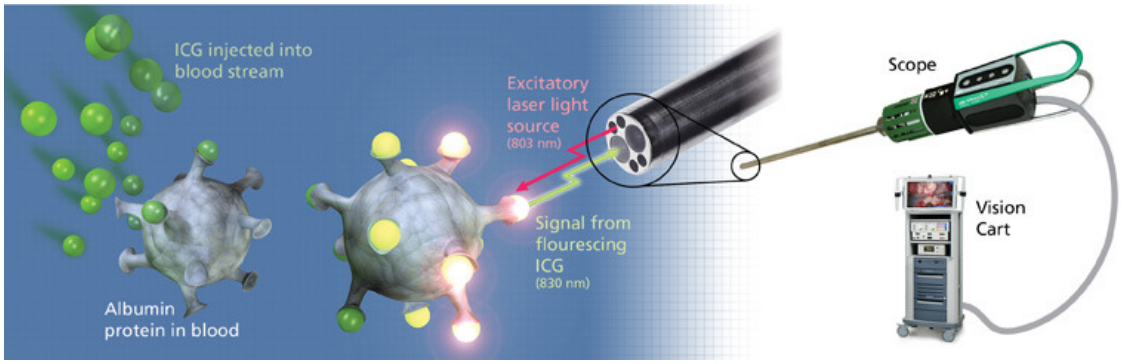
Figure 4. Clockwise from upper left: Spy Elite, Firefly, and Pinpoint machines, IC-view camera, Pinpoint scopes.

5.0mm PINPOINT Endoscopes



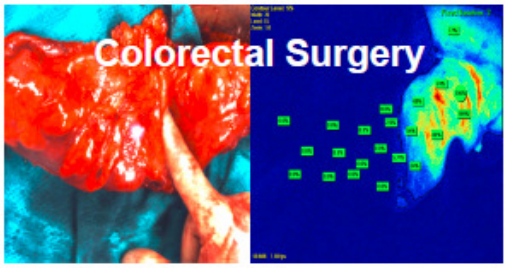
Source: Novadaq commercial material (personal communication) and Kamolz 2003 (12)

Figure 5. ICGA mechanism.

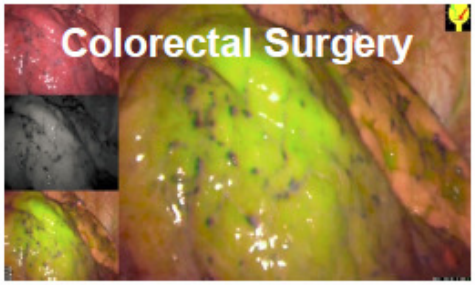


Source: Novadaq commercial material (personal communication)

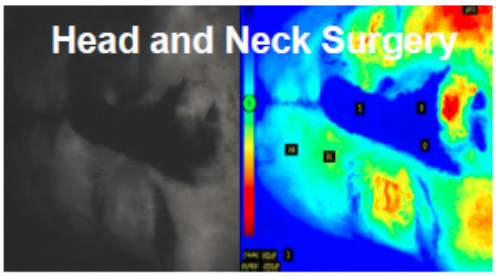
Figure 6. Images from ICGA produced by Spy Elite (upper left) and Pinpoint (upper right) in colorectal surgeries, and by Spy Elite in head and neck, vascular, and breast surgery.



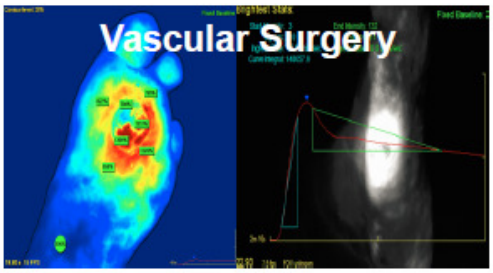
Assess tissue perfusion, guide transection margins



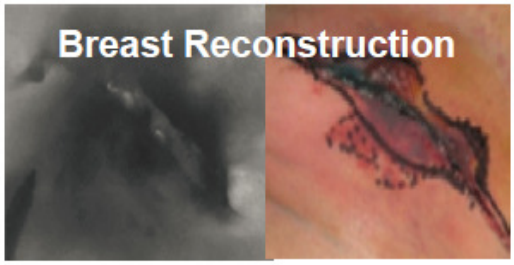
Assess tissue perfusion, healthy versus unhealthy tissue



Assess microvascular blood flow, anastomotic patency and perfusion



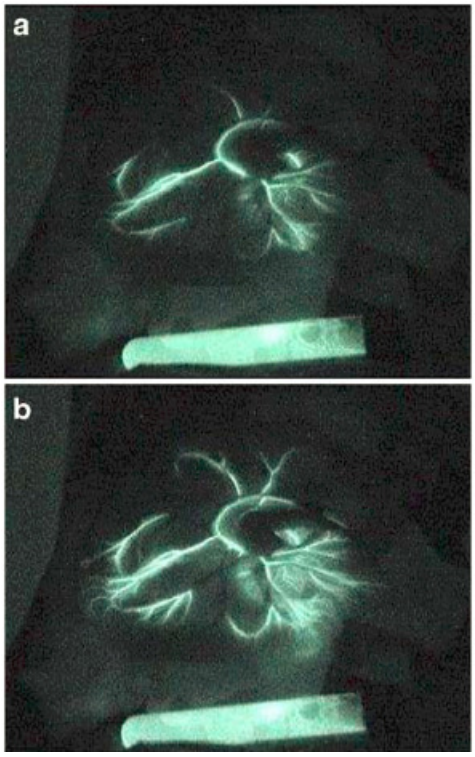
Assess blood inflow and outflow and tissue perfusion

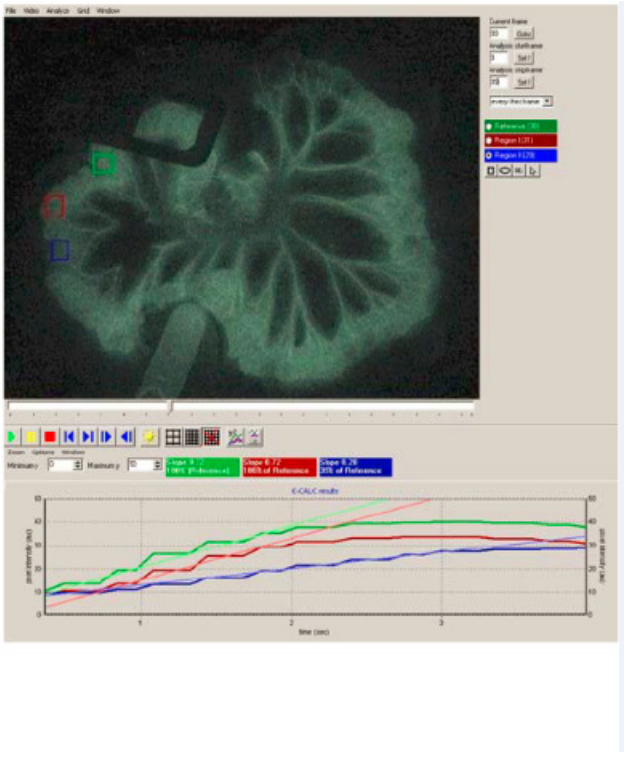


Assess tissue perfusion, segment healthy from abnormal tissue

Source: Novadaq commercial material (personal communication)
Note: Images on the left correspond to the alternative to use of ICGA (except for vascular surgery for which the alternative is on the right).

Figure 7. Images produced by (left) IC-view camera and (right) software analysis.





Source: Kamolz 2003 (12)

1.4 Guidelines on the use of the technology

Currently, there are no guidelines for the use of the technology in any indication.

1.5 Current usage in BC

Table 4 lists the four BC hospital sites reported to have the Novadaq equipment. Some sites have been using Spy Elite and Pinpoint in several indications, either routinely or in a trial.

Table 4. Current sites in BC where near-infrared devices are allocated and used.

Site	Devices and utilization		
	Spy Elite system - Novadaq (open surgeries)	Spy Pinpoint - Novadaq (laparoscopic surgeries)	Infrared 800 - Zeiss
UBC Hospital	Breast reconstructions (routine)	Biliary surgeries (routine)	Neurosurgery – arteriovenous malformations, bypass, aneurysm (routine)
Jim Pattison Surgery Centre (Surrey)	Breast reconstructions (routine)		
Eagle Ridge Hospital	Breast reconstructions (routine) Lymph node mapping – breast cancer (trial)		
Surrey Memorial Hospital		Esophagectomy surgeries (trial)	

1.6 Regulatory status

The Spy Elite system for open surgeries is licensed by Health Canada (n. 31977, first issued in 2001). It is intended "to image the coronary vasculature at the time of coronary artery bypass graft surgery. These images may be used to aid in locating vessels prior to the graft procedure. Post bypass graft, the images can be used to demonstrate and document graft patency" (13). The Spy Elite system is approved by the United States Food and Drug Administration (FDA) for use in cardiovascular surgery, plastic surgery, organ transplants, and

gastrointestinal surgery(14), but in Canada these indications are not listed under the current license.

The Spy Pinpoint system for laparoscopic surgeries is licensed by Health Canada under a broader scope (n. 81491, first issued in 2009) "to provide real-time endoscopic visible and near-infrared fluorescence imaging. Spy scope enables surgeons to perform routine visible light endoscopic procedures as well as further visually assess vessels, blood flow and related tissue perfusion with near-infrared imaging during minimally invasive surgery." (13) In the United States, Pinpoint is also indicated for "visual assessment of at least one of the major extrahepatic bile ducts (cystic duct, common bile duct or common hepatic duct), using near-infrared imaging. Fluorescence imaging of biliary ducts with the Pinpoint system is intended for use with the standard of care white light, and when indicated, intraoperative cholangiography. The device is not intended for standalone use for biliary duct visualization." (14)

ICG is sold separately from the devices. In Canada, the only supplier licensed by Health Canada is AKORN (DIN02014793). Some physicians and nurses raised the concern that a shortage of ICG in the market might affect the ability to perform ICGA at sites where the near-infrared devices are available.

1.7 Structure of report

Stakeholder perspectives and a Canadian jurisdictional scan are outlined in Chapters 2, 3, and 4. Chapter 5 is a summary of the evidence available on the technology for use in other indications and an assessment of the clinical and economic evidence for colorectal surgeries. The economic model is found in Chapter 6, and the budget impact is in Chapter 7.

Chapter 2 Jurisdictional Scan

Summary

Ten Canadian jurisdictions responded to the request for information. ICGA is performed in:

- *Neurosurgery (craniotomies, aneurysm clipping) in Nova Scotia and Alberta (Infrared 800)*
- *Plastic surgery reconstructions (breast, fingers, lower extremities) in Alberta (Spy Elite)*
- *Plastic surgery reconstructions in New Brunswick (Infrared 800)*
- *Lymphedema surgery in Alberta (Spy Elite)*
- *Colorectal surgeries (bowel perfusion) in Alberta (Spy Elite)*
- *Hernia repair in Alberta (Spy Elite)*

Two devices are currently in use: Spy Elite by Novadaq and Infrared 800 by Carl Zeiss. No MSP fee to perform ICGA has been reported. Some instances of ICG dye shortage has been reported in Alberta.

No written policy limiting or guiding the use of different devices was found. It seems the choice of device and indications is made by hospitals and physicians.

2.1 Objectives

To outline policies from across Canada about the use of near-infrared fluorescence detection devices for intraoperative indocyanine green angiography, indications for ICGA use, and whether ICGA has been publicly funded.

2.2 Methods

An environmental scan of the use of this technology in the Canadian provinces and territories was conducted by communicating with the appropriate contact person for each jurisdiction.

The Canadian Agency for Drugs and Technologies in Health (CADTH) liaison officers across Canada (policy and surgical program contacts) were contacted, and initial communication was done by the BC CADTH liaison officer. The Intergovernmental Relations network was also contacted and communication was done by policy analysts from the BC Ministry of Health. A

snowball sampling was used, and our team followed up with the resonders as necessary. The manufacturer was also contacted by the UBC research team.

There were three main questions of interest:

1. Which near-infrared fluorescence devices for ICGA have been purchased (model, manufacturer, etc.) and which indications have they been used for?
2. Has there been any shortage of the indocyanine green dye and how have the provinces been dealing with that?
3. Have physicians' fees to perform ICGA been charged on top of the surgical procedure fee?

The results were gathered and presented descriptively.

2.3 Results

Eight provinces and two territories provided details in response to the request (Alberta, Manitoba, New Brunswick, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, Quebec, Northwest Territories, and Yukon Territory). None of them had a written policy restricting public funding or use of the technology.

Northwest Territories, Prince Edward Island, and Yukon Territory confirmed no history of purchase or use of these devices. Manitoba, confirmed no history of purchase. However, Manitoba advises that 2 donated pieces of this technology are being utilized in patient treatment within the Winnipeg Regional Health Authority (WRHA). Newfoundland and Labrador, Ontario, and Quebec do not have a centralized database of deployment of this technology at the hospital level, so use and range of application were not available for the purposes of this review. The manufacturer estimates eight Spy imaging systems are placed in hospitals in Ontario and Quebec.

Nova Scotia reported performance of ICGA in some neurovascular cases, but no further detail on the device was obtained.

New Brunswick has reported a purchase of Infrared 800. So far it has been applied only for plastic surgery reconstructions, with no history of extra fees for ICGA and no shortage of the ICG dye.

Alberta provided the most detailed information on the types of the near-infrared fluorescence devices in use and indications:

- University of Alberta, Edmonton: uses Infrared 800 for neurosurgery (craniotomies, aneurysm clippings)
- Foothills Medical Centre, Calgary: uses Leica microscope for neurosurgery (craniotomies, aneurysm clippings)
- South Health Campus, Calgary: uses Spy Elite for plastic surgery reconstructions (free flap breast reconstruction, assessment of mastectomy flaps in cases of immediate breast reconstruction, digital replants, lower extremity flaps), lymphedema surgery, colorectal surgeries (bowel perfusion), skin flaps in hernia repair. There has been increasing interest from general surgery and orthopedic surgery in the use of the technology
- Misericordia Hospital, Edmonton: uses Spy Elite for breast reconstructions (TRAM flaps and Latissimus flap surgeries)

ICG dye shortage has been reported and is still an ongoing issue at University of Alberta. No shortage of ICG dye was reported by the other sites. No physician fee to perform ICGA has been charged on top of any surgery fee.

An international scan of types of cameras utilized in the different indications of ICGA at the hospital level was not feasible.

2.4 Conclusions

Within the respondent jurisdictions, there is no written policy limiting the coverage or guiding the use of near-infrared fluorescence detection devices for intraoperative ICGA. The choice of device and indications depends on hospital and physician judgment. Hospital-level data from more populated provinces (Quebec and Ontario), or at an international level, could have provided further insight into current practice but was not available for this review's scope and time frame.

Chapter 3 BC Context and Other Stakeholders' Perspectives

Summary

The clinical experience with the ICGA and Spy devices are concentrated in breast reconstructions and biliary surgeries at a limited number of sites. There is a great interest to expand the technology adoption to colorectal surgeries, which will have a noticeable impact on the health system given the volume of surgeries performed in BC (> 4,800/year).

In those surgeries, the use of the technology has the potential to decrease leak rates and the associated consequences for patients and the health care system—mortality, quality of life, long term disabilities, cost with treatment of complications and stoma care, impact in social and mental health, and stigma with regards to stoma and self-image.

Also, it can be used for research and training of surgeons. Currently, there are no guidelines for anastomosis assessment and it is mostly based on visual clinical judgment.

The main challenges for implementation are the capital costs and logistics for machine placement, cost of disposables, need for adequate infrastructure and logistics in the operating rooms, adequate supply of contrast, and potential adoption beyond colorectal surgeries.

3.1 Objective

To understand the BC experience with near-infrared fluorescence detection devices for intraoperative ICGA to date.

To determine the burden of illness, patterns of care, appropriate outcomes, and comparators for evaluation, capacity, and relevant implementation in BC as they relate to using ICGA for anastomosis assessment in colorectal surgeries.

3.2 Methods

Between September and November 2016, multiple telephone interviews and email inquiries were conducted with key informants to collect information to describe the current context for the use of the technology in BC. The interviewed participants included 12 individuals identified through a snowball sampling method as having a valuable perspective to inform the policy question. The participants included individuals working in the Greater Vancouver area (at

Vancouver Coastal Health and Fraser Health) and with a range of data/health care experience (two plastic surgeons, two general surgeons, one neurosurgeon, one cardiac surgeon, one gastroenterologist, two operating room registered nurses, two technicians from the manufacturer, two policy analysts from the Ministry of Health). Feedback was anonymized so no personally identifiable information was included.

A semistructured interview guide was developed to guide the interviews. This guide evolved over the course of the interviews, as questions were refined to reflect what had been learned through the previous interview(s).

3.3 Findings

3.3.1 Clinical experience with the technology in BC

The plastic surgery teams performing breast reconstructions at Eagle Ridge Hospital, Jim Pattison Surgery Centre, and UBC Hospital have been doing routine ICGA to assess flap perfusion using Spy Elite devices for several years. There is an interest in expanding the use of ICGA to other sites performing breast reconstruction, and to other plastic surgery reconstructions (fingers, limbs, trauma, etc.). The goal in those surgeries is to decrease the rate of necrosis, and, specifically in breast reconstructions, to support surgeons' decision making and confidence whether to perform more complex reconstructions, the timing for use of more costly resources (matrix, implant, expander) and decrease implant losses. A business case on the use of the technology was presented within Vancouver Coastal Health at the time the technology was adopted. The equipment could also be used for lymph node mapping during breast surgeries; the teams are still researching and considering this indication.

The neurosurgery team at UBC has also been routinely performing ICGA for years, using Infrared 800 devices. With some adaptation of the microscope setup, this equipment could be shared with other specialties, such as plastic surgery.

The general surgery team at UBC performs ICGA during biliary surgeries using the Spy Pinpoint device, which is specific for laparoscopic surgeries. The goal in these surgeries is to decrease bile duct injury by improving the visualization of the anatomy. This equipment could also be shared for other laparoscopic surgeries (colorectal, bariatric, gynecologic, etc.) provided it has the appropriate scope sets.

Eagle Ridge Hospital's plastic surgery team and Surrey Memorial Hospital's general surgery team have also been using Spy Elite to perform ICGA during lymph node mapping, and esophagectomies on trial studies (Table 4).

No cardiac surgeons or endoscopy team expressed interest in adopting the technology.

There was great interest from the general surgeons to adopt the technology (Spy Elite and Pinpoint) mainly for colorectal surgeries for anastomosis assessment (bowel perfusion) in open and laparoscopic surgeries. There is a concern about liability for using only clinical experience for anastomosis assessment. There is no history of use of ICGA or Spy devices in colorectal surgeries due to the lack of available equipment for general surgery operating rooms. The surgeons have learned about the Spy technology from colleagues at UBC using the equipment in other indications, colleagues in the United States using it for colorectal surgeries, and from conferences, studies, and the manufacturers' materials. They stated that other devices on the market (e.g., Stryker) to perform fluorescence angiography are inferior in image quality.

3.3.2 Burden of the complications and treatment options in colorectal surgery

In the context of colorectal surgeries, in one of the interviewed surgeon's experience, the leak rates in BC range from approximately 3 to 5 percent for colon surgeries and 15 percent for rectal surgeries. The lower in the intestine the resections are performed, the higher the expected leak rate.

Anastomotic leakage can be assessed as minor (where the leak is contained in perianastomotic space without peritonitis) or major (where the leak is not contained, leading to generalized peritonitis and sepsis). Minor (contained) leaks may be treated with antibiotics, bowel rest, and possible percutaneous drain, but are unlikely to lead to death. Major leaks mandate surgery to divert stool with a stoma, plus washout peritoneal lavage and drainage. The stoma may be temporary or permanent. Major leaks can lead to sepsis and death and have been associated with cancer recurrence. (e.g., Branagan et al 2005). (15)

3.3.3 Treatment protocols/clinical pathway/guidelines in colorectal surgery

Currently, there are no guidelines for anastomosis assessment. Some surgeons are using fluorescein dye and Wood lamp (ultraviolet lights); this has a higher risk of allergic reaction in the patient and steeper learning curve for the surgeon and is time-consuming and difficult to use in laparoscopic surgeries. Other surgeons are using only visual assessment and clinical judgment.

3.3.4 Potential size of patient population and usefulness of the technology under assessment

According to data from the Ministry of Health, in the last year, almost 4,800 colorectal surgeries were performed in BC (1).

In these surgeries, the goal of performing ICGA is to evaluate and improve perfusion in the anastomosis to decrease leak rates after resections and the associated consequences (sepsis, mortality, cancer treatment delay, and cancer recurrence).

As many surgeons and the manufacturer pointed out, once the machine is in place in the operating room, the technology has several other applications (e.g., liver transplant, esophagic surgeries, lymph node mapping, gynecologic surgeries, etc.). Other surgical teams are likely to be interested in adopting the technology, too.

3.3.5 Technology potential for illness and injury prevention

Performing ICGA during colorectal surgeries does not interfere with the primary illness but has the potential to decrease complications, thereby preventing injury and harm. It can also improve patients' well-being by indirectly decreasing the need for temporary or permanent stomas, which are known to interfere in the quality of life.

3.3.6 Technology potential for improving marginalized and disadvantaged population

The technology does not directly aim for marginalized and disadvantaged populations, but those patients face more challenges with stoma care (access to stoma care supplies, running water, basic hygiene conditions) and with complications in general (productivity loss, support systems, etc.)

3.3.7 Perspective on patient's experience (reported by clinicians or service providers)

The ICG dye has a better allergic profile than other contrast, so allergic reaction does not seem to be a concern for clinicians. However, the patient must still be asked about allergies and told about the contrast during the presurgical consultation, as with any other contrast.

3.3.8 Non-health benefits to patients (autonomy, convenience, comfort, and confidence)

Non-health benefits are related to avoidance of complications (e.g. leaks) and negative effects of the interventions or complications (e.g. death, intra-abdominal sepsis that frequently require prolonged ventilatory support, intensive care support and multiple surgical interventions, wound dehiscence, multiorgan failure, prolonged hospital stay, permanent colostomy). Patients who survive intra-abdominal sepsis are at risk for incisional herniation, mechanical bowel obstruction due to adhesions and chronic renal failure. All of the above can be associated with patient suffering, loss of income, potential long term disability and depression.

Patients have reported regretting their treatment decisions. They cite a lack of information and support to manage the lasting effects of the postoperative symptoms, and say they would have made a different decision in regards to the surgery had they known more before the procedure. (16)

For example, when patients survive complications with a permanent stoma that was not planned (or they were not informed about this possible outcome), they face many psychological, emotional and social changes in daily life (e.g., suffering, pain, deterioration, uncertainty about the future, fear of rejection). They can also face other setbacks, such as a range of social constraints, the possibility of outgassing and excrement leakage due to the lack of voluntary control or to flaws in the safety and quality of the collection bag, and other complications. Typically, such problems can be understood from the physical, psychological, social, and spiritual dimensions and lead to an adaptive process and change in lifestyle. Beyond the stigma, patients feel shame and embarrassment, feelings that result in self-isolation and loss of quality of life, self-esteem, body image, and interpersonal relations (especially the partner relationship). (17)

3.3.9 Other implementation considerations

Multiple surgeons noted that the potential for benefits in surgical education and training. They believe ICGA can improve the training of surgeons over time, thereby increasing surgeon confidence, improving intraoperative decision making, and allowing for changes in surgical technique in real time. ICGA can help surgeons better evaluate where to place ostomies, how much intestine tissue needs excision, and whether an ostomy can be avoided. It can allow immediate revisions in problematic anastomoses or sites with poor perfusion, avoiding complications and revision surgeries.

There is also potential for research. The machines' software systems capture data with every use, and surgeons and manufacturers' engineers are working to develop objective measurements of perfusion and tissue mapping that can be applied on the collected data.

3.3.10 Access to technology

The only patients with access to ICGA are those referred to surgery at one of the sites that can incorporate the technology (physical space and personal) and have the financial means to purchase the equipment. The technology has been used successfully for indications other than colorectal surgeries (Table 4).

3.3.11 Capacity for providing the technology in BC, and implementation challenges

Some health care providers noted that physical space might be a challenge in some operating rooms and that the device would not fit in with other equipment used for the same surgeries.

Surgeons and operating room staff need a certain amount of training to perform ICGA, and it is most effective to train "super users" (nurses and surgeons who perform high volumes of

surgery with the equipment). Extra staff (usually a registered nurse [RN]) is needed to manipulate the equipment.

Hospitals will need to evaluate their operating room capacity (staff, physical space, number of surgeries being performed) and allocate personnel to manipulate the equipment and accessories. Considerations include physical positioning in the operating room, moving the machine between operating rooms to increase usage efficiency, and time between surgeries for cleaning and sterilization.

It has been suggested that expanding the use of ICGA and purchasing new devices should be avoided until an adequate supply of contrast is established. This is critical to avoid the machines being idle. The ICG dye is considered a drug in Canada. Novadaq used to provide it in the disposable kits, but they are not licensed by Health Canada to commercialize drugs. The ICG dye is acquired through other licensed suppliers and there has been a history of shortage in BC.

There is no requirement for special credentials to perform ICGA.

In commercial materials from the manufacturer, the perceived competitors for the Spy system were the da Vinci with Firefly (the Firefly camera was manufactured by Novadaq for the da Vinci robot commercialized by Intuitive), the Laparoscopic near-infrared fluorescence system from Olympus, InfraVision from Stryker, and ViTOM II from Storz. Some technical comparisons (signal intensity, head imaging, resolution, quantification capability, ambient light interference) with Fluobeam, Photodynamic eye, and Visionsense stated their performance would not be comparable to the Spy systems.

The technical aspects and impact in the operating room operations need to be further analyzed with the users (surgeons and nurses) in case of proved effectiveness and implementation decisions.

3.3.12 Cost for the health system and patients

There are capital costs for the acquisition of the equipment, with different costs and components for open (Spy Elite) and laparoscopic (Spy Pinpoint) devices. There is also an annual maintenance fee that covers parts replacement.

The per-surgery cost of disposable materials includes drapes for open surgery devices and introducers and tubing for laparoscopic devices.

Surgeons had different opinions about whether there should be a fee to perform ICGA during surgery. One general surgeon was against extra fees, another asked if they would be paid to use the machine during surgery, and a plastic surgeon said he is trying to introduce a fee of approximately $50 dollars in the system to perform ICGA.

The contrast comes in 10 mL/2.5 mg per mL dose and needs to be used within six hours once diluted. Each test uses 1 mL and tests are usually performed a couple of times during surgery. The ideal range for reading with the camera is 2–5 minutes after injection.

Patients are not expected to incur any costs for the equipment or disposables.

3.3.13 Environmental impact

Adopting ICGA in every colorectal surgery will increase the amount of health care waste from the operating room (disposable drapes and introducers, ICG vials). However, avoided colostomies could reduce the waste associated with stoma care if a positive impact is observed in major leak rates and permanent stomas.

ICG is not a radioactive contrast, and in other settings has been suggested to decrease the need for radioactive contrast and personnel (lymph node mapping is under research).

3.3.14 Risk for successful implementation (financial, human resource, stakeholders, others)

The only apparent risks for successful implementation seem to be the need for infrastructure (space, logistics, staff, and training) in every hospital and availability of the contrast.

Financial risk is moderate since there is interest from other surgeon groups to adopt the technology. Once the machine is in place in the operating room, it might be used for additional indications, at an additional cost without a full understanding of whether the device would be effective and cost-effective for those other indications.

Chapter 4 Patient Experience

Summary

No literature on the patient experience of using ICGA was found. The result of this section is derived from the patient experience of colorectal surgery due to colorectal cancer. The major complaint about colorectal cancer from patients was impaired bowel function. The most common expected outcome of the surgery was improved bowel function. The core outcome sets for colorectal surgery should include oncologic outcomes, operative outcomes, and quality of life. Patients also reported gaps in the information provided before surgery about surgical outcomes and negative health effects of the surgery. Some patients expressed that they might have changed their decision had they known more about the negative effects of surgery. Patients also reported anxiety and fear around their future health status after the surgery.

4.1 Objective

To gain an understanding of the outcomes important to patients, to guide the evaluation of the clinical literature and health policy.

4.2 Patient experience from literature

A rapid review of qualitative studies was conducted by CADTH on behalf of the Health Technology Review (HTR) Office from the BC Ministry of Health to aid in meeting the overall objectives of this HTA (16).

CADTH found no published literature on the patient experience of ICGA in colorectal surgery. However, they found five studies on the patient experience on colorectal surgery due to colorectal cancer without ICGA (18-22). They found that “patients’ expectations of long-term functional outcomes are influenced by the cancer experience and the relative importance and imminence of cancer- and treatment-related events.” They reported patient experience based on preoperative expectations and postoperative experiences.

4.2.1 Preoperative expectations

The reviewers found that “the consensus meetings generated 12 core outcomes grouped into three categories: oncologic outcomes, operative outcomes, and quality of life. For operative outcomes, anastomotic leak, perioperative survival, surgical site infection, stoma rates and complications, and conversion to open operation (where appropriate) were the final core outcomes that the patient and provider groups came to a consensus on. For the patient quality of life, physical function, sexual function, fecal incontinence, and fecal urgency were the final core outcomes that the patient and provider groups came to a consensus on.” (18)

Another included study, Park 2014, reported that “the expectations that preoperative patients have of long-term functional outcomes can be viewed within the context of the cancer experience and the relative importance and imminence of cancer- and treatment-related events.” (19)

4.2.2 Postoperative experiences

In terms of postoperative experiences, the reviewers identified that “two of the studies reported that patients felt there were gaps in the information that was provided to them about surgical outcomes.” In one study, “of the respondents who reported that symptoms affected their lives greatly, 24–50 percent claimed they would have changed their treatment decisions had they known prior to the surgery about the lasting effects of these symptoms. Reasons for this regret were the presence of negative side effects and the lack of information about and support for addressing these negative effects.” (20)

The reviewer reported that “two of the studies reported the anxieties and fears that patients felt the postsurgical treatment of their conditions and how they tried to overcome

them. Steel et al. (2016) reported that 12 of 18 patients expressed worry about their health in the future, five reported actively trying not to worry because they felt they had done everything they could do to prevent another cancer, and seven were worried about local recurrence or developing cancer on another site." (21)

They also reported that "in this study [Tayler 2011], patients described anxiety about if and when their cancer might return, even though they knew they had successful treatment for early-stage colorectal cancer." (22)

4.3 Conclusions

The reviewers concluded that "core outcome sets for colorectal surgery have been identified based on the consensus of patient and providers as oncological, operative, and quality of life outcomes. The expectations that preoperative patients have of long-term functional outcomes can be viewed within the context of the cancer experience and the relative importance and imminence of cancer- and treatment-related events." Studies reporting on the view of postoperative patients indicated that there were gaps in the information provided about surgical outcomes before surgery. Patients stated that knowing about these outcomes before surgery might have changed their treatment decisions. Anxieties or fears after surgery were mainly about future health status and the local recurrence or development of cancer in another site. These findings are directly related to the main outcomes covered in this HTA: complications, survival, permanent stoma, and quality-adjusted life years (QALY).

Chapter 5 Assessment of Evidence

Summary

Four comparative nonrandomized studies and one single-arm study were included in the clinical effectiveness assessment. Anastomotic leakage was the most commonly reported outcome in the studies. The current evidence suggested that ICGA significantly reduced the risk of anastomotic leakage. The pooled estimate of risk ratio for leak was 0.55 [95% CI 0.35, 0.86]. The absolute risk reduction was 4 percent and number needed to treat was 25. Evidence for other outcomes was poor.

Due to the quality of evidence, it was not possible to rule out the possibility that part of the effect could be attributed to confounding factors. High risk of selection bias and lack of blinding could influence the estimates.

There is no evidence available to compare the Spy imaging systems to the other near-infrared fluorescence detection devices.

5.1 Objectives

1. To provide a summary of the entire evidence base on intraoperative ICGA utilization in other non-ophthalmologic indications.
2. To assess the published evidence on safety, effectiveness, and cost-effectiveness of the intraoperative ICGA for anastomosis assessment in colorectal surgeries (open or laparoscopic).

5.2 Methods

5.2.1 Inclusion criteria

Table 5 defines the patient population, inclusion criteria, and outcomes of interest for the colorectal surgery HTA.

Table 5. Inclusion criteria.

Patient Population	Intervention	Appropriate Comparators	Outcomes
Patients of any age undergoing colorectal surgeries due to any cause	ICGA assisted with any variation of Novadaq System (Spy, Pinpoint, Firefly) or another laser/near-infrared/ LED device assisting ICGA	Clinical judgment assisted with using patency tests (air or fluid leakage), endoscopic visualization techniques or microperfusion techniques (transabdominally or endoscopically, e.g., Doppler ultrasound, flowmetry, tonometry, spectroscopy, etc.)	**Clinical outcomes** Postoperative mortality Postoperative anastomotic complications (leak rate, stenosis, infection, etc.) Number of surgeries (revisions, perfusion-related operations) Quality of life Patient experience and satisfaction **Economic outcomes** Resource use (hospital admissions, readmissions, LOS) Cost (devices, procedure, revision) Utility measures ICERs, WTP, CEAC

Note: CEAC = cost-effectiveness acceptability curves; ICER = incremental cost-effectiveness ratio; ICGA = indocyanine green fluorescence angiography; LED = light-emitting diode; LOS = length of stay; WTP = willingness-to-pay.

5.2.2 Exclusion criteria

- Non-English-language publications
- Abstract/conference proceedings
- Letters and commentaries
- Nonintraoperative use of ICG
- Studies published before 2002

5.2.3 Literature search overview

Initial scoping search was undertaken using Medline in October 2016 to assess the volume and type of literature relating to the objectives. These scoping searches also informed the development of the final search strategies (Appendix A). For the scoping search, our search

strategy included search terms for intraoperative use of any equipment for indocyanine green fluorescence angiography for any non-ophthalmologic procedures. The search strategies were developed by an information specialist, with input from the reviewers. The strategies were designed to capture generic terms for indocyanine green fluorescence angiography. We searched relevant citations from 2002 to 2016. Published articles were identified in Medline and Embase via Ovid. Search results were imported into Endnote and Microsoft Excel for screening. The search is considered up to date as of October 13, 2016.

Articles relevant to colorectal surgery were identified during screening. Articles retrieved for full-text reading were separated by the type of publication, e.g., systematic reviews, randomized trials, and nonrandomized comparative studies. Economic studies were also sorted out for detailed reading at this point of the process.

5.2.4 Study selection and data extraction

One reviewer screened titles and abstracts and then full texts, following a specified protocol. A second reviewer confirmed the relevance of included studies. The study flow was summarized using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram (Figure 8).

Data was extracted into a standardized data extraction sheet (Appendix B). A reviewer extracted all the data for clinical outcomes, while another reviewer extracted all the data from economic analyses. Data were cross-checked by the two reviewers for errors. Any discrepancy was resolved by discussion.

5.2.5 Quality assessment

For the purposes of this project, we followed the 2011 report on hierarchy of evidence from the Centre for Evidence-based Medicine at University of Oxford (23). We first searched for any systematic review of randomized controlled trials (RCTs) (level 1). If the amount of evidence was deemed insufficient at this level, we searched for large-scale randomized trials (level 2). If the amount of evidence was deemed insufficient at this level, we searched for nonrandomized studies (level 3). Lower levels of evidence were considered hypothesis-generating and deemed insufficient for policy decision making.

Since the proper method for critical appraisal of systematic reviews of nonrandomized studies is still under debate, the systematic reviews of nonrandomized studies we found in our search were used for cross-reference only. We obtained the primary studies and critically appraised them with the Downs and Black checklist recommended by the Cochrane collaboration (24).

5.2.6 Data synthesis

Cochrane Review Manager Software, RevMan 5.3.5, was used to synthesize data for clinical outcomes using direct comparison. Dichotomous outcomes were analyzed by using risk ratio (RR) or odds ratio (OR). When we found a statistically significant RR or OR, we also calculated risk difference and number needed to treat (NNT) for the outcome when possible. Continuous outcomes were analyzed using weighted mean difference.

5.2.7 Subgroup analysis

We analyzed the following subgroups if possible:

1. Laparoscopic versus open surgery.
2. Protective stomas versus no stomas after primary surgery.

5.3 Search results

5.3.1 Scoping search

Our generic search in Medline and Embase retrieved 2,810 articles. HTA databases and a list of references provided by the manufacturer (227 articles) were cross-referenced to organize the evidence by indication and levels of evidence. Table 6 summarizes the volume of evidence to be examined for the technology assessment in each indication.

Table 6. Summary of the volume of evidence on the different indications of ICGA and hierarchy of evidence

Indication	Effectiveness review					Others			Total
	Review	Systematic review	RCT	Comparative study	Case series/ One arm cohort	Economic study	Guideline	Background	
Adrenalectomy				1					1
Biliary procedures/ cholecystectomy	8		2	11	12				33
Breast reconstruction	7			17	15	3			42
Cancer	10	1			1			1	13
Cancer genitourinary	4				2				6
Cancer pancreas	1								1
Cancer SLN bladder cancer	2				2				4
Cancer SLN breast	2		1	20	4				27
Cancer SLN colon				2					2
Cancer SLN gastric cancer				5	6			1	12
Cancer SLN groin cancer					2				2
Cancer SLN gynecologic cancers	4	1		17	11				33
Cancer SLN head/neck/oral/esophagectomy	4			5	7				16
Cancer SLN lung cancer				2	4				6
Cancer SLN multiple	7			2	1			1	11
Cancer SLN prostate	2			1	2				5
Cancer SLN skin cancer	1			12	3				16
Cancer SLN thoracic/lung					1				1
Cardio	6		3	6	6				21
Colorectal	7	4	1	6	18				36
Endoscopy	1								1
Extravasation of cytotoxic drugs				1					1
General article	20							4	24
GI	2	1		2	6				11

Indication	Effectiveness review						Others		
	Review	Systematic review	RCT	Comparative study	Case series/ One arm cohort	Economic study	Guideline	Background	Total
Hernia/abdominal wall repair	1		1	2	1				5
Liver surgery	2			2	6				10
Lymphography/lymphedema	1			1	8				10
Nephro	2			4	8				14
Neuro/general	4	1			4				9
Neuro/intracranial aneurysm	12			19	16			1	48
Neuro/MAV, carotids, others	6			8	20				34
Neuro/tumour	5	1			9				15
Plastic surgery other reconstructions	3			10	22				35
Robotic biliary					1				1
Robotic general	1								1
Robotic uro	1								1
Spinal surgery	1			2	6				9
Thoracic surgery				2	3				5
Thymectomy					1				1
Thyroid surgery	1			1	3				5
Vascular/wound	2			7	10		1	1	21
Total	137	9	8	168	221	3	1	8	556

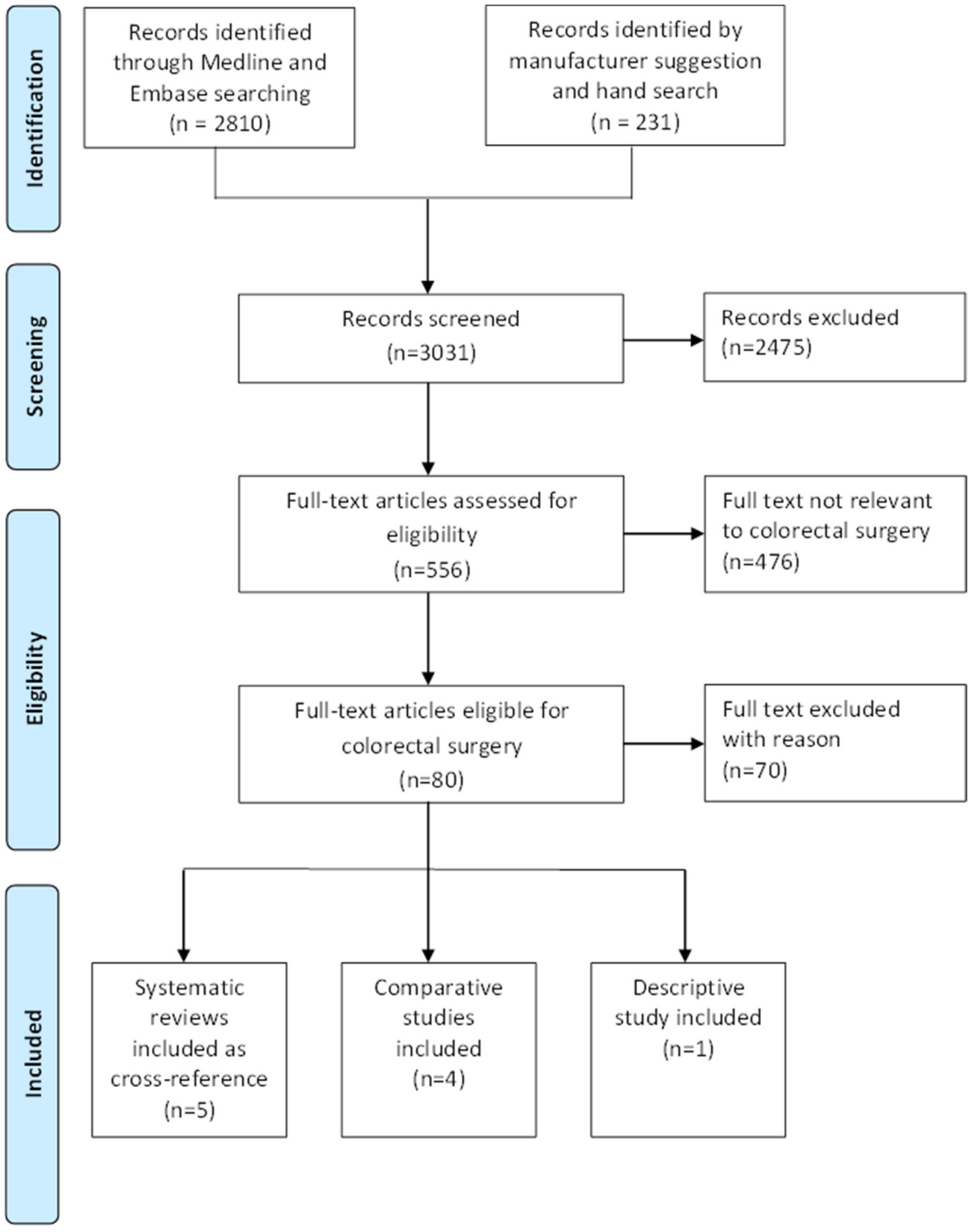
Note: Shaded indications are considered off-label in the United States.

5.3.2 Search results for colorectal surgery

The detailed flow of study selection for the evaluation in colorectal surgeries is presented in Figure 8.

Medline and Embase identified 2,810 citations. A list provided by the manufacturer and our own hand search found 231 citations. Two reviewers screened 3,031 citations and selected 556 citations for full-text review for all indications. We applied a filter to identify 80 citations relevant to colorectal surgery. After full-text review, we included five systematic reviews, four comparative nonrandomized studies, and one descriptive nonrandomized study for colorectal review. No economic analysis was found in our search for colorectal surgery.

Figure 8. PRISMA diagram.



5.4 Clinical effectiveness

5.4.1 Description of included studies

We included five systematic reviews, four nonrandomized comparative studies and one nonrandomized single-arm descriptive study (7, 25-33). We used the systematic reviews for cross-reference but did not report the findings because the included studies and methods varied between different systematic reviews, which led to different findings. Instead, we appraised and analyzed the primary studies ourselves. Three of the four comparative studies were a retrospective analysis of individual patient data. They compared the surgical outcomes of patients who received ICGA during surgery to those who did not. Two of the four comparative studies matched the profile of their participants based on age, sex, body mass index (BMI), and other variables. All of them reported the baseline characteristics. Two of the comparative studies examined ICGA with laparoscopic surgery, one examined ICGA with open surgery, and one examined a mix of laparoscopic and open surgery. None of the studies examined laparoscopic ICGA using solely Novadaq's machine. Therefore, we also included a single-arm descriptive study that examined only the laparoscopic ICG technology from Novadaq.

Overall, 1,224 patients were enrolled into the four comparative studies, in which 513 patients received ICGA during surgery and 711 patients did not receive ICGA. The single-arm descriptive study included 147 patients. The mean age ranged between 57 and 69 years, BMI ranged from 24 to 27 kg/m^2. Most of the participants needed colorectal resection because of colorectal cancer. The characteristics of included studies can be found in Appendix D.

5.4.2 Quality assessment

The quality of included studies was assessed using a checklist recommended by the Cochrane collaboration (24). We modified the checklist to fit the needs of this project (Appendix C). The included studies had a high risk of selection bias for being retrospective and nonrandomized. They also had a high risk of performance bias and detection bias due to the lack of blinding.

The risk of bias and confounding is generally higher in nonrandomized studies. Two of the studies attempted to minimize the confounding effect of selection bias by matching the patients. All of them reported the baseline characteristics and the categories that were different between groups. In addition, the anastomotic leak rate, which is the primary outcome in these studies, lay within the range of variation when compared with other larger observation studies of colorectal resection. However, such design features did not rule out the possibility that the effect estimate could be influenced by confounding factors. Taking this into account, the effect estimate of anastomotic leakage would likely to be overestimated in favor of ICGA.

5.4.3 Effect of intervention

5.4.3.1 **Mortality**

Kim 2015 reported no deaths in either group 30 days after the primary surgery (27).

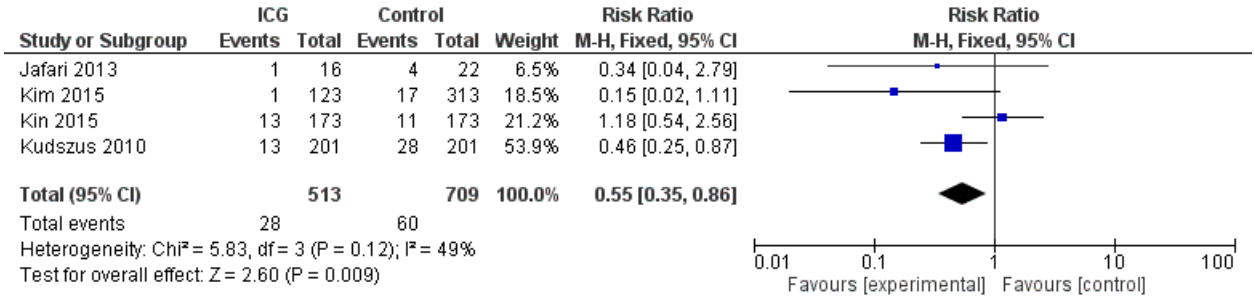
5.4.3.2 **Morbidity**

Kim 2015 reported 13/123 patients (10.6%) in the ICG group and 51/313 patients (16.3%) in the control group experienced morbidity (p=0.136) (27). Morbidity was not objectively defined in the studies.

5.4.3.3 **Anastomotic leaks**

Three of the four comparative studies reported the number of total anastomotic leaks (25, 27, 28). Kudszus 2010 reported the number of major leaks (29). In order to efficiently use the reported information, we used the ratio of major to total leaks from Murray 2016 (34) to estimate the number of total leaks in Kudszus 2010. We also determined from the reported baseline characteristics that the patient demographics of the included studies were similar enough that we could pool the data to estimate the RR of total leakage. Figure 9 shows the forest plot of the meta-analysis (using a fixed-effect model) and the RR of total anastomotic leakage, which is 0.55 [95% CI 0.35, 0.86; p=0.009]. The absolute risk reduction was 4% and NNT was 25.

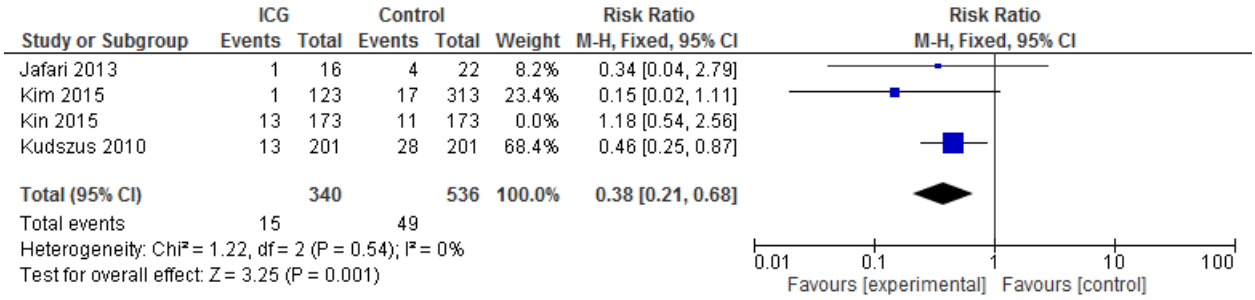
Figure 9. Forest plot of total anastomotic leaks.



Test for heterogeneity was not significant (Chi^2 p=0.12, I^2 = 49%). Although there is variation between studies, the heterogeneity test suggests that the variation is not large enough to raise concern about the validity of the pooled estimate. Despite that, sensitivity analysis was performed to identify the source of variation. Figure 10 shows the forest plot after excluding Kin 2015, which effectively eliminated all variation between studies in the estimate (I^2=0%). This test identified Kin 2015 as the sole source of variation within the pooled estimate.

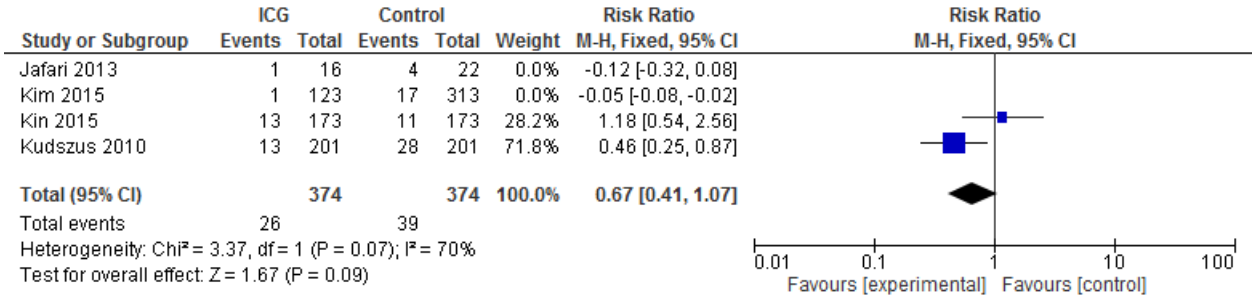
The RR without Kin 2015 was 0.38 [0.21, 0.68], p=0.001, absolute risk reduction was 6% and NNT was 17, which showed greater reduction of risk of leak with the use of ICGA.

Figure 10. **Risk of total leak without Kin 2015.**



Two studies compared the use of ICG camera in robot-assisted colorectal surgery. The effect of these two studies on the pooled estimate was explored in another sensitivity analysis. Figure 11 shows that heterogeneity increases without these two studies (I^2=70%), suggesting that the robotic studies did not cause any variation but enhanced the pooled estimate. The quality of evidence is therefore not affected with the robotic studies in the pooled estimate.

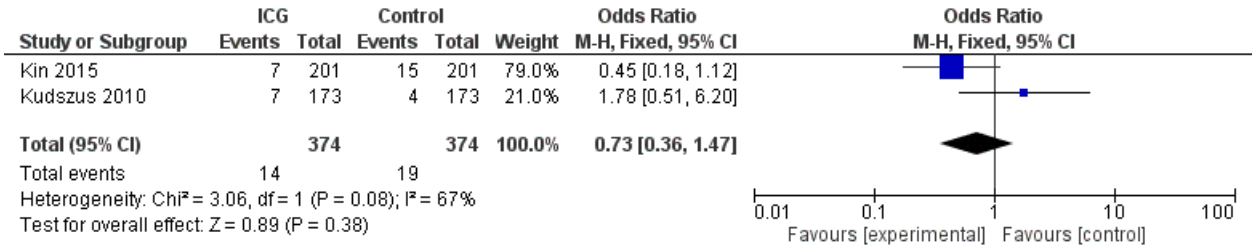
Figure 11. Sensitivity analysis without robotic assist studies.



5.4.3.4 **Reoperation due to anastomotic leak**

Two comparative studies reported the number of reoperations due to leaks (28, 29). Both had matched their patients, so pooling the results was deemed justifiable. The OR of operation due to leak was 0.73 [95% CI 0.36, 1.47] (Figure 12).

Figure 12. Forest plot of reoperation due to anastomotic leak.



5.4.3.5 Length of hospital stay

Three of the comparative studies reported the length of hospital stay (25, 27, 29). It was not possible to meta-analyze the length of stay with the two studies that reported the mean length of stay because Kudszus 2010 did not report the standard deviation or standard error of length of stay (Table 7).

Table 7. Length of hospital stay (in days).

Study	Non-ICGA group	ICGA group	Measurement
Kudszus 2010 (29)	21	19	Mean
Jafari 2013 (25)	5	4	Median
Kim 2015 (27)	7.6	7.7	Mean

5.4.3.6 Other outcomes

The included studies also reported other clinical outcomes, which are summarized in Table 8.

Table 8. Summary of other outcomes

Outcomes	Study	# of patients	% of patients with event
Sepsis	Jafari 2013	38	ICG: 1/16 (6%) Control 3/22 (13%)
Urinary tract infection	Jafari 2013	38	ICG: 2/16 (13%) Control: 2/22 (9%)
Urinary retention	Jafari 2013	38	ICG: 3/16 (19%) Control: 4/22 (18%)

	Kim 2015	436	ICG: 7/123 (5.7%) Control: 19/313 (6.1%)
Ileus (obstruction)	Jafari 2013	38	ICG: 6/16 (38%) Control: 4/22 (18%)
	Kim 2015	436	ICG: 2/123 (1.6%) Control: 13/313 (4.2%)
Bleeding	Jafari 2013	38	ICG: 1/16 (6%) Control: 2/22 (9%)
Wound infection	Jafari 2013	38	ICG: 1/16 (6%) Control: 3/22 (13%)
Enterocolitis	Kim 2015	436	ICG: 1/123(0.8%) Control: 1/313 (0.3%)
Respiratory infection	Kim 2015	436	ICG: 2/123 (1.6%) Control: 3/313 (3%)
Flatus passage	Kim 2015	436	ICG: 1.9 days +/- 0.9 Control: 2 days +/- 0.9

5.4.3.6.1 Outcomes from the descriptive study

Jafari 2015 enrolled 147 colorectal resection patients prospectively at 11 centres in the United States (33). The study was funded by Novadaq and used the laparoscopic ICGA machine from Novadaq (Pinpoint). The Pinpoint machine utilizes the same ICGA technology as the SPY Elite. Most patients needed colorectal resection due to diverticulitis (44%). It was different from the demographic in BC, where the most common cause for colorectal resection has been cancer (1).

Eight patients were not included in the analysis due to anastomosis greater than 5 cm, no anastomosis, or ileorectal anastomosis. The authors reported 24/139 (17.3%) morbidity rate and 2/139 (1.4%) leak rate. The authors concluded that Pinpoint was safe to be used in colorectal surgery and the patients whose anastomosis was revised due to inadequate blood flow during surgery did not experienced leak after surgery in the study.

5.4.4 Limitations

The quantity of evidence for using ICGA in colorectal surgery is limited. Only four comparative nonrandomized studies and one descriptive single-arm study were found. The amount of information obtained from the included studies allowed meta-analysis only on anastomotic leakage. The small amount of information obtained for other outcomes did not allow the drawing of definitive conclusions.

Although the effect on anastomotic leakage was statistically significant, it was not possible to rule out the effect of confounders. The included studies had high levels of risk of selection bias and performance bias. Although these risks are common in surgical observational studies, these biases could still significantly affect the estimates. Therefore, readers must interpret the results with caution, and consider that at least part of the effect was the result of confounding factors.

No studies directly comparing the Spy imaging systems with other near-infrared fluorescence detection devices were found. Firefly camera (studied in Kim 2015 and Jafari 2013) is also manufactured by Novadaq and considered a precursor of the Spy system. The assumption of similar "class effect" across ICGA devices was validated by two surgeons for the pooled estimates.

The study that solely used the Spy imaging system, Kin 2015, found the percentage of patients with leak higher in the Spy group compared with the control group (7.5% vs. 6.4%) but not significant. This variation did not cause significant heterogeneity in the pooled results, but it is not possible to rule out the possibility that the Spy system might perform differently from the other ICGA systems, due to the lack of comparative studies. In addition, the senior author of the article mentioned that he found the number of leaks in the control arm lower than usual, leading him to suspect study error (35). However, as of October 2016, no erratum was found for this study.

5.4.5 Overall summary of clinical effectiveness

- Four comparative studies and one single-arm descriptive study were included in this review. In total, 1,224 patients were enrolled in the comparative studies and 147

patients were enrolled in the descriptive study. The analysis of this sample size was able to show a significant difference in total leaks, which is not a rare serious adverse event in colorectal surgery.

- Two of the comparative studies matched participants. Other than matching, the included studies did not perform any other adjustment for confounders. Therefore, the studies had a high risk of bias due to lack of randomization and blinding.
- The baseline characteristics and methodology were similar enough across the included studies, and the assumption of similar "class effect" across ICGA devices allow meta-analysis of the effect on total leak. The current evidence suggested that ICGA significantly reduced the risk of anastomotic leakage. The pooled estimate of RR for total leak was 0.55 [95% CI 0.35, 0.86; p=0.009]. The absolute risk reduction was 4% and NNT was 25. Heterogeneity was not significant in the pooled estimate.
- Due to the high risk of selection bias and detection bias, it is possible that the pooled estimate could be affected by confounders. Limitation on the amount of data and the quality of current evidence prevented any adjustment of confounders or drawing any definitive conclusion about clinical effectiveness.
- It is not recommended to make decisions based on a single outcome estimate that could be influenced by confounders. Therefore, the result from the economic model, which partly addresses potential influences on the validity of the findings through sensitivity analysis, must be considered before drawing any conclusion.

- Although the study that used the Spy imaging system showed some variation from the pooled estimate, there was no evidence to indicate whether the Spy imaging system was superior or inferior to other near-infrared fluorescence detection devices.
- Parameters from other studies of colorectal surgery without ICGA were imputed in the model, which filled the gap of information left by the ICGA studies. The economic model could provide a better and more comprehensive picture of the effectiveness of ICGA in colorectal surgery.

5.5 Other studies that provided data for the economic model

Since studies about clinical effectiveness provided a limited amount of information, data from other studies that did not include ICGA was used to fill in the information gap. These studies were not under the scope of the research question for inclusion in the clinical effectiveness evaluation but they provided data for parameters in the economic model. The parameters and the studies that provided the data are listed in Table 9.

Table 9. Summary of studies that provided data for the parameters in the economic model.

Parameter	Values			Reference
Probability of having a stoma after primary surgery	Open surgery: 0.1588 Laparoscopic: 0.1171			Kang 2013 (36)
Probability of leakage in surgeries without the use of ICGA		Stoma	No stoma	Kang 2013 (36)
	Open	0.1606	0.1350	
	Laparoscopic	0.1414	0.0938	
Probability of major and minor leak	Major leak: 0.5479			Murray 2016 (34)
Mortality after leak	Major leak: 0.1641 Minor or no leak: 0.0314			Bakker 2014 (37)
Probability of permanent stoma	Minor leak or no complication: 0.085			Lindgren 2011 (38)
Increased risk in probability if:				
Major leakage	OR 10.5 (95% CI 5, 22.22)			
> 75 years old	OR 2 (95% CI 1.03, 4)			
QALY 30 days after surgery		No stoma		Jorden 2014 (39)
	Open	0.7800		
	Laparoscopic	0.8200		
Disutility of colostomy	0.09			Jeong 2016 (40)
QALY of living with or without stoma after surgery	Permanent stoma: 0.84			Smith 2006 (41)
Disutility of minor complication	Minor leak: 0.02			Brasel 1999 (42)

Note: Some values were calculated using the numbers from the original article.

5.6 Literature review of cost-effectiveness data

No cost-effectiveness studies or cost analysis related to the use of ICGA in colorectal surgeries were found.

Chapter 6 Economic Analysis for British Columbia

Summary

The best available evidence suggests that the use of intraoperative ICGA in colorectal surgeries for bowel perfusion assessment is likely cost-saving or cost-effective at conventional WTP levels compared with the current standard of care (visual clinical judgment) in most estimated scenarios and across most hospitals in the Province.

The estimates were most sensitive to four factors: leak rates for the local surgery teams, the effect of the technology in lowering leak rates, the incremental cost of leaks, and the capital cost per surgery (directly affected by the hospital-specific volume of surgery).

There is a moderate degree of uncertainty in the model. The effectiveness estimates were generated from observational studies. Adoption under controlled trial circumstances or monitored environment can confirm if the real-life benefits of the technology fall under the parameters used in the simulation model to confirm the cost-effectiveness.

6.1 Objective

To evaluate the cost-effectiveness of performing ICGA with Spy devices for colorectal surgeries in BC compared to routine care (clinical judgment alone).

6.2 Methods

We created a decision-analytic model for outcomes of colorectal surgeries to estimate the costs, health outcomes, and QALYs associated with performing ICGA during open and laparoscopic surgeries over a 20-year time horizon in BC.

6.2.1 Target population and subgroups

We stratified the BC population into four age subgroups (<50 years, 50–59 years, 60–69 years, and over 70 years). The analysis was performed separately within each subgroup. To generate population-based results, subgroup-specific results were weighted-averaged, with the weights being the prevalence of each subgroup in BC among the total number of surgeries performed.

6.2.2 Setting and location

The public health care system in BC, covering the entire population of the province, in the reference year of 2014/2015.

6.2.3 Study perspective

We chose a publicly funded health system perspective. Out-of-pocket expenses, third-party insurer costs, and productivity loss were not included.

6.2.4 Comparators

We compared ICGA with non-ICGA, the latter being the current standard of care.

6.2.5 Time horizon

We used a 20-year time horizon in the base-case analysis. Ten-year and lifetime time horizons were investigated in the sensitivity analyses.

6.2.6 Discount rate

A three-percent discount rate was applied to both costs and health outcomes. Alternative values were explored in sensitivity analyses.

6.2.7 Currency, price date, and conversion

All costs were inflated to 2015 Canadian dollars using the annual health and personal care Consumer Price Index for BC (43).

6.2.8 Choice of health outcomes

The main outcome of interest was the QALY, which captures both the length of time and quality of life associated with the different outcomes from colorectal surgery and the impact of corresponding complications. The secondary outcomes were number of deaths due to major leak, total number of complications (major and minor leak), and total number of patients with

permanent colostomy in the first year after surgery. The choice of secondary outcomes was based on clinical relevance.

6.2.9 Model structure

After evaluating the available evidence and consulting with surgeons, we created a decision tree to accommodate the most important immediate clinical outcomes that might be affected by the use of ICGA and result in long-term consequences for patients and the health system. These outcomes were major and minor leakage, death, and the need for temporary or permanent stoma. A Markov model with one-year cycles was created to extrapolate the outcomes from the decision tree to estimate the long-term impact on QALYs and costs (Figure 13).

6.2.10 Parameter sources and assumptions

Input parameters for the model came from the literature review (reported in Chapter 5), and analysis of administrative data from multiple databases within the Ministry of Health and health authorities (in particular the Discharge Abstract Database [DAD] and Medical Services Plan [MSP]). The analysis of administrative data allowed us to tailor the cost-effectiveness analysis to the BC context using local health service resource use data and costs.

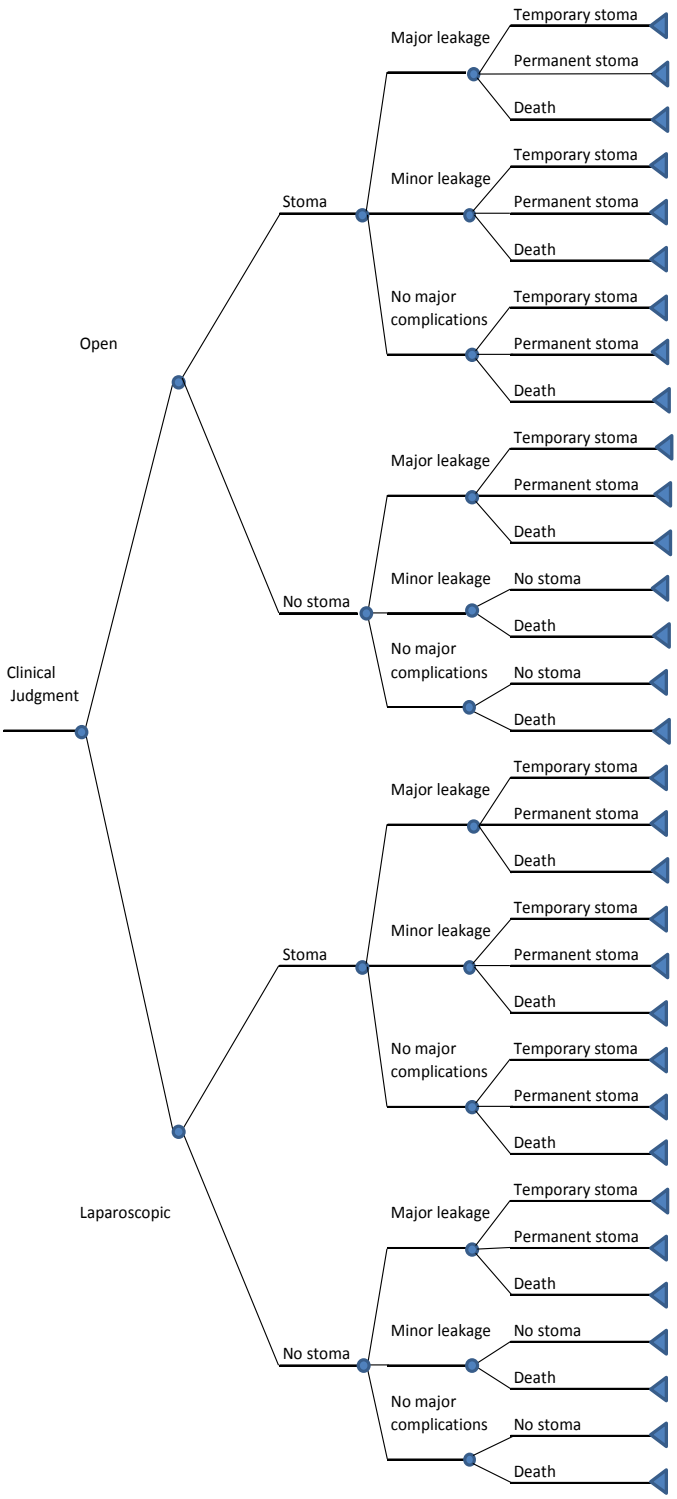
6.2.10.1 **The effectiveness of technologies**

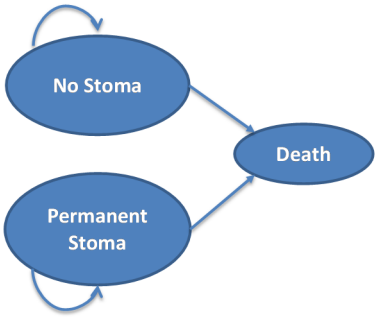
The leak rates associated with colorectal surgeries are a key parameter in determining the costs and health outcomes of ICGA use. Reported leaks rates varied substantially across observational studies and trials (27-29, 34-37). The leak rate is affected by a number of factors such as location of intestine resection (colon or rectum), surgeon experience, and patient characteristics (44).

For the surgeries performed without ICGA, we assume the baseline leak rates reported in an American nationwide inpatient registry (n= 72,055, from 2006–2009) published by Kang et al. 2013 (36). This registry reported the number of leaks by surgery technique (open vs. laparoscopic), with or without protective stoma performed in the initial surgery. This registry also is our reference for the probability of having a protective stoma by surgery technique (open vs. laparoscopic).

To model the effectiveness of the ICGA, we applied the calculated pooled OR of leakage reported in Chapter 5, based on the evidence available from ICGA studies using multiple devices, not exclusive to Spy. This approach assumes a similar "class effect" across ICGA devices which was also deemed plausible by the surgeons providing clinical advice to our group. The assumption of a class effect enables the use of larger data and accordingly results in more robust evidence and less uncertainty around the reported results.

Figure 13. Decision tree (left) and Markov model (right) structures.





Each terminal branch in the decision tree is connected to a separate copy of the Markov model, simulating the long-term outcomes for patients who experience all possible sequences of events modeled in the decision tree. The patients in the "Temporary stoma" branches of the decision tree enter the "No stoma" health state in the Markov Model.

6.2.10.2 **Proportion of major and minor leaks**

Based on surgeon input, we defined *minor leak* as requiring conservative treatment only (antibiotics, bowel rest, and possible percutaneous drain) and *major leak* as mandating surgical treatment (surgery to divert stool with a stoma, washout peritoneal lavage and drainage). Another registry (n=23,58), published by Murray et al. (34), provided data on the probability of leaks that required surgical treatment.

6.2.10.3 **Mortality**

Surgery risks and immediate complications were assumed to occur within a short time after the surgery and therefore were modelled in the decision tree component of the model. Surgical mortality was extracted from a Dutch registry (n=15,667) for patients with and without leaks (37). Based on surgeon input, we assumed minor leaks should not lead to death. Therefore, we assumed the same probability of surgical mortality for patients with minor leaks and those without any leaks.

Background mortality rate was extracted from Canadian life tables for BC (2010–2012) published by Statistics Canada (45). For patients with diverticulitis, aside from mortality due to immediate complications, background mortality rate was assumed to be similar to that of the general population. For patients undergoing surgery for colorectal cancer, higher mortality rate (due to cancer recurrence) was modelled for the first five years. After five years, the mortality rate of these patients was assumed to be equal to that of the general population. To estimate annual mortality rates for the first five years in this group, we derived the parameters of a Weibull survival curve based on one-year survival data published by Maringe et al 2013 (46) and

five-year survival data from the Canadian Cancer Society (47). Separate Weibull curves were fitted for each subgroup of patients according to cancer stage at the time of diagnosis.

6.2.10.4 **Probability of a protective stoma being permanent**

We extracted the probability of permanent stoma after a colorectal surgery from Lindgren et al. (38). This study also reported the effects of age and leakage on the probability of permanent stoma, which were used to make this parameter variable across subgroups.

6.2.10.5 **Health state utility values (utilities)**

We assumed the utility value published by Smith et al 2006 for surviving colorectal surgery without a permanent stoma. (41) We then calculated the utility value for surviving colorectal surgery with a permanent stoma, subtracting the values published by Jeong et al (40) for having a colostomy. We adjusted the utilities for the initial 30 days after surgery using the utility values by surgery technique (open or laparoscopic) published by Jordan et al 2014 (39). We used the utility values for patients with major complications published by Miller et al 2000 (48) to calculate the reduction in QALYs when a major leak occurred. For minor leaks, we used the reduction in QALYs published by Brasel et al 1999 (42). The reduction in QALYs due to complications was assumed only to the first cycle (first year) in the model.

6.2.10.6 **Costs**

The cost for device acquisition, annual maintenance, and disposables for the test were provided by the manufacturer. The cost composition for the laparoscopic device accessories were based on an average set with spare camera/cable/scopes (in case of malfunction or contamination during the procedure). Anal introducers for laparoscopic surgeries were assumed to be used in only 30 percent of the laparoscopic surgeries.

The weighted average capital cost per surgery was assumed to be an average of the individual hospital capital cost (IHCC) per surgery.

$$IHCC = \frac{\begin{array}{c} hospital\ cost\ with\ machines\ acquisition \\ and\ replacement\ + maintenance\ over\ time\ (volume\ dependent) \end{array}}{\begin{array}{c} \%\ of\ surgery\ a\ hospital\ performs\ in\ BC\ (volume\ dependent) * \\ projected\ number\ of\ surgeries\ for\ BC\ over\ 20\ years\ (discounted) \end{array}}$$

The IHCC was estimated based on operating room capacity for elective surgeries and number of machines needed, dividing the 2014/2015 number of surgeries by each hospital in the province (separately for laparoscopic and open surgeries since they require different machines) by operating room capacity. The HTR office analyst team obtained the patient volume from each hospital from the DAD and MSP database (Appendix E). We assumed that operating rooms are used for 5 business days per week, 52 weeks per year. We assumed no more than two surgeries booked per day in each room, to account for preparation and anesthesia time (personal communication with head nurse of general operating room), and potential additional operative time associated with ICGA. We also assumed each room would accommodate 20 percent overtime for emergency surgeries without the need for extra rooms or machines. We then projected the number of surgeries for the next 20 years, to check if more machines would need to be purchased over time to accommodate the surgeries. Since the yearly fluctuation of number of surgeries was not relevant, we assumed the initial number of machines purchased would remain sufficient for the demand. We adopted a 10-year depreciation model, after which the machines and accessories would be retired and replaced. The total costs with acquisition of the devices, replacement in 10 years, and annual maintenance were divided by the projected number of surgeries for the next 20 years. Because capital costs are accrued over the time horizon while the purchases are made at time 0, capital

cost was calculated such that its discounted value represent the net present value of the price of the machine. Projected numbers of machines and capital costs per hospital can be found in Appendix E).

Costs for the ICGA dye were extracted from the BC Clinical and Support Services Society (BCCSSS) database (49).

Average MSP and hospital costs (6-month and 12-months costs, BC fiscal year 2014/2015) were extracted from DAD and MSP database and calculated individually for each group of patients according to surgery technique, presence of protective stoma, and occurrence of major and minor complications. The complete methodology used to calculate MSP and hospital costs is described in Appendix F. These cost estimates include the costs of the initial surgery, subsequent procedures, and hospital admissions up to 12 months after the initial surgery, to include any cost consequence due to different surgery techniques and complications. The cost estimates from 6 to 12 months are correlated with the costs from 0 to 6 months, so for the probabilistic model, we used the average costs and variance from the first 6 months, and for the second semester, we applied the calculated ratio change in cost for the second period of the first cycle.

6.2.11 Analytic methods

For the base-case analysis, we calculated a single set of outcomes for surgeries, with or without the use of ICGA, by weighted-averaging outcomes within each age subgroup. Weights represented the age distribution of patients who underwent colorectal surgeries in BC in 2014/2015. Base-case results and all subgroup-specific results were calculated from a deterministic analysis. We also performed a probabilistic sensitivity analysis using Monte Carlo

simulation with 20,000 iterations to evaluate the degree of uncertainty in the base-case results. Results of the probabilistic sensitivity analysis are reported as the cost-effectiveness (CE) plane and the cost-effectiveness acceptability curve (CEAC). For the probabilistic sensitivity analysis, probability distributions were assigned to each uncertain model parameter, as follows:

- Beta distributions for the majority of transition probabilities (e.g., baseline risk of leakage, surgical mortality, baseline risk of permanent stoma).
- Lognormal distributions for the OR of leakage when using ICGA, and the effects of age and leakage on the risk of permanent stoma.
- Weibull distribution for cancer survival after surgery.
- We assigned normal distribution for utilities since the variance found in the data was small and distribution was reasonably contained in the (-1,1) interval. For the disutility of colostomies and minor complications, we used an arbitrary 0.25 coefficient of variance due to lack of evidence on the variance of this parameter in the literature.
- Gamma distributions were used for all cost parameters.

The choice of parameters for the above-mentioned distribution was based on the degree of uncertainty reported in the original studies (representing the sampling variability due to the finite size of the studies, as well as between-study heterogeneity when results were pooled estimates from a meta-analysis of individual studies). The price of devices and disposables were assumed to be known, because price is subject to negotiation.

We did not assume any uncertainty around the proportion in laparoscopic surgeries or in the distributions of surgeries by age group due to the large sample size of the source (n>4,800).

We conducted univariate deterministic sensitivity analyses to evaluate the effect of changes in key assumptions on the results. We evaluated changes in the baseline rate of leakage in patients undergoing colorectal surgeries without ICGA, alternative discounting values (0% and 5%), variations on the OR of leakage when using ICGA, subgroup analysis of population submitted to colorectal surgeries (i.e., 100% cancer patients) and surgery technique (i.e., 100% laparoscopic surgeries).

In determining the best strategy, we compared the incremental cost-effectiveness ratio (ICER) against a willingness-to-pay (WTP) of $50,000 per QALY gained.

6.2.12 Study parameters

Table 10, Table 11, and Table 12 describe the study parameters used in the model.

Table 10. Model input for transition probabilities

Probability of protective stoma	Distribution	Mean	alpha	beta	Source
Open	Beta	0.1588	10775	57055	Kang 2013
Laparoscopic	Beta	0.1171	495	3730	
Probability of leakage without ICGA					
Open with stoma	Beta	0.1606	1730	10775	Kang 2013
Open without stoma	Beta	0.1350	7705	57055	
Laparoscopic with stoma	Beta	0.1414	70	495	
Laparoscopic without stoma	Beta	0.0938	350	3730	
Probability of leak being major					
Major	Beta	0.5479	440	803	Murray 2016
Perioperative mortality					
In general	Beta	0.0314	455	14036	Baker 2014
If leakage occurs	Beta	0.1641	193	983	
Probability of stoma being permanent					
After minor leak or no complication	Beta	0.085	20	214	Lindgren 2011
OR of leakage if performing ICGA		**Mean**	**mu**	**sigma**	
With any device (pooled)	Lognormal	0.55	-0.598	0.2280	NMA Chapter 5
With any device (excluding Spy study – Kin 2015)		0.38			
With any device (excluding robotic studies)		0.65			
OR of stoma being permanent					
After major leak	Lognormal	10.5	5	22.22	Lindgren 2011
If > 75 years old	Lognormal	2	1.03	4	
Probability of Cancer Survival			**lambda**	**k**	
Stage I	Weibull		353.016	0.528	Canadian Cancer Society Maringe 2013
Stage II	Weibull		23.730	0.688	
Stage III	Weibull		1.586	0.621	

Note: CI = confidence interval; ICGA = indocyanine green angiography; lb = low boundary; ub = upper boundary.

Table 11. Model input for other parameters

Proportion of surgeries in BC by technique	%	Source
Open	0.56267	HTR Office DAD MSP Database
Laparoscopic	0.43733	
Proportion of surgeries within age subgroups		
<50 y	0.11916	HTR Office DAD MSP Database
50–59	0.16855	
60–69	0.27825	
70+	0.43403	
Proportion of cancer cases among patients submitted to colorectal surgeries in BC	0.67688	HTR Office DAD MSP Database
Proportion of cancer stages among cancer patients submitted to colorectal surgery		
Stage I	0.42072	Maringe 2013
Stage II	0.33212	
Stage III	0.24715	

Note: HTR = health technology review office; DAD = discharge abstract data; MSP = medical services plan.

Table 12. Model input for utilities and costs

Utilities	Distribution	Mean	SE			Source
Living without a stoma (noS)	Normal	0.84	0.025			Smith 2006
30 days after open surgery	Normal	0.78	0.08			Jordan 2014
30 days after laparoscopic surgery	Normal	0.82	0.05			Jordan 2014
Major Complications (Pain and Surgical Comp)	Normal	0.50	0.059			Miller 2000
Colostomy disutility	Normal	-0.09	0.0225			Jeong 2006
Minor complications disutility	Normal	-0.02	0.005			Brasel 1999
Costs (2015 CAD$)		**Mean**	**SE**	**alpha**	**beta**	
Near-infrared cameras and accessories						
Spy Elite (open surgery)		[redacted]				Novadaq 2016 price list
Spy Pinpoint (laparoscopic surgery)		[redacted]				
Warranty/maintenance fee (per year, per machine)		[redacted]				
Disposable drapes (per open surgery)		[redacted]				
Disposable introducers (per laparoscopic surgery)		[redacted]				
Capital cost of machine per surgery (include purchase, replacement and maintenance fees) **		[redacted]				Calculated
ICG dye (per surgery)		[redacted]				BCCSSS
Stoma supplies (year cost)	Gamma	1,210		23,777	0.05	
Hospital Costs up to 6-months (includes surgery costs)		**Mean**	**SE**	**alpha**	**beta**	
Open surgery with stoma and major leak	Gamma	99,039	10,093	979,654	0.10	HTR Office/ DAD/ MSP
Open surgery with stoma and minor leak	Gamma	73,320	4,705	1,151,788	0.06	
Open surgery with stoma and no complication	Gamma	21,948	724	671,112	0.03	
Open surgery without stoma and major leak	Gamma	102,040	16,718	627,785	0.16	
Open surgery without stoma and minor leak	Gamma	49,354	3,721	659,899	0.08	
Open surgery without stoma and no complication	Gamma	13,494	325	564,996	0.02	
Laparoscopic surgery with stoma and major leak	Gamma	110,369	23,227	528,642	0.21	
Laparoscopic surgery with stoma and minor leak	Gamma	54,002	4,143	709,546	0.08	
Laparoscopic surgery with stoma and no complication	Gamma	17,317	602	501,915	0.03	
Laparoscopic surgery without stoma and major leak	Gamma	85,564	31,792	232,128	0.37	
Laparoscopic surgery without stoma and minor leak	Gamma	26,140	995	692,358	0.04	
Laparoscopic surgery without stoma and no complication	Gamma	10,508	161	689,898	0.02	
Hospital Costs from 6 to 12 months (relative to 6 month costs)		**%**				
Open surgery with stoma and major leak		11.03%				HTR Office/ DAD/ MSP
Open surgery with stoma and minor leak		10.62%				
Open surgery with stoma and no complication		23.58%				
Open surgery without stoma and major leak		3.62%				
Open surgery without stoma and minor leak		17.30%				
Open surgery without stoma and no complication		18.33%				
Laparoscopic surgery with stoma and major leak		3.17%				

Laparoscopic surgery with stoma and minor leak		21.61%				
Laparoscopic surgery with stoma and no complication		24.10%				
Laparoscopic surgery without stoma and major leak		15.07%				
Laparoscopic surgery without stoma and minor leak						
Laparoscopic surgery without stoma and no complication		11.47%				
MSP Costs up to 6-months (includes surgery)		**Mean**	**SE**	**alpha**	**beta**	
Open surgery with stoma and major leak	Gamma	11,640	596	228,962	0.05	HTR Office/
Open surgery with stoma and minor leak	Gamma	10,307	388	276,143	0.04	DAD/
Open surgery with stoma and no complication	Gamma	6,016	119	305,425	0.02	MSP
Open surgery without stoma and major leak	Gamma	13,544	1,673	110,542	0.12	
Open surgery without stoma and minor leak	Gamma	8,333	333	209,940	0.04	
Open surgery without stoma and no complication	Gamma	4,110	61	281,228	0.01	
Laparoscopic surgery with stoma and major leak	Gamma	12,650	1,500	107,533	0.12	
Laparoscopic surgery with stoma and minor leak	Gamma	9,102	415	201,197	0.05	
Laparoscopic surgery with stoma and no complication	Gamma	4,979	113	220,474	0.02	
Laparoscopic surgery without stoma and major leak	Gamma	12,913	2,598	64,700	0.20	
Laparoscopic surgery without stoma and minor leak	Gamma	5,750	117	283,683	0.02	
Laparoscopic surgery without stoma and no complication	Gamma	3,492	39	318,175	0.01	
MSP Costs from 6 to 12 months (relative to 6-month costs)		**%**				
Open surgery with stoma and major leak		14.32%				HTR Office/
Open surgery with stoma and minor leak		17.80%				DAD/
Open surgery with stoma and no complication		28.45%				MSP
Open surgery without stoma and major leak		8.38%				
Open surgery without stoma and minor leak		16.91%				
Open surgery without stoma and no complication		26.02%				
Laparoscopic surgery with stoma and major leak		9.85%				
Laparoscopic surgery with stoma and minor leak		27.40%				
Laparoscopic surgery with stoma and no complication		30.59%				
Laparoscopic surgery without stoma and major leak		9.51%				
Laparoscopic surgery without stoma and minor leak		20.89%				
Laparoscopic surgery without stoma and no complication		**25.30%**				

Note: BCCSSS = BC Clinical and Support Services Society database; DAD = discharge abstract data; lb = low boundary; MSP = Medical services plan; SE = standard error; ub = upper boundary.

**See individual capital costs per hospital in Appendix E.

6.3 Results

6.3.1 Costs and outcomes – population level

Without ICGA for colorectal surgeries, for every 1,000 patients submitted to surgery, it is expected that 122 complications would occur, leading to 11 deaths due to major leak and 53 patients who will be left with a permanent stoma. Over a 20-year time horizon, the average QALY score would be 8.51 per patient, with total costs of $29,716 per patient. Of the total costs, $11,692 per patient (39%) would be spent on addressing complications (Table 13).

With intraoperative ICGA, for every 1,000 patients submitted to surgery, these numbers are expected to drop to 71 complications leading to 6 deaths due to major leak and 38 patients left with a permanent stoma. Over a 20-year time horizon, the average QALY score would be 8.56 per patient, with total costs of $28,811 per patient; of this amount, $6,826 per patient (23%) will be spent on complications.

Table 13. Death due to major leak, number of complications, number of permanent stoma, total costs, and total QALY over a 20-year time horizon (per patient).

	Death due major leak	Complications (major + minor)	Permanent stoma	Complication Costs	Total Costs*	QALYs*
No ICGA	0.011	0.122	0.053	$11,692	$29,716	8.510
ICGA	0.006	0.071	0.038	$6,826	$28,811	8.559

Note: QALY = quality –adjusted life years.
* Costs and QALY are discounted.

6.3.2 Incremental costs and outcomes – population level

Over a 20-year time horizon, the use of intraoperative ICGA is cost-saving and associated with positive QALY gains compared to the standard of care in BC (no ICGA). Per every thousand patients submitted to surgery with the use of the technology, 50 complications, 5 deaths* due to major leak and 15 permanent stomas are expected to be avoided and 50 QALYs gained. BC would see a cost saving of $905 per patient, on average (Table 14).

Table 14. Cost-effectiveness of the use of intraoperative ICGA in colorectal surgeries in BC over a 20-year time horizon (results are expressed per patient).

	ICGA vs. no ICGA
ICER / QALY	dominant
ICER / Complications avoided	dominant
ICER / Death avoided	dominant
ICER / Permanent stoma avoided	dominant
Incremental costs	-905
Incremental QALY	0.050
Complications avoided	0.05
Deaths avoided	0.005
Permanent stoma avoided	0.015

Note: ICER = incremental cost-effectiveness ratio; QALY = quality –adjusted life years.
Note: Dominant = the intervention costs less and is at least as effective as the comparator.

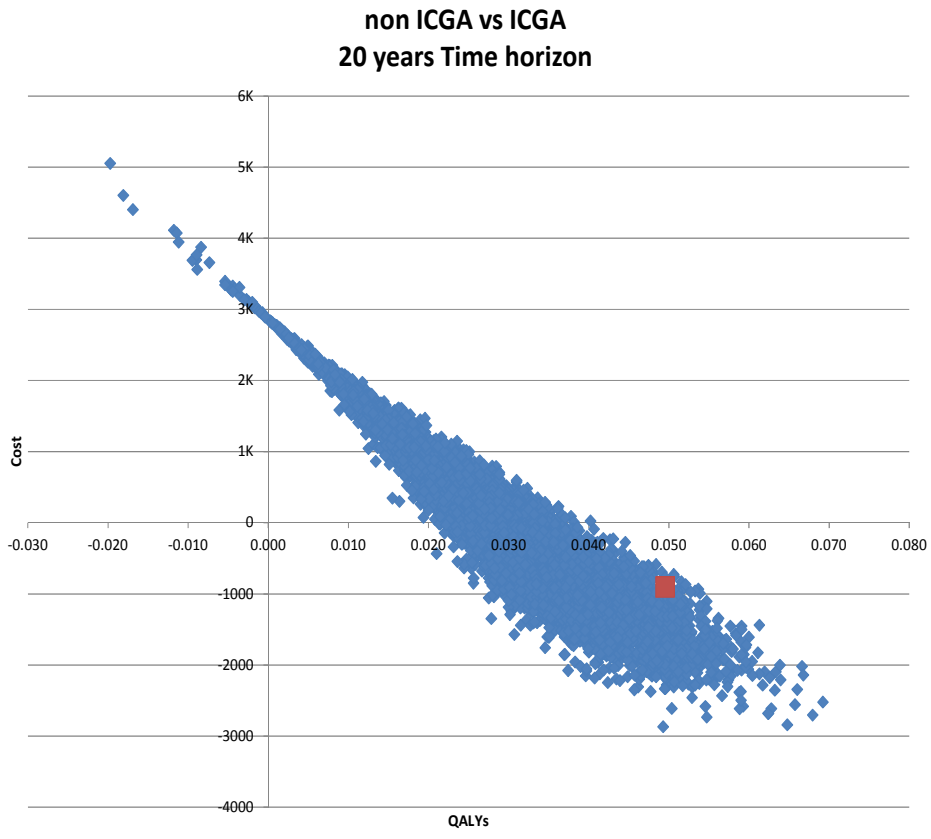
6.3.3 Characterizing uncertainty – probabilistic analysis

The probabilistic model for a 20-year time horizon showed some degree of uncertainty. The cloud in the cost-effectiveness plane spread over three quadrants, but the majority fell into the southeast quadrant, showing that surgery performed with ICGA is usually beneficial and results in lower overall costs when compared to those performed with no ICGA (i.e., the technology is less costly and more effective) (Figure 14). The cost-effectiveness acceptability

* Deaths avoided during the time horizon of the model. If running the model in a lifetime time horizon, eventually every patient will die.

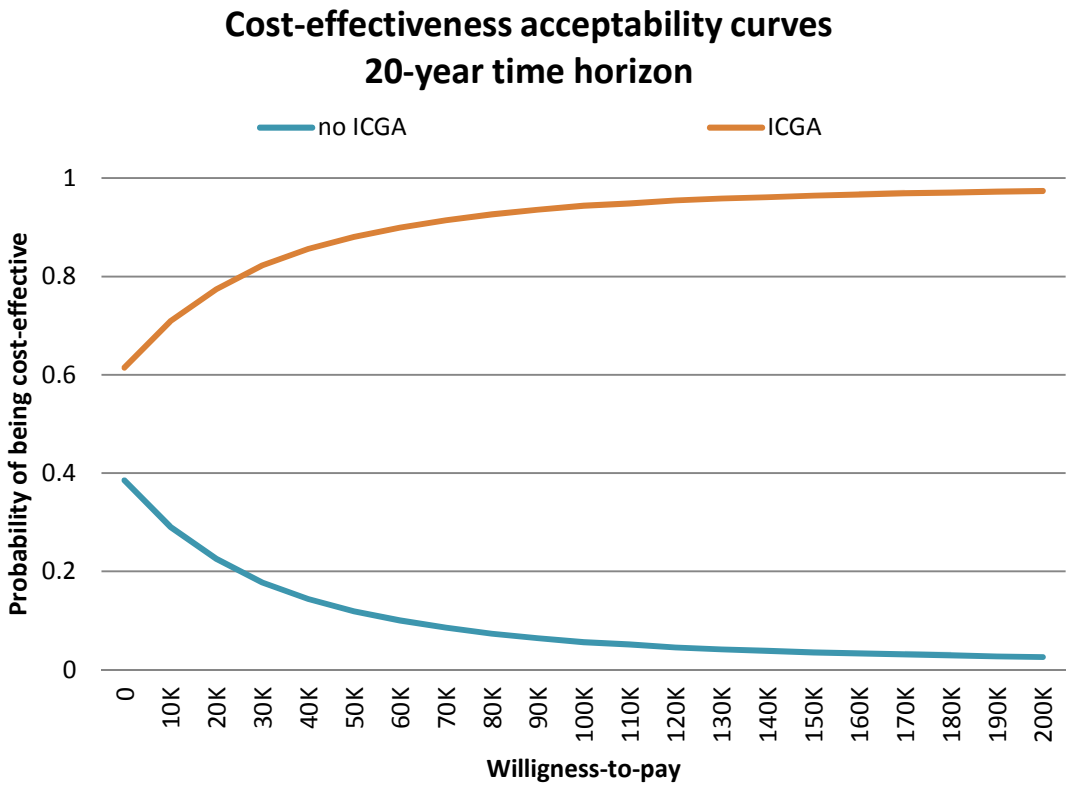
curve (CEAC) quantifies the uncertainty by demonstrating the probable cost-effectiveness of ICGA at a given WTP (Figure 15). Even though in some simulations the surgeries performed with ICGA were associated with lower QALY and higher costs (northwest quadrant in the cost-effectiveness plane), ICGA had a high probability of being cost-effective. For example, for a WTP of $0 per QALY gain in a 20-year period, the probability of ICGA being cost-saving was 61%. At a WTP of $50,000 per QALY gain in a 20-year period, the probability of ICGA being cost-effective was 88%.

Figure 14. Cost-effectiveness plane of probabilistic analysis over a 20-year time horizon.



Note: the red squares represent the ICER from the deterministic analysis.

Figure 15. Cost-effectiveness acceptability curve at different thresholds of willingness-to-pay.



Several deterministic sensitivity analyses were conducted (Table 16) and the results were similar to those from the base-case analysis, with ICGA being dominant in most scenarios.

Some scenarios where the technology would have a positive incremental cost were:

1. *If the baseline leak rates in the BC population undergoing surgery were 70% lower than the values used in the model for the base-case (*Table 15*)*. In this case, surgeries with ICGA would result in an incremental cost per patient of $1,666 and an ICER of $106,142 per QALY gained. This demonstrates that in clinical contexts with extreme low leak rates (2–4%), the use of ICGA might not be considered cost-effective relative to conventionally accepted levels of cost-effectiveness (WTP $50,000/QALY).

Table 15. Leak rates for patients undergoing surgery without ICGA.

	Base-case values		Sensitivity analysis (70% lower)	
Technique	**Stoma**	**No stoma**	**Stoma**	**No stoma**
Open	0.1606	0.1350	0.0482	0.0405
Lap	0.1414	0.0938	0.0424	0.0282

2. *If the effect of the use of ICGA in decreasing leak rates were the minimum effect observed in the clinical studies (upper bound of confidence interval of the pooled OR =0.86)*. In this case, surgeries with ICGA would result in an incremental cost per patient of $1,736 and an ICER of $117,352 per QALY gained.
3. *If the hospital and MSP costs of patients with complications were lower than estimates applied in the model, reducing the gap in costs of patients with or without complications.* For instance, in the base-case analysis, a patient undergoing an open colorectal surgery with a protective stoma and who developed a major complication had a hospital cost almost four times higher than a patient undergoing the same surgery who did not present any complications. A 40% decrease in nominal cost of patients with complication resulted in an incremental costs of using ICGA of $959 and an ICER of $19,358 per QALY gained. At the extreme, if patients with complications cost only 10% more (hospital and MSP costs) than patients with no complications, the incremental cost of using ICGA would reach $2,648 per patient, resulting in an ICER of $53,473 per QALY gained.

4. *If the capital cost per surgery surpasses $[redacted]*. In clinical settings where the capital cost is higher than this threshold, the technology is no longer cost-saving. Two sensitivity analyses with the highest capital costs estimated for the province (Appendix E) produced ICERs of $350,247 per QALY and $83,249 per QALY.
5. *Assuming hospital and MSP costs below the observed average costs*. When assuming median costs instead of average costs, surgeries with ICGA would result in an incremental cost per patient of $404 and an ICER of $8,158 per QALY gained. Assuming the 25th cost percentile instead the ICER per QALY goes to $8,158.

Most of the sensitivity analysis scenarios resulted in ICER estimates that would be considered cost-effective under a WTP of $50,000 per QALY. The cut-off point for capital cost so the ICER falls below the same threshold is approximately $[redacted] per surgery (holding all the other parameters in the model unchanged.) The cut-off point for effectiveness is a decrease in leak rates due to the use of the technology of 21% (OR = 0.785). And if a patient with complications (minor or major) cost at least 30% more (hospital and MSP costs) than a patient without complications, the technology would also be considered cost effective under the same threshold.

Table 16. Univariate deterministic sensitivity analysis.

	ICER / QALY	ICER / complication avoided	ICER / death avoided	ICER / permanent stoma avoided	Incremental costs	Incremental QALY	Complications avoided	Deaths avoided	Permanent stoma avoided
Base-case (20-year time horizon)	dominant	dominant	dominant	dominant	- 905	0.050	0.051	0.005	0.015
Baseline leak rate 30% higher	dominant	dominant	dominant	dominant	- 1,906	0.063	0.06	0.006	0.019
Baseline leak rate 70% lower	106,142	103,551	1,151,508	345,334	1,666	0.016	0.02	0.001	0.005
OR leakage with ICGA 0.35 - lower bound	dominant	dominant	dominant	dominant	- 2,731	0.073	0.08	0.007	0.023
OR leakage with ICGA 0.86 - upper bound	117,352	114,531	1,273,609	381,617	1,736	0.015	0.02	0.001	0.005
OR excluding Spy study (OR 0.38)	dominant	dominant	dominant	dominant	- 2,450	0.070	0.07	0.006	0.021
OR excluding robotic studies (OR 0.65)	dominant	dominant	dominant	dominant	- 29	0.038	0.04	0.004	0.012
100% cancer patients	dominant	dominant	dominant	dominant	- 868	0.043	0.05	0.005	0.015
100% non-cancer patients	dominant	dominant	dominant	dominant	- 995	0.067	0.05	0.005	0.015
100% open surgeries	dominant	dominant	dominant	dominant	- 1,604	0.056	0.06	0.005	0.017
100% laparoscopic surgeries	dominant	dominant	dominant	dominant	- 6	0.041	0.04	0.004	0.013
10-year time horizon	dominant	dominant	dominant	dominant	- 843	0.033	0.05	0.005	0.015
Lifetime time horizon	dominant	dominant	dominant	dominant	- 944	0.060	0.05	0.005	0.015
Discount 0%	dominant	dominant	dominant	dominant	- 952	0.062	0.05	0.005	0.015
Discount 5%	dominant	dominant	dominant	dominant	- 882	0.044	0.05	0.005	0.015
20% decrease in cost of complications	540	527	5,863	1,757	27	0.050	0.05	0.005	0.015
40% decrease in costs of complications	19,358	18,890	210,057	62,963	959	0.050	0.05	0.005	0.015
Hospital and MSP costs of complications only 10% higher than costs with no complications	53,473	52,179	580,243	173,922	2,648	0.050	0.05	0.005	0.015
Capital cost per surgery = [redacted]	350,247	341,775	3,800,607	1,139,194	17,343	0.050	0.05	0.005	0.015

	ICER / QALY	ICER / complication avoided	ICER / death avoided	ICER / permanent stoma avoided	Incremental costs	Incremental QALY	Complications avoided	Deaths avoided	Permanent stoma avoided
Capital cost per surgery = [redacted]	83,249	81,235	903,350	270,770	4,122	0.050	0.05	0.005	0.015
Median hospital and MSP costs (instead of average)	8,158	7,961	88,523	26,534	404	0.050	0.05	0.005	0.015
25th percentile hospital and MSP costs (instead of average)	33,881	33,062	367,654	110,201	1,678	0.050	0.05	0.005	0.015
75th percentile hospital and MSP costs (instead of average)	dominant	dominant	dominant	dominant	- 2,208	0.050	0.05	0.005	0.015

Note: ICER = incremental cost-effectiveness ratio; ICGA = indocyanine green fluorescence angiography; MSP = BC Medical Services Plan; OR = odds ratio; QALY = quality-adjusted life years.

6.4 Discussion

Incorporating the best available evidence into a decision-analytic simulation model showed that the use of intraoperative ICGA in colorectal surgeries for bowel perfusion assessment is likely cost-saving or cost-effective in the majority of the simulated scenarios compared with the current standard of care (visual clinical judgment) at a wide range of WTP values for a QALY.

The economic analysis has some limitations due to no RCT comparing ICGA to clinical judgment available. The effectiveness estimates came from comparative non-randomized studies with risk of selection bias and performance bias. Although the effect on anastomotic leakage was statistically significant, it was not possible to rule out the effect of confounders. These risks are common in surgical observational studies, and these biases could still significantly affect the estimates. Therefore, readers must interpret the results with caution, and perhaps adopt the technology under a controlled trial to assess if the effectiveness of the ICGA and the baseline leak rates in control groups would be within the range modelled in this economic evaluation (baseline leak rates in colorectal surgeries between 2.8% and 16%, and decrease in leak rates due to the technology adoption are at least 21%).

Also, despite our best efforts to include the relevant costs associated with the use of the technology, downstream costs with the treatment of baseline diseases beyond one year after surgery were not included in the analysis. For instance, cancer treatment occurring in hospital in the first year after surgery is captured in the cost data. However, if the decrease in leaks after colorectal cancer resection decreases recurrence of disease, and consequent cancer treatment

costs after one year, these are not reflected in the economic estimates. Therefore, the cost savings of the complications avoided could be underestimated.

Additionally, the hospital and MSP cost estimates for patients with and without complications were based on administrative data not collected for research purposes and several assumptions in coding practices. Some published data from other countries on the cost of leaks showed great variability between settings and there is no standardized way of measuring those costs (Table 17). Despite that, costs associated with complications are substantially increased in every setting. The estimated costs attributed to complications in our model (39%) are similar to the costs of complications in 29 different hospitals in the Netherlands (31%). (50) Sensitivity analysis with extreme low values of relative costs for complications showed the technology would still be considered cost-effective.

Table 17. Cost of complications of colorectal surgeries in different settings

Outcome	With leak or complications	Without leak or complications	Ratio compared to no leak/no complications	$ year	Location
HTR Data – hospital costs, initial admission costs, do not include MSP) - range				CAD$ 2014/2015	BC HTR Data(5)
Major leak	$71,407 to $101,000	$9,340 to $16,717	4.9 to 8		
Minor leak	$19,121 to $53,980		2 to 3.5 uncontrolled		
HTR Data – hospital costs, 6 months costs, do not include MSP) - range				CAD$ 2014/2015	BC HTR Data(5)
Major leak	$85,564 to $102,040	$10,508 to $21,948	4.5 to 8.14		
Minor leak	$26,140 to $73,320		2.48 to 3.65 uncontrolled		
Inpatient costs (not sure if includes physician costs) – include all complications (leakage, reoperation, infection, DVT, respiratory infections)				AUS$ 2009	AUS and NZ Gordon 2010 (51)
Rectal resection with complications (30 days)	$33,277	$18,094	1.83		
Colon procedures with complications (30 days)	$30,899	$14,283	2.16 uncontrolled		
Mean cost savings for an intervention decreasing complications in 25% (small effect)		$24,960			
In hospital costs (included initial surgery and re-admission in 30 days; includes all supplies, labor, and depreciation of equipment, overhead costs)	Mean $72,905 (sd 94,723)	Mean $44,308 (sd 52,168)	Regression model after controlling all covariates showed costs of patients with leak were 0.8 times higher	Jan2008-Dec 2010	USA (600 hospitals, 99,879 patients)
Anastomotic leaks in colorectal surgery increase the total clinical and economic burden by a factor of 0.6–1.9 for a 30-day re-admission, postoperative infection, LOS, and hospital costs.				Not clear if adjusted for 2010 US$	Hammond 2014(52)
Mean total cost per discharge	$37,042	$13,674	2.7	US$ 2009	USA

Outcome	With leak or complications	Without leak or complications	Ratio compared to no leak/no complications	$ year	Location
(not much detail of what this cost includes or how long was the follow-up)			uncontrolled		Hashemi 2012(53)
Costs with complications after colorectal cancer surgeries (costs of primary admissions and the 90 days after discharge)			Mixed model with random effects	€ 2012	Netherlands (29 hospitals, 6,768 patients) Govaert 2015(50)
Minor complications	€9,061 Increase in 21% in the primary admission and 47% after discharge compared to no complications	No complications €7,470			
Major complications (include pulmonary, neurologic, infections, etc.**)**	€23,616 Increase in 216% in the primary admission and 109% after discharge compared to no complications		1–2.1		
Anastomotic leakage	€33,486	No leakage € 11,821	3		

Note: sd = standard deviation

Chapter 7 Budget Impact

Summary

The BC health care system should expect a progressive increase in the number of primary colorectal surgeries due to population growth and aging. Policy changes that lead to decreased complications from these surgeries can substantially reduce costs and mortality. Implementing intraoperative ICGA can be cost-saving. Due to efficiency aspects, the average capital cost of ICGA can range from $[redacted] to $[redacted] per surgery.

If implemented in high-volume hospitals, the technology can reduce mortality by 32 percent, and the incremental costs with the new technology ($85.9 million over 20 years) are expected to be immediately offset by cost savings related to complications, assuming those resources could be reallocated. Implementing ICGA in every hospital in BC would have a higher incremental cost for the new technology ($144.9 million), and could still be offset by complications avoided.

Health authorities should expect peaks of incremental costs with the technology in the acquisition year and replacement year (10-year depreciation assumed) beyond the costs of dye, disposables, and annual maintenance of the machines.

7.1 Objective

To evaluate the budget impact of a policy change in BC to incorporate the use of intraoperative ICGA in colorectal surgeries using the Spy imaging system.

7.2 Methods

Three scenarios were created to evaluate the budget impact in BC:

1. The status quo scenario represents the current clinical practice with no near-infrared cameras in place for ICGA during colorectal surgeries.
2. Scenario A assumes a Spy imaging system would be available for every colorectal surgery performed in BC as required (open or laparoscopic system).
3. Scenario B assumes a Spy imaging system would be available for colorectal surgeries performed in high-volume hospitals (those where volume of surgery ≥ the average number of surgeries per year among BC hospitals) and/or teaching

hospitals (clinical academic campuses) (54). This scenario was created to evaluate a measured incorporation of the technology, as these sites might be able to collect data to further the research in this area and mitigate the risks of early adoption under non-optimal levels of evidence. Costs of a formal research process (data collection, analysis, etc.) were not included. The list of BC hospitals with and without an academic affiliation can be found in Appendix E.

In all scenarios, it was assumed that all health care costs, including cost of the devices, were paid by the public health care system.

The same Markov model as in the economic evaluation (Figure 13) was used for budget impact analysis. However, the model was configured to simulate the dynamic population impact over 20 years (2018 to 2037). The subgroup weights were assigned based on Statistics Canada's projected population growth and aging during this period. (55)

It was assumed that surgery capacity would accommodate all the projected colorectal surgeries of the aging population, based initially on the numbers of surgeries performed in 2014/2015 (1). Capital costs with the devices acquisition and yearly maintenance per machine were included, and assumed to incur under the budget for the health authorities. The overall budget impact on the province is presented, as well as an estimation for the health authority and MSP portions.

Number of surgeries and costs were not discounted, and inflation was not applied following the ISPOR guidelines for budget impact (56). Costs were expressed in 2015 Canadian dollars. No changes in price units during the period were assumed (meaning that any nominal change in price in the future would equate to the inflation rate).

Total numbers of complications and permanent stomas avoided, deaths avoided after major leakage, total costs, and costs with ICGA equipment and disposables were the outcomes of interest.

7.3 Results

Table 18 shows the main results for the budget impact evaluation. Given the growth and aging of the population in BC, it is estimated that the number of colorectal surgeries will increase from 5,182 surgeries per year in 2018 to 7,297 surgeries per year in 2037 (relative change of 41 percent), for a total of 126,005 primary surgeries over 20 years. Results for each year are available in Appendix G.

7.3.1 Status quo

For the status quo scenario in BC (no use of ICGA during surgeries), the health care costs to treat patients requiring colorectal surgeries (and their short-term consequences) was estimated to be $3.7 billion over 20 years. It was predicted to increase from $151.1 million per year in 2018 to $217 million per year in 2037 (Table 18). This scenario predicted 15,340 complications (major and minor leaks), 1,379 deaths due to major leaks, and 5,842 patients surviving with a permanent stoma. Estimates for each individual year are available in Appendix G.

7.3.2 Intraoperative ICGA in 100% of colorectal surgeries (Scenario A)

Incorporating the use of ICGA in every hospital in BC, to be used in 100% of colorectal surgeries performed are expected to avoid 6,394 complications, 575 deaths after major leaks[1] and 1,745 permanent stomas. The expected budget impact over 20 years is a net saving of $279.3 million to the health authorities, and $42.7 million in physician fees representing an overall net saving of $322.0 million for the health care system over 20 years due to fewer complications (Table 18).

The annual budget impact decreases over time, from an additional $7.9 million in 2018 to $22 million in savings in 2037 as a result of the reduced health care costs associated with complications (hospital admissions, surgeries, stoma supplies, physicians' fees, etc.).

Savings due to physician fees associated with the management of those patients after the initial surgery were predicted to immediately drop by $1.8 million in 2018 and continue to drop by $2.5 million in 2037.

The increase in costs with ICGA devices and disposables in the acquisition years (2018 and 2028) were estimated to be $26.6 to 27.2 million. The costs with the devices maintenance and ICGA disposables in the years in between acquisition ranged from $4.5–5.6 million (Appendix G). Incremental costs for health authorities in years 1 and 11 of $9.7 million and $5.7 million, respectively, are expected due to device acquisition and replacements and turn to cost-saving every year after that. However, the costs with the new technology are expected to be

[1] Deaths avoided during the time horizon of the model. If running the model in a lifetime time horizon, eventually every patient will die.

completely offset over 20 years by the decrease in costs with complications, assuming a reallocation of those resources to the purchase of ICGA devices and disposables.

7.3.3 Intraoperative ICGA in teaching hospitals (Scenario B)

Incorporating the use of ICGA only in high-volume and/or teaching hospitals in BC, would provide ICGA in 77.9 percent of all surgeries and be expected to avoid 4,982 complications, 448 deaths[2] from major leaks and 1,359 permanent stomas were expected to be avoided. The weighted-averaged capital costs of ICGA per surgery decreases from $[redacted] to $[redacted] due to greater efficiency in the application of the technology. The expected budget impact over 20 years is a net saving of $244.7 million for the health authorities, $33.2 million in physician fees related representing an overall net saving of $277.9 million to the health system (Table 18) due to fewer complications.

The annual budget impact shows immediate cost savings of $2.3 million in 2018 to $17.7 million in 2037 as a result of the reduced costs associated with complications (hospital admissions, surgeries, stoma supplies, physician fees, etc.).

Savings in physician fees associated with the management of those patients after the initial surgery are expected to immediately drop $1.4 million in 2018 to $1.9 million in 2037.

The increase in costs with ICGA devices and disposables in the acquisition years (2018 and 2028) are estimated to be $12.3 to 12.8 million. The costs of device maintenance and ICGA disposables in the years in between acquisition ranged from $2.9 to $3.8 million (Appendix G).

[2] Deaths avoided during the time horizon of the model. If running the model in a lifetime time horizon, eventually every patient will die.

Incremental costs for health authorities in years 1 (2018) and 11 (2028) for device acquisition and replacement are completely offset by cost avoidances due to reduced complications, assuming a reallocation of those resources.

Table 18. Total costs and annual budget impact for BC for management of colorectal surgeries and its consequences in year 1 and 11 (when machines are expected to be purchased and replaced), year 2,12,20 (costs with disposables and maintenance), and cumulative over 20 years.

		2018	2019	2028	2029	2037	Total	2018–2037
Scenario	Volume of primary surgeries	5,182	5,307	6,379	6,494	7,297		126,005
Status quo no ICGA	N. deaths due leak	57	58	70	71	80		1,379
	N. Complications	631	646	777	791	888		15,340
	N. Permanent stomas	242	248	296	301	337		5,842
	Total health care cost	151.1 M	155.0 M	188.3 M	191.8 M	217.0 M		3.7 B
	MSP Portion	30.3 M	31.0 M	37.3 M	38.0 M	42.7 M		737.2 M
	HA Portion	120.8 M	123.9 M	150.9 M	153.8 M	174.3 M		3.0 B
ICGA in 100% of colorectal surgeries	N. Deaths due Leak	33	34	41	41	47		804
	Impact on Mortality	-24	-24	-29	-30	-33		-575
	N. Complications	368	377	453	461	518		8946
	Impact on Complications	-263	-269	-324	-330	-370		-6394
N. machines required	N. Permanent stomas	170	174	207	211	236		4097
	Impact on Stomas	-72	-74	-88	-90	-101		-1745
[redacted]**Spy Elite**	Health Care Cost	135.3 M	138.7 M	168.1 M	171.2 M	193.4 M		3.3 B
	MSP Portion	28.6 M	29.3 M	35.2 M	35.8 M	40.2 M		694.5 M
[redacted]**Spy Pinpoint**	HA Portion	106.7 M	109.4 M	132.9 M	135.4 M	153.2 M		2.6 B
	Capital costs with acquisitions	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
	Capital costs with maintenance	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
	Total Health Care + Capital Costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
	Total Budget Impact compared to Status Quo	7.9 M	-14.7 M	3.6 M	-19.0 M	-22.0 M		-322.0 M
	MSP Budget Impact compared to Status Quo	-1.8 M	-1.8 M	-2.2 M	-2.2 M	-2.5 M		-42.7 M
	HA Budget Impact compared to Status Quo	9.7 M	-12.9 M	5.7 M	-16.8 M	-19.5 M		-279.3 M
	ICGA Costs Disposables	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
	Total ICGA Costs (Disposables + Capital Costs)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
	Cost Avoided with Complications (Health System)	-18.7 M	-19.2 M	-23.7 M	-24.1 M	-27.6 M		-466.9 M
	HA Cost Avoided with Complications	-16.9 M	-17.4 M	-21.5 M	-21.9 M	-25.1 M		-424.2 M

		2018	2019	2028	2029	2037	Total 2018–2037
ICGA in 77.9% of colorectal surgeries **[redacted]Spy Elite** **[redacted]Spy Pinpoint**	N. deaths due to leak	38	39	47	48	54	931
	Impact on mortality	-18	-19	-23	-23	-26	-448
	N. Complications	426	436	524	534	600	10358
	Impact on Complications	-205	-210	-252	-257	-289	-4982
	N. Permanent stomas	186	190	227	231	258	4483
	Impact on Stomas	-56	-58	-69	-70	-78	-1359
	Health care cost	138.8 M	142.3 M	172.5 M	175.8 M	198.6 M	3.4 B
	MSP portion	29.0 M	29.6 M	35.6 M	36.3 M	40.8 M	704.0 M
	Health authority portion	109.8 M	112.6 M	136.9 M	139.5 M	157.9 M	2.7 B
	Capital costs with acquisitions	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Capital costs with maintenance	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Total health care + capital costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Total budget impact compared to status quo	-2.3 M	-12.0 M	-5.6 M	-15.4 M	-17.7 M	-277.9 M
	MSP budget impact compared to status quo	-1.4 M	-1.4 M	-1.7 M	-1.7 M	-1.9 M	-33.2 M
	HA budget impact compared to status quo	-902.8 K	-10.6 M	-4.0 M	-13.7 M	-15.8 M	-244.7 M
	ICGA costs disposables	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Total ICGA costs (disposables + capital costs)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Cost Avoided with Complications (Health System)	-14.6 M	-15.0 M	-18.4 M	-18.8 M	-21.5 M	-363.8 M
	HA Cost Avoided with Complications	-13.2 M	-13.6 M	-16.8 M	-17.1 M	-19.6 M	-330.6 M

7.4 Discussion

The budget impact analysis considered population growth and aging in BC over the next 20 years. In the status quo scenario, the health care system could expect an average increase of two percent per year in the number of colorectal surgeries, assuming the prevalence of diseases leading to surgery remains the same within each age subgroup. The anticipated cost over this time is around $3.7 billion, with 1,379 deaths after major leaks.

Complications, especially anastomotic leaks, can have a substantial impact on costs (50). Policy changes incorporating the use of intraoperative ICGA can decrease mortality and costs for the province and health authorities due to complications avoided. The average capital costs of ICGA per surgery can range from $[redacted] (if implemented in every hospital without distinction) to $[redacted] per surgery (if implemented in high-volume hospitals only where each machine will have higher usage). If implemented in high-volume hospitals only, the incremental costs of the new technology ($85.9 million over 20 years) is expected to be immediately offset by the cost savings in hospital care and physician fees due to complications avoided (estimated at $277.9 million assuming there will be reallocation of those resources), and mortality due to complications is expected to decrease 32 percent. If implemented in every hospital thorough BC, the incremental costs with the new technology ($144.9 million over 20 years) are still offset over time by the costs of complications avoided ($322.0 million, assuming those resources will be reallocated), and mortality due to complications is estimated to decrease 42 percent. However, two peaks of incremental costs for the health authorities, of $9.7 million and 5.7 million, are expected in year 1 and year 11 of the technology implementation due to device

acquisition and replacements. Costs associated with the downstream treatment of baseline diseases beyond one year after surgery is not included in the analysis.

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Appendix A Search strategies

A.1 Medline

Database: ePub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
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1 Fluorescein Angiography/ (20545)
2 (fluoresce$ adj6 (angiograph$ or videoangiograph$)).mp. (24200)
3 1 or 2 (24200)

4 Angiography/ (57905)
5 angiography, digital subtraction/ or cerebral angiography/ or coronary angiography/ (93329)
6 angiography.mp. (240863)
7 video angiograph$.mp. (126)
8 videoangiograph$.mp. (362)
9 microscopy, fluorescence/ or microscopy, fluorescence, multiphoton/ (73076)
10 surgery, computer-assisted/ or robotic surgical procedures/ (14548)
11 diagnosis, computer-assisted/ or image interpretation, computer-assisted/ (58498)
12 or/4-11 (382014)

13 Fluorescent Dyes/ (64059)
14 Indocyanine Green/ (6150)
15 or/13-14 (69799)

16 Coloring Agents/ (43265)
17 Fluorescent Dyes/ (64059)
18 Coloring Agents/ (43265)
19 Indocyanine Green/ (6150)
20 Fluorescence/ (36244)
21 Indocyanine Green.mp. (9284)
22 fluoresce$.mp. (653110)
23 or/16-22 (694064)

24 bs.fs. [blood supply] (324233)
25 Regional Blood Flow/ (62379)
26 mt.fs. [methods] (3125056)
27 or/24-26 (3408926)

28 su.fs. [surgery] (1756091)

29 exp surgical procedures, operative/ or reconstructive surgical procedures/ (2739671)
30 Intraoperative Care/ or Monitoring, Intraoperative/ or Intraoperative Period/ (44263)
31 intra operative.mp. (10086)
32 intraoperative.mp. (137821)
33 or/28-32 (3338140)

34 3 and (15 or 27 or 33) (11073)
35 12 and 23 and (27 or 33) (36107)
36 15 and 27 and 33 (2619)
37 or/34-36 (38710)

38 limit 37 to yr="2002 -Current" (27029)
39 limit 38 to English language (26021)
40 limit 38 to humans (15340)
41 comment/ or editorial/ or letter/ or news/ (1705805)
42 40 not 41 (14595)

43 SPY Elite.mp. (14)
44 (SPY adj40 angiography).mp. (35)
45 (SPY adj50 (fluoresce$ or imag$ or system)).mp. (125)
46 I-SPY.mp. (42)
47 (SPY adj40 surgery).mp. (12)
48 (SPY adj40 green).mp. (47)
49 (SPY adj2 machine).mp. (2)
50 (pinpoint adj10 (system or imag$ or fluoresce$)).mp. (203)
51 or/43-50 [SPY system] (369)
52 FDPM imager.mp. (0)
53 Mini FLARE.mp. (12)
54 photodynamic eye.mp. (31)
55 hypereye medical system.mp. (15)
56 fluobeam.mp. (14)
57 ic-view.mp. (11)
58 visual navigator.mp. (2)
59 prototype surgical navigation system.mp. (0)
60 leica fl800.mp. [article in Spanish] (1)
61 infrared 800.mp. (24)
62 (firefly adj7 (system or surgical or surgery or robotic or da vinci)).mp. (165)
63 laparoscopic near-infrared fluorescence system.mp. (0)
64 Near-Infrared Fluorescence Imaging.kw. (40)
65 (laparoscopic and near-infrared fluorescence).mp. (61)
66 64 or 65 (96)
67 or/43-66 (731)

68 limit 67 to yr="2002 -Current" (617)
69 limit 68 to English language (597)
70 limit 69 to humans (318)
71 comment/ or editorial/ or letter/ or news/ (1705805)
72 70 not 71 (313)

73 or/42,72 (14803)

74 exp *eye/ (241486)
75 exp *Ophthalmologic Surgical Procedures/ (71416)
76 exp *Eye Diseases/ (425949)
77 exp *Visual Acuity/ (14827)
78 or/74-77 [Ophthaolmology] (593438)
79 73 not 78 [Search results before filters] (9848)

Reviews
80 limit 79 to "reviews (maximizes specificity)" (31)

81 limit 79 to systematic reviews (68)

82 meta-analysis/ (74900)
83 meta-analysis as topic/ (15527)
84 technology assessment, biomedical/ or technology, high-cost/ (9870)
85 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf,kw. (105659)
86 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf,kw. (17171)
87 (data synthes* or data extraction* or data abstraction*).ti,ab,kf,kw. (18434)
88 (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf,kw. (19382)
89 (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf,kw. (6897)
90 (meta regression* or metaregression*).ti,ab,kf,kw. (4875)
91 (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp. (186585)
92 (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. (139980)
93 (cochrane or (health adj2 technology assessment) or evidence report).jw. (20689)
94 (comparative adj3 (efficacy or effectiveness)).ti,ab,kf,kw. (9629)
95 (outcomes research or relative effectiveness).ti,ab,kf,kw. (7058)
96 ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab,kf,kw. (1460)
97 or/82-96 [CADTH SR Filter] (307872)

98 79 and 97 (62)

99 Meta-Analysis as Topic/ (15527)
100 meta analy$.tw. (104170)
101 metaanaly$.tw. (1695)
102 Meta-Analysis/ (74900)
103 (systematic adj (review$1 or overview$1)).tw. (93419)
104 exp Review Literature as Topic/ (9154)
105 or/99-104 (191835)
106 cochrane.ab. (51572)
107 embase.ab. (52648)
108 (psychlit or psyclit).ab. (907)
109 (psychinfo or psycinfo).ab. (15194)
110 (cinahl or cinhal).ab. (17547)
111 science citation index.ab. (2770)
112 bids.ab. (419)
113 cancerlit.ab. (637)
114 or/106-113 (83702)
115 reference list$.ab. (14541)
116 bibliograph$.ab. (14429)
117 hand-search$.ab. (5273)
118 relevant journals.ab. (1067)
119 manual search$.ab. (3276)
120 or/115-119 (34645)
121 selection criteria.ab. (27817)
122 data extraction.ab. (14110)
123 121 or 122 (39574)
124 Review/ (2209340)
125 123 and 124 (27462)
126 comment/ or editorial/ or letter/ (1539003)
127 animal/ not (animal/ and human/) (4301359)
128 or/126-127 (5779179)
129 105 or 114 or 120 or 125 (229969)
130 129 not 128 [SIGN SR Filter] (217485)

131 79 and 130 (37)

132 80 or 81 or 98 or 131 (93)

133 limit 79 to "reviews (best balance of sensitivity and specificity)" (1151)

134 133 not 132 (1081)

135 79 not (132 or 134) [Remaining ref once reviews removed] (8674)

RCTs

136 limit 135 to "therapy (best balance of sensitivity and specificity)" (109)

137 Randomized Controlled Trial.pt. (434179)
138 Pragmatic Clinical Trial.pt. (438)
139 randomized controlled trials as topic/ or intention to treat analysis/ or pragmatic clinical trials as topic/ (112919)
140 Randomized Controlled Trial/ (434179)
141 Randomization/ (89435)
142 Random Allocation/ (89435)
143 Double-Blind Method/ (140059)
144 Double-Blind Studies/ (140059)
145 Single-Blind Method/ (23017)
146 Single-Blind Studies/ (23017)
147 Placebos/ (33758)
148 (random* or sham or placebo*).ti,ab,hw,kf,kw. (1213324)
149 ((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw. (204699)
150 ((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw. (586)
151 or/137-150 [CADTH RCT Filter] (1236978)

152 135 and 151 (283)

153 Randomized Controlled Trials as Topic/ (111217)
154 randomized controlled trial/ (434179)
155 Random Allocation/ (89435)
156 Double Blind Method/ (140059)
157 Single Blind Method/ (23017)
158 clinical trial/ (506784)
159 clinical trial, phase i.pt. (16806)
160 clinical trial, phase ii.pt. (27366)
161 clinical trial, phase iii.pt. (12068)
162 clinical trial, phase iv.pt. (1261)
163 controlled clinical trial.pt. (91862)
164 randomized controlled trial.pt. (434179)
165 multicenter study.pt. (213454)
166 clinical trial.pt. (506784)
167 exp Clinical Trials as topic/ (304628)
168 or/153-167 (1172767)
169 (clinical adj trial$).tw. (278519)
170 ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw. (149065)
171 PLACEBOS/ (33758)
172 placebo$.tw. (186419)

173 randomly allocated.tw. (21686)
174 (allocated adj2 random$).tw. (24564)
175 or/169-174 (513706)
176 168 or 175 (1371367)
177 letter/ (945129)
178 historical article/ (342845)
179 case report.tw. (249142)
180 or/177-179 (1523667)
181 176 not 180 [SIGN RCT Filter] (1339172)

182 135 and 181 (401)

183 or/136,152,182 [RCT references] (558)

184 135 not 183 [Remaining ref once reviews & RCTs removed] (8116)

185 limit 184 to "economics (best balance of sensitivity and specificity)" (193)

186 Economics/ (26809)
187 exp "Costs and Cost Analysis"/ (203717)
188 Economics, Nursing/ (3944)
189 Economics, Medical/ (8939)
190 Economics, Pharmaceutical/ (2660)
191 exp Economics, Hospital/ (21941)
192 Economics, Dental/ (1892)
193 exp "Fees and Charges"/ (28635)
194 exp Budgets/ (13001)
195 budget*.ti,ab,kf. (23387)
196 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. (183054)
197 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 (216180)
198 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf. (120258)
199 (value adj2 (money or monetary)).ti,ab,kf. (1758)
200 exp models, economic/ (12206)
201 economic model*.ab,kf. (2460)
202 markov chains/ (11693)
203 markov.ti,ab,kf. (16608)
204 monte carlo method/ (23412)
205 monte carlo.ti,ab,kf. (38300)

206 exp Decision Theory/ (10636)
207 (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. (16957)
208 or/186-207 [CADTH Econ Filter] (587619)

209 184 and 208 (145)

210 Economics/ (26809)
211 "costs and cost analysis"/ (44800)
212 Cost allocation/ (1995)
213 Cost-benefit analysis/ (68350)
214 Cost control/ (21073)
215 Cost savings/ (10095)
216 Cost of illness/ (21441)
217 Cost sharing/ (2177)
218 "deductibles and coinsurance"/ (1568)
219 Medical savings accounts/ (501)
220 Health care costs/ (32258)
221 Direct service costs/ (1116)
222 Drug costs/ (13699)
223 Employer health costs/ (1083)
224 Hospital costs/ (9164)
225 Health expenditures/ (15883)
226 Capital expenditures/ (1973)
227 Value of life/ (5529)
228 exp economics, hospital/ (21941)
229 exp economics, medical/ (13990)
230 Economics, nursing/ (3944)
231 Economics, pharmaceutical/ (2660)
232 exp "fees and charges"/ (28635)
233 exp budgets/ (13001)
234 (low adj cost).mp. (36024)
235 (high adj cost).mp. (10452)
236 (health?care adj cost$).mp. (7048)
237 (fiscal or funding or financial or finance).tw. (108862)
238 (cost adj estimate$).mp. (1815)
239 (cost adj variable).mp. (38)
240 (unit adj cost$).mp. (1981)
241 (economic$ or pharmacoeconomic$ or price$ or pricing).tw. (224513)
242 or/210-241 [SIGN Economic Filter] (574390)

243 184 and 242 (85)

244 or/185,209,243 [Economic References] (270)

245 184 not 244 [Remaining ref once reviews & RCTs & Econ removed] (7846)

246 Epidemiologic studies/ (7322)
247 exp case control studies/ (822757)
248 exp cohort studies/ (1606365)
249 Case control.tw. (100171)
250 (cohort adj (study or studies)).tw. (130025)
251 Cohort analy$.tw. (5312)
252 (Follow up adj (study or studies)).tw. (43160)
253 (observational adj (study or studies)).tw. (67637)
254 Longitudinal.tw. (184162)
255 Retrospective.tw. (370544)
256 Cross sectional.tw. (239422)
257 Cross-sectional studies/ (230182)
258 or/246-257 [SIGN Observational Filter] (2342972)

259 245 and 258 [Observational references] (506)

260 245 not 259 [Remaining ref once reviews & RCTs & Econ & Obs removed] (7340)

SPY M9 Other #1
261 exp Breast/ (41006)
262 260 and 261 (46)
263 su.fs. [surgery] (1756091)
264 260 and 263 (637)
265 "Indocyanine Green"/ (6150)
266 260 and 265 (427)
267 Reconstructive Surgical Procedures/ (40532)
268 Surgery, Plastic/ (25047)
269 267 or 268 (62575)
270 260 and 269 (25)
271 262 or 264 or 266 or 270 (823)
272 260 not 271 (6517)
273 fluorescein angiography/ (20545)
274 272 and 273 (75)

275 262 or 264 or 266 or 270 or 274 (898)
276 260 not 275 (6442)

SPY M9 Other #2
277 exp Neoplasms/ (2919562)
278 276 and 277 (1578)

SPY M9 Other #3

279 276 not 278 (4864)

Search Summary

Reviews
132 80 or 81 or 98 or 131 (93)

133 limit 79 to "reviews (best balance of sensitivity and specificity)" (1151)

134 133 not 132 (1081)

RCT References
183 or/136,152,182 [RCT references] (558)

Economic References
244 or/185,209,243 [Economic References] (270)

Observational References
259 245 and 258 [Observational references] (506)

Other References
260 245 not 259 [Remaining ref once reviews & RCTs & Econ & Obs removed] (7340)

A.2 Embase

Database: Embase <1974 to 2016 October 13>
Search Strategy:
---

1 indocyanine green angiography/ (2886)
2 indocyanine green fluorescence angiography/ (2)
3 near infrared indocyanine green fluorescence angiography/ (1)
4 intraoperative indocyanine green fluorescence angiography/ (1)
5 laser assisted indocyanine green fluorescence angiography/ (1)
6 or/1-5 (2887) [Search #1]

7 fluorescence imaging/ or autofluorescence imaging/ or voltage sensitive dye imaging/ (16384)
8 fluorescence imaging system/ (379)
9 fluorescence angiography/ (17445)
10 Spy fluorescent imaging system/ (1)
11 exp angiography/ (353803)
12 or/7-11 (369744)

13 indocyanine green/ (10036)
14 12 and 13 (3313)

15 6 or 14 (5285) [Search #2]

16 exp surgery/ (4164879)
17 intra operative.mp. (17645)
18 intraoperative.mp. (138556)
19 su.fs. [Surgery] (1851200)
20 or/16-19 (4575531)

21 6 and 20 (1095) [Search #1 & Surgery]

22 12 and 13 and 20 (1920) [Search #2 & Surgery]

23 21 or 22 (2526) [Search #1 or #2 & Surgery]

24 exp perfusion/ (242529)
25 vascularization/ (143833)
26 blood flow/ (78961)
27 artery blood flow/ (14263)
28 vein blood flow/ or portal vein blood flow/ (12168)
29 exp organ blood flow/ (153532)
30 or/24-29 (567659)

31 6 and 30 (440) [Search #1 & Perfusion]

32 12 and 13 and 30 (756) [Search #2 & Perfusion]

33 31 or 32 (966) [Search #1 or #2 & Perfusion]

34 23 or 33 (2871) [Total Search #1 or #2 Combined]

35 limit 34 to yr="2002 -Current" (2495)
36 limit 35 to English language (2343)
37 limit 36 to human (2099)
38 limit 37 to (conference abstract or conference proceeding or editorial or letter or note) (529)
39 37 not 38 (1570) [Final for Search #1 or #2 - Tests]

40 (FDPM adj5 (imag$ or system)).mp. (5)
41 Mini FLARE.mp. (40)
42 Mini-FLARE.dv. (10)
43 or/41-42 (40)

44 SPY Elite.mp. (33)
45 SPY Elite.dv. (16)
46 (SPY adj40 angiography).mp. (41)
47 (SPY adj50 (fluoresce$ or imag$ or system)).mp. (205)
48 I-SPY.mp. (141)
49 (SPY adj40 surgery).mp. (29)
50 (SPY adj40 green).mp. (48)
51 (SPY adj2 machine).mp. (1)
52 SPY.dv. (51)
53 (pinpoint adj10 (system or imag$ or fluoresce$)).mp. (291)
54 Novadaq.dv. (50)
55 or/44-54 [SPY system] (672)
56 photodynamic eye.mp. (94)
57 indocyanine green/ (10036)
58 56 and 57 (87)
59 Photodynamic eye.dv. (28)
60 or/58-59 (89)
61 hypereye medical system.mp. (36)
62 HyperEye.dv. (21)
63 or/61-62 (39)
64 fluobeam.mp. (29)
65 fluobeam.dv. (9)
66 or/64-65 (29)
67 ic-view.mp. (31)
68 IC-View.dv. (23)
69 or/67-68 (31)
70 visual navigator.mp. (5)
71 Visual Navigator.dv. (3)
72 or/70-71 (5)
73 prototype surgical navigation system.mp. (0)
74 chinese academy of sciences.dv. [Protoype surgical nav system] (4)
75 or/73-74 (4)
76 leica fl800.mp. (2)
77 Leica FL800.dv. (1)
78 Leica.dv. (414)
79 indocyanine green/ (10036)
80 78 and 79 (4)
81 or/76-77,80 (5)
82 infrared 800.mp. (24)
83 infrared 800.dv. (6)
84 or/82-83 (24)
85 (firefly adj7 (system or surgical or surgery or robotic or da vinci)).mp. (260)
86 indocyanine green/ (10036)
87 85 and 86 (32)

88 FIREFLY.dv. (28)
89 or/87-88 (50)
90 laparoscopic near-infrared fluorescence system.mp. (0)
91 Near-Infrared Fluorescence Imaging.kw. (105)
92 (laparoscopic and near-infrared fluorescence).mp. (125)
93 or/90-92 (223)
94 olympus.dv. (6287)
95 93 and 94 (2)
96 INFRARED.dv. (134)
97 Fluorescence.dv. (142)
98 Near-Infrared Fluorescence Imaging.dv. (0)
99 da vinci.dv. (1475)
100 or/96-99 (1747)
101 indocyanine green/ (10036)
102 100 and 101 (31)
103 or/40,43,55,60,63,66,69,72,75,81,84,89,95,102 [Machines] (976) [Total Search #3 for Machines]

104 limit 103 to yr="2002 -Current" (906)
105 limit 104 to English language (862)
106 limit 105 to human (662)
107 limit 106 to (conference abstract or conference proceeding or "conference review" or editorial or letter or note) (251)
108 106 not 107 (411) [Final Search #3 for Machines]

109 39 or 108 (1821) [Search #1, #2, #3]

110 exp *eye surgery/ (78651)
111 *retina fluorescein angiography/ (1398)
112 exp *eye disease/su [Surgery] (79173)
113 *retina angiography/ (147)
114 exp *tuberculosis/ (140473)
115 (DNA or RNA).ab. (1248126)
116 or/110-115 (1517534) [Unwanted topics]

117 109 not 116 (1574) [Final Search #1, #2, #3]

118 limit 117 to medline status (103)

119 "review"/ (2169943)
120 117 and 119 (214)

121 "systematic review"/ (141558)
122 117 and 121 (30)

123 limit 117 to "reviews (best balance of sensitivity and specificity)" (250)

124 meta-analysis/ (149710)
125 systematic review/ (141558)
126 meta-analysis as topic/ (21377)
127 "meta analysis (topic)"/ (35237)
128 "systematic review (topic)"/ (25868)
129 technology assessment, biomedical/ or technology, high-cost/ (11780)
130 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf,kw. (128215)
131 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf,kw. (23021)
132 (data synthes* or data extraction* or data abstraction*).ti,ab,kf,kw. (21450)
133 (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf,kw. (23017)
134 (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf,kw. (9744)
135 (meta regression* or metaregression*).ti,ab,kf,kw. (5894)
136 (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp. (296370)
137 (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. (175339)
138 (cochrane or (health adj2 technology assessment) or evidence report).jw. (18682)
139 (comparative adj3 (efficacy or effectiveness)).ti,ab,kf,kw. (13366)
140 (outcomes research or relative effectiveness).ti,ab,kf,kw. (10157)
141 ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab,kf,kw. (2599)
142 or/124-141 [CADTH SR Filter] (433681)

143 117 and 142 (49)

144 meta analysis/ (149710)
145 ((meta adj analy$) or metaanalys$).tw. (132504)
146 (systematic adj (review$1 or overview$1)).tw. (111651)
147 or/144-146 (233895)
148 cancerlit.ab. (687)
149 cochrane.ab. (59633)
150 embase.ab. (60806)
151 (psychlit or psyclit).ab. (965)
152 (psychinfo or psycinfo).ab. (14277)
153 (cinahl or cinhal).ab. (18038)
154 science citation index.ab. (2777)
155 bids.ab. (521)
156 or/148-155 (95252)

157 reference lists.ab. (13618)
158 bibliograph$.ab. (17586)
159 hand-search$.ab. (5995)
160 manual search$.ab. (3710)
161 relevant journals.ab. (1075)
162 or/157-161 (37802)
163 data extraction.ab. (16245)
164 selection criteria.ab. (26174)
165 163 or 164 (40841)
166 review.pt. (2193237)
167 165 and 166 (19324)
168 letter.pt. (955954)
169 editorial.pt. (518498)
170 animal/ (1738760)
171 human/ (17915730)
172 170 not (170 and 171) (1322238)
173 or/168-169,172 (2781162)
174 147 or 156 or 162 or 167 (277963)
175 174 not 173 [SIGN SR filter] (269747)

176 117 and 175 (24)

177 or/120,122-123,143,176 [Total Reviews] (254)

178 117 not 177 (1320) [Remaining References]

179 limit 178 to "therapy (best balance of sensitivity and specificity)" (61)

180 "Randomized Controlled Trial (topic)"/ (121545)
181 Randomized Controlled Trial/ (455746)
182 Randomization/ (82887)
183 Double Blind Procedure/ (136727)
184 Single Blind Procedure/ (26237)
185 Placebo/ (324165)
186 (random* or sham or placebo*).ti,ab,hw,kf,kw. (1574504)
187 ((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw. (248088)
188 ((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw. (758)
189 intention to treat analysis/ (17415)
190 or/180-189 [CADTH RCT Filter] (1607373)
191 178 and 190 (70)
192 Clinical trial/ (981265)
193 Randomized controlled trial/ (455746)
194 Randomization/ (82887)
195 Single blind procedure/ (26237)

196 Double blind procedure/ (136727)
197 Crossover procedure/ (53343)
198 Placebo/ (324165)
199 Randomi?ed controlled trial$.tw. (147173)
200 Rct.tw. (22013)
201 Random allocation.tw. (1621)
202 Randomly allocated.tw. (26394)
203 Allocated randomly.tw. (2201)
204 (allocated adj2 random).tw. (852)
205 Single blind$.tw. (18542)
206 Double blind$.tw. (173652)
207 ((treble or triple) adj blind$).tw. (632)
208 Placebo$.tw. (246894)
209 Prospective study/ (380738)
210 or/192-209 (1758150)
211 Case study/ (91725)
212 Case report.tw. (323396)
213 Abstract report/ or letter/ (1000880)
214 or/211-213 (1406958)
215 210 not 214 (1707978)
216 210 not 214 [SIGN RCT Filter] (1707978)

217 178 and 216 (192)

218 or/179,191,217 [Total RCTs] (215)

219 178 not 218 (1105) [Remaining References]

220 limit 219 to "economics (best balance of sensitivity and specificity)" (36)

221 Economics/ (224455)
222 Cost/ (57002)
223 exp health economics/ (730048)
224 Budget/ (28231)
225 budget*.ti,ab,kw. (29658)
226 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kw. (217641)
227 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 (287221)
228 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kw. (163487)
229 (value adj2 (money or monetary)).ti,ab,kw. (2363)

230 Statistical Model/ (147521)
231 economic model*.ab,kw. (3290)
232 Probability/ (73088)
233 markov.ti,ab,kw. (20701)
234 monte carlo method/ (29954)
235 monte carlo.ti,ab,kw. (35796)
236 Decision Theory/ (2696)
237 Decision Tree/ (8942)
238 (decision* adj2 (tree* or analy* or model*)).ti,ab,kw. (22991)
239 or/221-238 [CADTH Economic Filter Embase] (1330573)

240 219 and 239 (28)

241 Socioeconomics/ (124289)
242 Cost benefit analysis/ (75190)
243 Cost effectiveness analysis/ (125860)
244 Cost of illness/ (16759)
245 Cost control/ (61538)
246 Economic aspect/ (115102)
247 financial management/ (111290)
248 Health care cost/ (159716)
249 Health care financing/ (12685)
250 Health economics/ (37045)
251 Hospital cost/ (17914)
252 (fiscal or financial or finance or funding).tw. (133853)
253 Cost minimization analysis/ (3046)
254 (cost adj estimate$).mp. (2545)
255 (cost adj variable$).mp. (186)
256 (unit adj cost$).mp. (3209)
257 or/241-256 [SIGN Economic Filter Embase] (785004)

258 219 and 257 (12)

259 or/220,240,258 [Total Economic] (47)

260 219 not 259 (1058) [Remaining References]

261 Clinical study/ (244727)
262 case control study/ (121412)
263 Family study/ (25049)
264 Longitudinal study/ (104137)
265 Retrospective study/ (504715)
266 Prospective study/ (380738)
267 Randomized controlled trials/ (121545)

268 266 not 267 (376128)
269 Cohort analysis/ (294740)
270 (Cohort adj (study or studies)).mp. (180072)
271 (Case control adj (study or studies)).tw. (99525)
272 (follow up adj (study or studies)).tw. (53204)
273 (observational adj (study or studies)).tw. (99083)
274 (epidemiologic$ adj (study or studies)).tw. (88405)
275 (cross sectional adj (study or studies)).tw. (128949)
276 or/261-265,268-275 [SIGN Observational Filter Embase] (1808504)

277 260 and 276 [Total Observational] (146)

278 260 not 277 (912) [Remaining References]

279 6 and 20 and 260 (358)
280 278 not 279 (613)
281 9 and 13 and 280 (59)
282 280 not 281 (554)

Appendix B Data extraction sheet

Article number	
Type of study	
Title and Reference (First author)	
Year of publication	
n. patients (studies in case of SR)	
Matching?	
Inclusion criteria	
Patients	
Intervention & comparator	
Device	
Surgical technique	
Follow up period & outcome measured	
Exclusion criteria	
Study characteristics	
Population	
Intervention	
Comparison	
Outcomes	
Mortality	
Morbidity	
Surgical revision due to leak	
Length of stay	
Anastomotic leak	
Sepsis	
Revision	
UTI	
Urinary retention	
Ileus	
Bleeding	
Wound infection	
Enterocolitis	
Respiratory infection	
Flatus passage	

Appendix C Critical appraisal of nonrandomized study

Critical appraisal of observational study (Down and black method)	Kudszus 2010	Jafari 2013	Kim 2015	Kin 2015	Jafari 2015
Generalization					
Were the subject asked to participate in the study representative of the findings of the entire population from which they were recruited?	Y	Y	Y	Y	Y
Were those subjects, who were prepared to participate, representative of the entire population from which they were recruited?	Y	Y	Y	Y	Y
Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of the patients received?	N	N	N	N	N
Selection bias (confounding) & attrition bias					
Were the patients in different intervention groups recruited from the same population?	Y	Y	Y	Y	NA
Were the patients in different intervention groups recruited over the same period of time?	N	N	N	N	NA
Were study subjects randomized to intervention groups?	N	N	N	N	N
Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was completed and irrevocable?	N	N	N	N	N
Was there adequate adjustment for confounding for the main findings? (Methodological or statistical)	Y	N	N	Y	N
Was loss of patients to follow-up taken into account?	U	Y	Y	Y	Y
Performance bias and detection bias					
Was an attempt made to blind study subjects to the intervention they have received?	N	N	N	N	N
Was an attempt made to blind those measuring the main outcome of the intervention?	N	N	N	N	N
If any of the results of the study were based on data dredging, was it made clear?	N	Y	Y	Y	Y

Critical appraisal of observational study (Down and black method)	Kudszus 2010	Jafari 2013	Kim 2015	Kin 2015	Jafari 2015
In trial, do the analyses adjust for the different lengths of follow-up of patients?	N	N	N	N	N
Were the statistical tests used to assess the main outcomes appropriate?	Y	NA	Y	Y	NA
Was compliance with the intervention reliable?	Y	Y	Y	Y	Y
Was the main outcome measures use accurate?	Y	Y	Y	Y	Y
Reporting bias					
Is the hypothesis/aim/objective of the study clearly described?	Y	Y	Y	Y	Y
Are the main outcomes to be measured clearly described in the introduction or method section?	Y	Y	Y	Y	Y
Are the characteristics of the patients included in the study described?	Y	Y	Y	Y	Y
Is the intervention of interest clearly described?	Y	Y	Y	Y	Y
Is the distribution of principal confounders in each group of subjects to be compared clearly described?	Y	N	N	Y	NA
Are the main findings of the study clearly described?	Y	Y	Y	Y	Y
Does the study provide estimates of the random variability in the data for the main outcomes?	Y	N	Y	Y	N
Have all important adverse events that may be a consequence of the intervention been reported?	N	Y	Y	N	Y
Have the characteristics of patients lost to follow-up been described?	N	Y	NA	NA	N
Have actual probability value been reported (p value)?	Y	N	Y	Y	NA
Power					
Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?	N	N	Y	N	NA

Note: NA indicates not applicable in that category; a no (N) answer indicate high risk of bias in the category; a yes (Y) answer indicates low risk of bias in the category; an unknown answer (U) indicates unknown risk of bias in the category.

Appendix D Characteristics of included studies

Part 1

Article	Kudszus 2010	Jafari 2013	Kim 2015
Type of study	Comparative retrospective	Comparative retrospective	Comparative prospective
Title and reference (first author)	Kudszus 2010	Jafari 2013	Kim 2015
Year of publication	2010	2013	2015
n. patients (studies in case of SR)	402 (201 v 201)	40 (16 v 24)	436 (123 v 313)
Matching?	Matched	Unmatched	Unmatched
Inclusion criteria			
Patients	All patients who had been treated surgically for colorectal cancer in our institution between 1998 and 2008 were identified. Between 2003 and 2008, all anastomosis or resection margins in colorectal resections were investigated intraoperatively using LFA to objectify tissue perfusion in the anastomotic region. Patients were matched for age (<70 years, ≥70 years, according to the smallest age difference, no matching with an age difference >20 years), T-stage (T1–T3 or T4), type of resection (right hemicolon, segmental colonic resections, and left hemicolon and rectum), type of anastomosis (hand or stapled), defunctioning stoma, intraoperative administration of blood, resection under	Rectal cancer cases treated surgically via robot-assisted low- and ultralow ANTERIOR resection, as well intersphincteric resection (ISR) between 2011 and 2012.	A consecutive cohort of 436 patients with rectal cancer Medical Centre (Seoul, Korea) during 2010–2014 were prospectively enrolled. Among these patients, the 123 consecutive patients who had surgery in or after 2013 received ICG fluorescent imaging (ICG+ group), while the 313 patients who had surgery before 2013 did not receive ICG fluorescent imaging (ICG– group).

	emergency conditions, and body mass index.		
Intervention & comparator	All patients underwent surgery either laparoscopically or conventionally. Laser fluorescence angiography was performed in all cases by a commercially available system (IC-View®, Pulsion Medical Systems AG, Munich, Germany). This system consists of a digital video camera with a mounted laser (p= 0.16 W, λ=780 nm) and an infrared filter. To visualize and analyze tissue perfusion, regions of interest (i.e., anastomosis or resection margins prepared for anastomosis as well as a loop of normal small intestine serving as the internal control) are positioned in front of a tripod-mounted camera while the surrounding tissues are covered by sterile drapes.	Intravenous injection of 6–8 mg of ICG. The bowel was then visualized via NIR laparoscopy, and the surgeon decided whether to revise the point of transection of either the proximal or distal bowel based on the ICG perfusion assessment. Firefly was one of the systems used in the study.	The da Vinci Si® high-definition (HD) vision system (Firefly ™, Intuitive Surgical, Sunnyvale, CA, USA) was used to enable fluorescent image acquisition, using ICG dye injection and a NIRF camera in addition to a white light image (12). For each specific procedure, 10 mg ICG (25 mg/vial) was intravenously injected immediately after completion of colorectal mobilization and anastomosis or prior to lymph node sampling. Perfusion status was assessed to determine the transection point in the left or sigmoid colon after colorectal mobilization.
Device (Manufacturer)	IC-view (Pulsion)	Firefly for Da Vinci robotic system (Novadaq)	Firefly for Da Vinci robotic system (Novadaq)
Surgical technique	Mixed laparoscopic or conventional	Laparoscopic robotic assisted	Laparoscopic robotic
Follow up period & outcome measured	Anastomotic leakage Duration of hospital stay	Intraoperative factors including operative time, estimated blood loss (EBL), intraoperative occurrences, and level of anastomosis were collected. Postoperative complications including anastomotic leak, bleeding, urinary tract infection, urinary retention, ileus, sepsis, cardiac occurrences, and wound infection were collected. Anastomotic leak was defined as any disruption of the anastomosis occurring within 60 days of surgery as visualized by contrast enema study or endoscopy. Reoperation and readmission	AL was identified as any disruption of the anastomosis, including leakage, abscess and enteric fistula, verified by water-soluble contrast enema, pelvic computed tomography and clinical findings, and observed for at least 6 months after the take-down of diversion or anastomosis without diversion. Anastomotic stricture was identified as impeded passage of examination tools by manual rectal examination or colonoscopy. Other general morbidities were evaluated postoperatively for 1 month. Mean follow-

		rates were analyzed	up period (± SD) was 11.6 ± 4.4 months for the ICG+ group and 35.8 ± 12.3 months for the ICG– group
Exclusion criteria	NA	NA	NA

Article	Kudszus 2010		Jafari 2013			Kim 2015			
Study characteristics									
Population		LFA	Control		ICG	Control		(with ICG), n = 123	(no ICG), n = 313	p
	Age (years)	69.0± 21.8	67.8±25.2	Age	58	63	Sex, male/female	73/50	192/121	0.744
	Height (cm)	168.0 ±18.2	170.0±18. 8	Sex	75%M	73%M	Age, years	57±10	58±10	0.328
	Weight (kg)	73.0± 28.4	73.5±30.8	BMI	27	27	ASA physical status, I/II/III	26/89/8	74/233/6	0.048
	BMI	25.7± 7.8	25.3±8.4	ASA	2.3	2.5	Comorbidity, yes	42 (34.1)	118 (37.7)	0.51
	Male gender (%)	42.2	42.2	Preoperative chemotherapy/ radiotherapy (%)	63	68	BMI, kg/m2	23.9±3.3	23.7±2.7	0.474
				Rectal cancer stage (%)			Prior abdominopelvic surgery	11 (8.9)	27 (8.6)	1
				I	37	54	Preoperative CRT	23 (18.7)	96 (30.9)	0.012
				II	25	9	Tumour distance from the AV, cm	6.4±3.7	6.1±3.2	0.369
				III	38	27	Operation, LAR/uLAR with ISR	52/71	108/205	0.151
				IV	0	9	Concurrent ileal diversion, yes	45 (36.6)	106 (33.9)	0.655
				Obesity (%)	44	27	Operation, uLAR with ISR	44 (97.8)	96 (90.6)	0.175
				Anemia (%)	25	23	Prior abdominopelvic surgery	2 (4.4)	5 (4.7)	1
				Diabetes mellitus (%)	0	18	Restrictive mesocolon	4 (8.9)	5 (4.7)	0.452
				Hypertension (%)	25	23	Intraoperative events	3 (6.7)	1 (0.9)	0.079

Article	Kudszus 2010	Jafari 2013			Kim 2015			
		Chronic kidney disease (%)	6	9	Total operative time, min	164±34	186±41	<0.001
		Hyperlipidemia (%)	13	9	Robot console time, min	58±14	70±19	<0.001
		Cardiac disease (%)	19	9	Docking time, min	2±1	3±2	<0.001
		Pulmonary disease (%)	6	23	ICG flushing timed, s Mesocolon/ colon wall, left	42±18/51± 24	NA	NA
		Hypothyroidism (%)	6	5	Stage, 0/I/II/III	9/39/34/41	20/109/8 4/100	0.932
		History of alcohol (%)	6	0				
		History of tobacco (%)	13	27				
Intervention	Laser fluorescence angiography IC-View®, Pulsion Medical Systems AG, Munich, Germany	ICG NIR The NIR camera system is provided by multiple manufacturers including Olympus Corporation (Tokyo, Japan), Karl Storz GmbH (Tuttlingen, Germany), Stryker Corporation (Portage, MI, USA), and Novadaq Technologies (Ontario, Canada)			ICG			
Comparison	without LFA	Without ICG NIR (retro unmatched)			No ICG			
Conclusion*	There was an overall reduction in the absolute revision rate of 4% in the LFA group and a significantly reduced rate of revision in the subgroup analysis of patients undergoing elective colorectal resections, in patients older than 70 years and in patients with hand-sewn anastomosis. This demonstrates that LFA is a method that may	ICG fluorescence may play a role in anastomotic tissue perfusion assessment and affect the AL rate. Larger prospective studies are needed to further validate this novel technology.			ICG imaging during RA SSO [robot-assist sphincter-saving operations] provides accurate real-time knowledge of the perfusion status at or near the anastomosis, specifically reducing AL [anastomotic leak] in patients who may incur bowel ischaemia.			

Article	Kudszus 2010	Jafari 2013	Kim 2015
	significantly reduce not only the rate of severe complications in colorectal surgery but also the hospital length of stay.		

*Please note that individual studies might have different objectives than this HTA as well as differences in statistical power, and therefore might arrive at a different conclusion than the meta-analysis.

Note: ASA = American Society of Anesthesiologists; AV = anal verge ; BMI = body mass index; CRT = chemoradiotherapy ; ICG = indocyanine green; ISR = intersphincteric resection; LAR = lower anterior resection; LFA = laser fluorescence angiography; NIR = near infrared ; NIRF = near infrared fluorescence ; uLAR =ultra-low anterior resection.

Part 2

Article	Kin 2015	Jafari 2015
Type of study	Comparative retrospective	Descriptive prospective
Title and reference (first author)	Kin 2015	Jafari 2015
Year of publication	2015	2015
n. patients (studies in case of SR)	173 v 173	147
Matching?	Matched	NA
Inclusion criteria		
Patients	Patients ≥18 years of age who underwent elective colon or rectal resections with a primary anastomosis were included. Patients were case matched in a 1:1 ratio using the criteria of sex, age (±5 years), level of anastomosis (±1 cm), history of neoadjuvant pelvic radiation therapy, and use of a diverting loop ileostomy.	Patients were eligible for enrollment if they were over 18 years old and were scheduled for a laparoscopic left colectomy or anterior resection with a planned anastomosis located 5 to 15 cm from the anal verge.
Intervention & comparator	For the angiography group, 3 mL of indocyanine green dye followed by a 10-mL saline flush was injected into a peripheral vein, and real-time fluorescence images using the Spy Imaging System. Portions of the bowel with greater fluorescence relative to other areas indicated better perfusion. Bowel with poor perfusion was resected back to well-perfused bowel, even if it had seemed viable on gross examination. Reassessment of proximal bowel perfusion was not conducted after excision. Perfusion of the distal rectal stump was not evaluated, because the angiography system often could not visualize structures in the pelvis, especially in laparoscopic cases.	During the surgical procedure, the Pinpoint Endoscopic Fluorescence Imaging System (Novadaq) was used to assess perfusion of colonic tissue at two critical steps of the operation: the planned point of proximal transection just before bowel resection and completion of the anastomosis (“baseline image”), and after completion of the anastomosis, when the integrity of the mucosal aspect of the completed anastomosis was assessed via proctoscopy.
Device (manufacturer)	SPY Imaging System - Elite and Pinpoint (Novadaq)	Pinpoint endoscopic fluorescence imaging system (Novadaq)
Surgical technique	Open	Laparoscopic
Follow up period & outcome measured	The primary outcome was anastomotic leak occurring within 60 days of the initial operation. An anastomotic leak was defined by at least one of the following criteria: 1) an anastomotic defect noted on physical examination,	The primary end points were the feasibility and safety of fluorescence angiography during low anterior resection and left colectomy. Secondary endpoints included clinical outcomes of the

Article	Kin 2015				Jafari 2015	
	2) an anastomotic defect confirmed in the operating room, 3) an anastomotic defect seen on proctoscopy, 4) radiologic evidence of a leak consisting of either a defect in the anastomosis and an adjacent fluid collection, or stranding or the extravasation of rectal contrast into the extraluminal space, or 5) clinical evidence of a leak such as feculent output from a pelvic drain. The secondary outcome was whether the results of intraoperative fluorescence angiography changed surgical management.				procedures performed. The incidence of major postoperative clinical complications with a minimum 30-day post-procedure follow-up was collected. Major post-operative clinical complications included clinically evident anastomotic leak, radiologic anastomotic leak (when prompted by clinical suspicion), and post-operative fever and delay in return of bowel function.	
Exclusion criteria	NA				Patients with a history of adverse reaction or known allergy to ICG, iodine, or iodine dyes were not eligible. Pregnant and/or lactating patients were excluded.	
Study characteristics						
Population	Variable	Angiography (N = 173)	No angiography (N = 173)	p	n=139	
	Age, y, mean ± SD	58.2 ± 13.2	58.2 ± 13.2	0.9	Age, y, mean±SD	58±14
	Sex, % – Men	54	54		Sex, n (%)	
	BMI, kg/m2, mean ± SD	27.0 ± 4.9	26.5 ± 5.3	0.33	Male	74 (53.2)
	Smoking status, % (Never smoker/ Former smoker/ Current smoker)	65 /25/ 10	60/29 /11	0.6	Race, n (%)	
	Diabetes mellitus, %	13	10	0.5	Asian	
	Anemia, %	26	30	0.53	Black or African American	14 (10.0)
	Hemoglobin, g/dL, mean ± SD	13.2 ± 1.5	13.1 ± 1.8	0.91	Hispanic	7 (5.0)
	Surgical indications, % (Diverticular disease/Cancer/IBD)	27.0/57.0/2.3	18.0/61.0/3.5	0.18	Hispanic	10 (7.2)
					Middle Eastern	2 (1.4)
					White	106 (76.3)
					Body mass index (BMI), kg/m2, mean±SD	29±6
					BMI > 30, n (%)	42 (30.2)

Article	Kin 2015	Jafari 2015	
		BMI 30, n (%)	97 (69.8)
		American Society of Anesthesiologists, n (%)	
		I	17 (12.2)
		II	73 (52.5)
		III	46 (33.1)
		IV	3 (2.2)
		Diagnosis, n (%)	
		Diverticulitis	61 (43.9)
		Rectal cancer	35 (25.2)
		Colon cancer	29 (20.9)
		Polyp	6 (4.3)
		Procidentia	4 (2.9)
		Crohn's disease	1 (0.7)
		Colovesical fistula	1 (0.7)
		Radiation stricture	1 (0.7)
		Sigmoid volvulus	1 (0.7)
		Preoperative chemotherapy, n (%)	13 (9.4)
		Preoperative radiation therapy, n (%)	15 (10.8)
Intervention	ICG	ICG	
Comparison	without ICG (matched retrospectively)	NA	

Note : BMI = body mass index; IBD = ischemic bowel disease; ICG = indocyanine green; NA = not applicable; SD = standard deviation.

Article	Kin 2015	Jafari 2015
Type of study	Comparative retrospective	Descriptive prospective
Title and reference (first author)	Kin 2015	Jafari 2015
Year of publication	2015	2015
n. patients (studies in case of SR)	173 v 173	147
Matching?	Matched	NA
Inclusion criteria		
Patients	Patients ≥18 years of age who underwent elective colon or rectal resections with a primary anastomosis were included. Patients were case matched in a 1:1 ratio using the criteria of sex, age (±5 years), level of anastomosis (±1 cm), history of neoadjuvant pelvic radiation therapy, and use of a diverting loop ileostomy.	Patients were eligible for enrollment if they were over 18 years old and were scheduled for a laparoscopic left colectomy or anterior resection with a planned anastomosis located 5 to 15 cm from the anal verge.
Intervention & comparator	For the angiography group, 3 mL of indocyanine green dye followed by a 10-mL saline flush was injected into a peripheral vein, and real-time fluorescence images using the Spy imaging system. Portions of the bowel with greater fluorescence relative to other areas indicated better perfusion. Bowel with poor perfusion was resected back to well-perfused bowel, even if it had seemed viable on gross examination. Reassessment of proximal bowel perfusion was not conducted after excision. Perfusion of the distal rectal stump was not evaluated, because the angiography system often could not visualize structures in the pelvis, especially in laparoscopic cases.	During the surgical procedure, the Pinpoint Endoscopic Fluorescence Imaging System (Novadaq) was used to assess perfusion of colonic tissue at two critical steps of the operation: the planned point of proximal transection just before bowel resection and completion of the anastomosis ("baseline image"), and after completion of the anastomosis, when the integrity of the mucosal aspect of the completed anastomosis was assessed via proctoscopy.
Device (manufacturer)	Spy imaging system - Elite and Pinpoint (Novadaq)	Pinpoint Endoscopic Fluorescence Imaging System (Novadaq)
Surgical technique	Open	Laparoscopic
Follow-up period & outcome measured	The primary outcome was anastomotic leak occurring within 60 days of the initial operation. An anastomotic leak was defined by at least one of the following criteria: 1) an anastomotic defect noted on physical examination, 2) an anastomotic defect confirmed in the operating room, 3) an anastomotic defect seen on proctoscopy, 4) radiologic evidence of a leak consisting of either a defect in the anastomosis and an adjacent fluid collection, or stranding or the	The primary end points were the feasibility and safety of fluorescence angiography during low anterior resection and left colectomy. Secondary endpoints included clinical outcomes of the procedures performed. The incidence of major postoperative clinical complications with a minimum 30-day post-procedure follow-up was collected. Major postoperative clinical complications included

Article	Kin 2015				Jafari 2015	
	extravasation of rectal contrast into the extraluminal space, or 5) clinical evidence of a leak such as feculent output from a pelvic drain. The secondary outcome was whether the results of intraoperative fluorescence angiography changed surgical management.				clinically evident anastomotic leak, radiologic anastomotic leak (when prompted by clinical suspicion), and postoperative fever and delay in return of bowel function.	
Exclusion criteria	NA				Patients with a history of adverse reaction or known allergy to ICG, iodine, or iodine dyes were not eligible. Pregnant and/or lactating patients were excluded.	
Study characteristics						
Population	Variable	Angiography (N = 173)	No angiography (N = 173)	p	n=139	
	Age, y, mean ± SD	58.2 ± 13.2	58.2 ± 13.2	0.9	Age, y, mean±SD	58±14
	Sex, % – Men	54	54		Sex, n (%)	
	BMI, kg/m^2, mean ± SD	27.0 ± 4.9	26.5 ± 5.3	0.33	Male	74 (53.2)
	Smoking status, % (Never smoker/ Former smoker/ Current smoker)	65 /25/ 10	60/29 /11	0.6	Race, n (%)	
	Diabetes mellitus, %	13	10	0.5	Asian	
	Anemia, %	26	30	0.53	Black or African American	14 (10.0)
	Hemoglobin, g/dL, mean ± SD	13.2 ± 1.5	13.1 ± 1.8	0.91	Hispanic	7 (5.0)
	Surgical indications, % (Diverticular disease/Cancer/IBD)	27.0/57.0/2.3	18.0/61.0/3.5	0.18	Hispanic	10 (7.2)
					Middle Eastern	2 (1.4)
					White	106 (76.3)
					BMI, kg/m^2, mean±SD	29±6
					BMI > 30, n (%)	42 (30.2)
					BMI 30, n (%)	97 (69.8)
					American Society of Anesthesiologists, n (%)	
					I	17 (12.2)
					II	73 (52.5)

Article	Kin 2015	Jafari 2015	
		III	46 (33.1)
		IV	3 (2.2)
		Diagnosis, n (%)	
		Diverticulitis	61 (43.9)
		Rectal cancer	35 (25.2)
		Colon cancer	29 (20.9)
		Polyp	6 (4.3)
		Procidentia	4 (2.9)
		Crohn's disease	1 (0.7)
		Colovesical fistula	1 (0.7)
		Radiation stricture	1 (0.7)
		Sigmoid volvulus	1 (0.7)
		Preoperative chemotherapy, n (%)	13 (9.4)
		Preoperative radiation therapy, n (%)	15 (10.8)
Intervention	ICG	ICG	
Comparison	without ICG (matched retrospectively)	NA	
Conclusion*	Intraoperative fluorescence angiography to assess the perfusion of the colon conduit for anastomosis was not associated with colorectal anastomotic leak. Perfusion is but one of multiple factors contributing to anastomotic leaks. Additional studies are necessary to determine whether this technology is beneficial for colorectal surgery.	PINPOINT is a safe and feasible tool for intraoperative assessment of tissue perfusion during colorectal resection. There were no anastomotic leaks in patients in whom the anastomosis was revised based on inadequate perfusion with FA [fluorescence angiography].	

*Please note that individual studies might have different objectives than this HTA as well as differences in statistical power, and therefore might arrive at a different conclusion than the meta-analysis.

Note : BMI = body mass index; IBD = ischemic bowel disease; ICG = indocyanine green; NA = not applicable; SD = standard deviation.

Appendix E List of BC hospitals, corresponding volumes of colorectal surgeries in 2014/2015, and estimated number of machines needed to provide ICGA in every surgery, and estimated capital costs per surgery.

	Hospital	Laparoscopic surgeries	Undefined or open surgeries	All colorectal surgeries	N. of devices needed		% surgeries per hospital	Capital Cost per surgery ($)
					Spy pinpoint (laparoscopic surgeries)	Spy Elite (open surgeries)		
Interior	Cariboo Memorial Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	East Kootenay Regional Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Kelowna General Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Kootenay Boundary Regional Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Penticton Regional Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Royal Inland Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Shuswap Lake General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Vernon Jubilee Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Fraser	Abbotsford Regional Hospital and Cancer Centre	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Burnaby Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Chilliwack General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Delta Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Eagle Ridge Hospital and Health Care Centre	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Jim Pattison Outpatient Care and Surgery Centre	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Langley Memorial Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Peace Arch District Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Ridge Meadows Hospital and Health Care Centre	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Royal Columbian Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Surrey Memorial Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Va	B.C. Children's Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Hospital	Laparoscopic surgeries	Undefined or open surgeries	All colorectal surgeries	N. of devices needed		% surgeries per hospital	Capital Cost per surgery ($)
					Spy pinpoint (laparoscopic surgeries)	Spy Elite (open surgeries)		
	Lions Gate Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Mount Saint Joseph Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Powell River General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Richmond Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Sechelt Hospital/shíshálh Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	St. Paul's Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	UBC Health Sciences Centre*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Vancouver General Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Vancouver Island	Campbell River and District General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Cowichan District Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Nanaimo Regional General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Royal Jubilee Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Saanich Peninsula Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	St. Joseph's General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Victoria General Hospital*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	West Coast General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Northern	Dawson Creek and District Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Fort St. John General Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	G.R. Baker Memorial Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Mills Memorial Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Prince Rupert Regional Hospital	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	The University Hospital of Northern British Columbia*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Total n. surgeries in 2014/2015 ->				[redacted]	[redacted]	[redacted]	**Average Capital**	[redacted]
Projected number of surgeries over 20 years				[redacted]				

	Hospital	Laparoscopic surgeries	Undefined or open surgeries	All colorectal surgeries	N. of devices needed		% surgeries per hospital	Capital Cost per surgery ($)
					Spy pinpoint (laparoscopic surgeries)	Spy Elite (open surgeries)		
(discounted) ->							**cost**	

Data source: MSP & DAD, 2014/15.

Note: Some patients may have multiple services at different hospitals. Cases < 5 have been suppressed.

* Teaching hospital, according to CIHI peer groups in the electronic DAD reports.

¥ Capital cost per surgery above the cut-off ($5,700) to produce cost-effective ICERs under a WTP threshold of $50,000/QALY.

Appendix F Methodology used by HTR Office to determine hospital costs and MSP costs of patients with or without complications

The data provided shows the estimated hospital and MSP costs per patient for the 12 patient groups identified in the clinical pathway and is divided into 3 timeframes: the initial hospital stay; the 6 month period following the initial date of admission; and the 365 day period following the initial date of admission. Below is a description of how the estimates were derived.

1. The MSP and DAD databases were queried to identify patients that underwent their first colorectal surgery in a BC hospital in 2014/15 (did not have colorectal surgery in 2013/14), for which a MSP fee was paid. Only patients that had their first colorectal surgery in 2014/15 were included. The DAD intervention codes and MSP fee items used are listed below.

2. Billed MSP fee items were reconciled to each patient's surgery to determine whether their first surgery was open or laparoscopic.

3. MSP and PharmaNet data was used to determine whether the surgeries included a stoma.

Using PharmaNet data, patients were counted as having a stoma if they had their first PharmaNet claim for ostomy supplies within 100 days of discharge after their first surgery.

4. DAD data was used to identify whether patients had a diagnosis of sepsis (ICD-10: A40, A41) within 30 days of their first surgery. If a patient had a diagnosis of sepsis then they were considered to have had a major leak.

5. To differentiate patients with minor complications from those with no complications, across patients that did not have sepsis, it was assumed that patients with an initial length of stay in hospital that was at or below the 75th percentile had no complications and those above the 75th percentile had minor complications.

6. To estimate hospital costs, resource intensity weights (RIW) in DAD were summed for each patient across the 365 day period following their first admission date for colorectal surgery. 2015/16 RIWs were used, which have a value of $5,850 per weighted case.

7. MSP costs were estimated by summing expenditures on MSP fee items for each patient across the 365 day period following their first admission date for colorectal surgery.

8. Descriptive statistics were calculated for each of the 12 patient groups across 3 timeframes.

DAD intervention codes

1.NM.87.^^	Excision partial, large intestine
1.NM.89.^^	Excision total, large intestine
1.NM.91.^^	Excision radical, large intestine
1.NQ.87.^^	Excision partial, rectum
1.NQ.89.^^	Excision total, rectum

MSP Fee Items

FITM_CD	FITM	FITM_DSCR
07449	RESECTION OF COLONIC INJURY	RESECTION OF COLONIC INJURY
07455	EMERGENCY RESECTION OF OBSTRUCTED COLON	EMERGENCY RESECTION OF OBSTRUCTED COLON, WITH LAVAGE AND ANASTOMOSIS
07565	TAKEDOWN PELVIC POUCH TO INCLUDE ILEOSTOMY - OPEN	TAKE-DOWN OF PELVIC POUCH, TO INCLUDE ILEOSTOMY - OPEN
07566	RECTAL MUCOSECTOMY, ILEOANAL ANASTOMOSIS	RECTAL MUCOSECTOMY AND ILEOANAL ANASTOMOSIS
07567	PROCTECTOMY WITH RECTAL MUCOSECTOMY - OPEN	PROCTECTOMY WITH RECTAL MUCOSECTOMY, ILEOANAL ANASTOMOSIS, CREATION OF A ILEAL RESERVOIR (S OR J) WITH OR WITHOUT LOOP ILEOSTOMY - OPEN
07569	COLECTOMY AND HEMIPROCTECTOMY - OPEN	COLECTOMY AND HEMIPROCTECTOMY - OPEN
07570	COLO-COLOSTOMY OR ENTERO-COLOSTOMY - OPEN	COLO-COLOSTOMY OR ENTERO-COLOSTOMY - OPEN
07580	RECTAL TUMOR EXCISION BY POSTERIOR PARASACRAL	EXCISION OF RECTAL TUMOUR BY POSTERIOR PARASACRAL, TRANSACRAL OR TRASCOCCYGEAL APPROACH (KRASKE)
07588	COLOSTOMY OR ILEOSTOMY - LOOP - END - OPEN	COLOSTOMY OR ILEOSTOMY - END - OPEN

FITM_CD	FITM	FITM_DSCR
07589	TOTAL PROCTOCOLECTOMY SYNCHRONOUS ABDOMINAL PORTIO	TOTAL PROCTOCOLECTOMY - WITH PERINEAL EXCISION OF RECTUM AND ILEOSTOMY - SYNCHRONOUS - ABDOMINAL PORTION - OPEN
07636	SMALL INTESTINE RESECTION/WITH ANASTOMOSIS - OPEN	RESECTION OF SMALL INTESTINE - WITH ANASTOMOSIS - OPEN
07640	COLECTOMY,TOTAL,ABDOMINAL,WITHOUT PROCTECTOMY/OPEN	COLECTOMY - TOTAL, ABDOMINAL, (WITHOUT PROCTECTOMY) - OPEN NOTE: INCLUDES ILEOSTOMY OR ILEOPROCTOSTOMY
07641	PROCTOCOLECTOMY TOTAL WITH PERINEAL EXCISION-OPEN	TOTAL PROCTOCOLECTOMY - WITH PERINEAL EXCISION OF RECTUM AND ILEOSTOMY - OPEN - SINGLE SURGEON
07643	ENTEROENTEROSTOMY	Enteroenterostomy
07645	COLOSTOMY OR ILEOSTOMY - LOOP - OPEN	COLOSTOMY OR ILEOSTOMY - LOOP - OPEN
07647	CLOSURE OF LOOP ENTEROSTOMY WITH RESECTION	CLOSURE OF LOOP ENTEROSTOMY, LARGE OR SMALL INTESTINE - WITH RESECTION AND ANASTOMOSIS
07648	REVISION OF COLOSTOMY, ILEOSTOMY - SIMPLE INCISION	REVISION OF COLOSTOMY, ILEOSTOMY - SIMPLE INCISION OR SCAR, ETC.
07649	REVISION OF COLOSTOMY, ILEOSTOMY - RADICAL	REVISION OF COLOSTOMY, ILEOSTOMY - RADICAL; RECONSTRUCTION WITH BOWEL RESECTION
07658	EXTERIORIZATION OF BOWEL	Exteriorization of large bowel lesion (carcinoma, perforation, etc.)
07662	ABDOMINO-PERINEAL RESECTION (SINGLE SURGEON)-OPEN	ABDOMINO-PERINEAL RESECTION - SINGLE SURGEON - OPEN
07663	ABDOMINO-PERINEAL RESECTION (SYNCHRONOUS ABDOMINAL	ABDOMINO-PERINEAL RESECTION - SYNCHRONOUS ABDOMINAL PORTION - OPEN
07664	PROCTECTOMY,COMBINED WITH ABDOM RESECTION/PERINEAL	PROCTECTOMY, IN COMBINATION WITH ANY ABDOMINAL RESECTION - SYNCHRONOUS - PERINEAL PORTION
07672	COMPLETE RECTAL PROLAPSE	COMPLETE RECTAL PROLAPSE-TRANSABDOMINAL RECTOPEXY OR TRANSPERINEAL DELORME PROCEDURE NOTES:

FITM_CD	FITM	FITM_DSCR
		I) PAID IN ADDITION TO TRANSABDOMINAL RESECTION OF COLON OR RECTUM IF REQUIRED II) NOT PAID IN ADDITION TO 72666 ALTEMEIER PROCEDURE.
72601	CAECOSTOMY TUBE FOR DECOMPRESSION-LAP. (EXTRA)	CAECOSTOMY TUBE FOR DECOMPRESSION - LAPAROSCOPIC (EXTRA) NOTES: I) RESTRICTED TO GENERAL SURGEONS. II) IF CONVERSION TO OPEN PROCEDURE IS REQUIRED, BILL UNDER THE APPROPRIATE OPEN PROCEDURE AT 100% PLUS FEE ITEM 04001 AT 50%.
72620	RESECTION OF SMALL INTESTINE-WITH ENTEROSTOMY/OPEN	RESECTION OF SMALL INTESTINE - WITH ENTEROSTOMY; WITHOUT ANASTOMOSIS (DOES NOT INCLUDE SEPARATE ENTEROSTOMIES OR RESECTIONS) - OPEN
72621	MOBILIZATION OF SPLENIC FLEXURE-EXTRA-OPEN	MOBILIZATION (TAKE-DOWN) OF SPLENIC FLEXURE PERFORMED IN CONJUNCTION WITH PARTIAL COLECTOMY - EXTRA (NOT APPLICABLE TO RIGHT OR LEFT HEMICOLECTOMY) OPERATION ONLY-OPEN
72622	RESECTION - COLON - LIMITED - OPEN	Limited resection of colon - open
72623	RESECTION - COLON - LIMITED - LAPAROSCOPIC	Limited resection of colon -laparoscopic
72624	HEMICOLECTOMY - RIGHT - OPEN	Hemicolectomy; right - open
72625	HEMICOLECTOMY - RIGHT - LAPAROSCOPIC	Hemicolectomy; right - laparoscopic
72626	HEMICOLECTOMY - LEFT - OPEN	Hemicolectomy; left - open
72631	HEMICOLECTOMY - LEFT - LAPAROSCOPIC	Hemicolectomy; left - laparoscopic
72632	SIGMOID RESECTION - OPEN	Sigmoid resection - open
72633	SIGMOID RESECTION - LAPAROSCOPIC	Sigmoid resection - laparoscopic
72634	SIGMOID RESECTION/END COLOSTOMY - OPEN	SIGMOID RESECTION - WITH END COLOSTOMY AND CLOSURE OF DISTAL SEGMENT OR MUCOUS FISTULA (HARTMANN TYPE PROCEDURE) - OPEN
72635	ANTERIOR RESECTION - RECTOSIGMOID-CARCINOMA - OPEN	ANTERIOR RESECTION OF RECTOSIGMOID FOR CARCINOMA (LOW PELVIC ANASTOMOSIS;

FITM_CD	FITM	FITM_DSCR
		COLOPROCTOSTOMY) WITH OR WITHOUT PROTECTIVE STOMA - OPEN
72636	PROCTECTOMY - ABDOMINAL/TRANSANAL	PROCTECTOMY; ABDOMINAL AND TRANSANAL APPROACH; COLOANAL ANASTOMOSIS (WITH OR WITHOUT PROTECTIVE COLOSTOMY) - SYNCHRONOUS ABDOMINAL PORTION
72640	PARTIAL RIGHT COLECTOMY (CAECUM) - OPEN	PARTIAL RIGHT COLECTOMY (CAECUM) WITH REMOVAL OF TERMINAL ILEUM AND ILEOCOLOSTOMY - OPEN
72641	CAECOSTOMY, TUBE FOR DECOMPRESSION(EXTRA)-OPEN	CAECOSTOMY, TUBE FOR DECOMPRESSION (EXTRA)-OPEN
72644	REVISION OF COLOSTOMY, ILEOSTOMY - WITH REPAIR	REVISION OF COLOSTOMY, ILEOSTOMY - WITH REPAIR OF PARACOLOSTOMY HERNIA REQUIRING LAPAROTOMY
72645	CONTINENT ILEOSTOMY - OPEN	CONTINENT ILEOSTOMY (KOCH PROCEDURE) - OPEN
72646	COLOSTOMY OR ILEOSTOMY - MULTIPLE BIOPSIES	COLOSTOMY OR ILEOSTOMY - MULTIPLE BIOPSIES (E.G. FOR HIRSCHSPRUNG DISEASE) - EXTRA - OPERATION ONLY
72647	INTESTINAL STRICTUROPLASTY - SINGLE	Intestinal strictoplasy (enterotomy and enterorrhaphy) with or without dilation for intestinal obstruction - single
72648	INTESTINAL STRICTUROPLASTY - MULTIPLE	Intestinal strictoplasy (enterotomy and enterorrhaphy) with or without dilation for intestinal obstruction - multiple (two or more)
72651	RECONSTRUCTION HARTMANN PROCEDURE - OPEN	RECONSTRUCTION HARTMANN PROCEDURE WITH OR WITHOUT PROTECTIVE COLOSTOMY - OPEN
72652	HARTMAN PROCEDURE - RECONSTRUCTION - LAPAROSCOPIC	Reconstruction Hartmann procedure with or without protective colostomy - laparoscopic
72654	FISTULA - CLOSURE/BOWEL RESECTION	Closure of fistula; enterovesical, colovesical or colovaginal - with bowel resection (extra to 72653)
72662	PROCTECTOMY, COMPLETE - SYNCHRONOUS ABDOMINAL	Proctectomy; complete (for congenital megacolon) abdominal and perineal

FITM_CD	FITM	FITM_DSCR
		approach with pull through procedure and anastomosis (e.g. Swenson, Duhamel or Soave type operation) - synchronous abdominal
72664	PROCTECTOMY, COMPLETE - SUBTOTAL/TOTAL COLECTOMY	Proctectomy, complete (for congenital megacolon), abdominal and perineal approach; with pull through procedure and anastomosis (e.g. Swenson, Duhamel, or Soave type operation) - with subtotal or total colectomy, with multiple biopsies
72665	PROCTECTOMY, PARTIAL - WITHOUT ANASTOMOSIS	Proctectomy, partial, without anastomosis, perineal approach
72666	ALTEMEIER TRANSPERINEAL EXCISION OF RECTAL PROCIDE	ALTEMEIER TRANSPERINEAL EXCISION OF RECTAL PROCIDENTIA WITH ANASTOMOSIS NOTE: I) INCLUDES LEVATOR MUSCLE IMBRICATION (70671). II) SPHINCTEROPLASTY(70666) IS PAID IN ADDITION IF PERFORMED THROUGH A SEPARATE INCISION. II) COLOSTOMY PAID IN ADDITION IF REQUIRED.
72669	EXCISION OF RECTAL TUMOUR, 0 TO 2.5 CM	EXCISION OF RECTAL TUMOUR, TRANSANAL APPROACH TO INCLUDE OPERATIVE SIGMOIDOSCOPY - 0 TO 2.5 CM - OPERATION ONLY
72670	TUMOR - RECTAL - EXCISION - 2.6 TO 5 CM.	EXCISION OF RECTAL TUMOUR, TRANSANAL APPROACH TO INCLUDE OPERATIVE SIGMOIDOSCOPY - 2.6 TO 5 CM (OPERATION ONLY)
72671	EXCISION OF RECTAL TUMOUR GREATER THAN 5 CM	EXCISION OF RECTAL TUMOUR, TRANSANAL APPROACH TO INCLUDE OPERATIVE SIGMOIDOSCOPY - GREATER THAN 5 CM (OPERATION ONLY)
72673	TRANSANAL ENDO. MICRO. RESECTION OF RECTAL TUMOUR	TRANSANAL ENDOSCOPIC MICROSURGICAL RESECTION OF RECTAL TUMOUR NOTES: I) PAID ONLY IF A SEALED AND INSUFFLATING OPERATING

FITM_CD	FITM	FITM_DSCR
		PROCTOSCOPE IN EMPLOYED WITH VISUALIZATION VIA AN ENDOSCOPIC CAMERA (NOT UNDER DIRECT VISION). II) NOT PAID WITH 70683, 72669, 72670 AND 72671. III) RESECTION OF ONE ADDITIONAL LESION IS PAYABLE AT 50% ONLY IF COMPLETE REMOVAL, REPOSITIONING AND REINSERTION OF THE INSUFFLATING OPERATING PROCTOSCOPE IS REQUIRED. IV) IF PROCEDURE IS CONVERTED TO OPEN, BILL UNDER THE APPROPRIATE OPEN PROCEDURE AT 100% AND 04001 AT 50%. V) FEE ITEMS SY00715, SY10714, SY00716, AND SY00718 ARE INCLUDED IF DONE AT THE SAME TIME. VI) RESTRICTED TO GENERAL SURGERY.
72715	COLOSTOMY OR ILEOSTOMY - LOOP - LAPAROSCOPIC	COLOSTOMY OR ILEOSTOMY - LOOP - LAPAROSCOPIC
72720	RESECTION SMALL INTESTINE/ENTEROSTOMY-LAPAROSCOPIC	RESECTION OF SMALL INTESTINE WITH ENTEROSTOMY; WITHOUT ANASTOMOSIS (DOES NOT INCLUDE SEPARATE ENTEROSTOMIES OR RESECTIONS) - LAPAROSCOPIC
72721	MOBILIZATION OF SPLENIC FLEXURE - LAP (EXTRA)	MOBILIZATION(TAKE-DOWN) OF SPLENIC FLEXURE PERFORMED IN CONJUNCTION WITH PARTIAL COLECTOMY-LAPAROSCOPIC-EXTRA (NOT APPLICABLE TO RIGHT OR LEFT HEMICOLECTOMY) (OPERATION ONLY) NOTES: I) RESTRICTED TO GENERAL SURGEONS. II) IF CONVERSION TO OPEN PROCEDURE IS REQUIRED, BILL UNDER THE APPROPRIATE OPEN PROCEDURE AT 100%.

FITM_CD	FITM	FITM_DSCR
72734	SIGMOID RESECTION-WITH END COLOSTOMY-LAPAROSCOPIC	SIGMOID RESECTION - WITH END COLOSTOMY AND CLOSURE OF DISTAL SEGMENT OR MUCOUS FISTULA (HARTMANN TYPE PROCEDURE) - LAPAROSCOPIC
72736	RESECTION OF SMALL INTESTINE WITH ANASTOMOSIS	RESECTION OF SMALL INTESTINE WITH ANASTOMOSIS - LAPAROSCOPIC
72740	PARTIAL RIGHT COLECTOMY - LAPAROSCOPIC	PARTIAL RIGHT COLECTOMY (CAECUM) WITH REMOVAL OF TERMINAL ILEUM AND ILEOCOLOSTOMY - LAPAROSCOPIC
72741	TOTAL PROCTOCOLECTOMY-SINGLE SURGEON/LAPAROSCOPIC	TOTAL PROCTOCOLECTOMY - WITH PERINEAL EXCISION OF RECTUM AND ILEOSTOMY - SINGLE SURGEON - LAPAROSCOPIC
72745	CONTINENT ILEOSTOMY (KOCH PROCEDURE) LAPAROSCOPIC	CONTINENT ILEOSTOMY (KOCH PROCEDURE) - LAPAROSCOPIC
72755	ANTERIOR RESECTION OF RECTOSIGMOID - LAPAROSCOPIC	ANTERIOR RESECTION OF RECTOSIGMOID FOR CARCINOMA (LOW PELVIC ANASTOMOSIS; COLOPROCTOSTOMY) WITH OR WITHOUT PROTECTIVE STOMA - LAPAROSCOPIC
72760	COLECTOMY - TOTAL, ABDOMINAL - LAPAROSCOPIC	COLECTOMY - TOTAL, ABDOMINAL, (WITHOUT PROCTECTOMY) - LAPAROSCOPIC NOTE: INCLUDES ILEOSTOMY OR ILEOPROCTOSTOMY
72762	ABDOMINO-PERINEAL RESECTION-SINGLE SURGEON	ABDOMINO-PERINEAL RESECTION - SINGLE SURGEON - LAPAROSCOPIC
72763	ABDOMINO-PERINEAL RESECTION-SYNCHRONOUS	ABDOMINO-PERINEAL RESECTION - SYNCHRONOUS ABDOMINAL PORTION - LAPAROSCOPIC
72765	TAKE-DOWN OF PELVIC POUCH - LAPAROSCOPIC	TAKE-DOWN OF PELVIC POUCH, TO INCLUDE ILEOSTOMY - LAPAROSCOPIC
72767	PROCTECTOMY WITH RECTAL MUCOSECTOMY-LAPAROSCOPIC	PROCTECTOMY WITH RECTAL MUCOSECTOMY, ILEOANAL ANASTOMOSIS, CREATION OF ILEAL RESERVOIR (S OR J) WITH OR WITHOUT LOOP ILEOSTOMY - LAPAROSCOPIC
72769	COLECTOMY AND HEMIPROCTECTOMY - LAPAROSCOPIC	COLECTOMY AND HEMIPROCTECTOMY - LAPAROSCOPIC

FITM_CD	FITM	FITM_DSCR
72770	COLO-COLOSTOMY OR ENTERO-COLOSTOMY-LAPAROSCOPIC	COLO-COLOSTOMY OR ENTERO-COLOSTOMY - LAPAROSCOPIC NOTE: PCV72770 APPLIES TO UNPREPARED, NON-RESECTABLE BOWEL OBSTRUCTIONS. IN ALL OTHER INSTANCES, 07643 IS APPLICABLE INSTEAD.
72788	COLOSTOMY OF ILEOSTOMY - END - LAPAROSCOPIC	COLOSTOMY OR ILEOSTOMY - END - LAPAROSCOPIC
72789	TOTAL PROCTOCOLOECTOMY - SYN.ABD.PORTION	TOTAL PROCTOCOLECTOMY - SYNCHRONOUS - ABDOMINAL PORTION - LAPAROSCOPIC

Appendix G Budget impact for BC in total costs of management of colorectal surgeries and its consequences

		2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	Total
Volume of primary surgeries		55,182	5,307	5,432	5,558	5,677	5,797	5,917	6,037	6,153	6,265	6,379	6,494	6,611	6,726	6,833	6,941	7,042	7,136	7,220	7,297	126,005
Status quo no ICGA	N. Deaths due Leak	57	58	59	61	62	63	65	66	67	69	70	71	72	74	75	76	77	78	79	80	1,379
	N. Complications	631	646	661	677	691	706	720	735	749	763	777	791	805	819	832	845	857	869	879	888	15,340
	N. Permanent stomas	242	248	253	259	264	270	275	280	286	291	296	301	306	311	316	321	325	329	333	337	5,842
	Total Health Care Cost	151.1 M	155.0 M	158.9 M	162.8 M	166.4 M	170.2 M	173.9 M	177.6 M	181.2 M	184.7 M	188.3 M	191.8 M	195.4 M	199.0 M	202.4 M	205.8 M	208.9 M	211.9 M	214.6 M	217.0 M	3.7 B
	MSP Portion	30.3 M	31.0 M	31.8 M	32.5 M	33.2 M	33.9 M	34.6 M	35.3 M	36.0 M	36.7 M	37.3 M	38.0 M	38.7 M	39.4 M	40.0 M	40.6 M	41.2 M	41.8 M	42.2 M	42.7 M	737.2 M
	HA Portion	120.8 M	123.9 M	127.1 M	130.3 M	133.2 M	136.2 M	139.3 M	142.3 M	145.2 M	148.0 M	150.9 M	153.8 M	156.8 M	159.7 M	162.4 M	165.1 M	167.7 M	170.1 M	172.3 M	174.3 M	3.0 B
ICGA in 100% of colorectal surgeries 42 Spy Elite, 38 Spy Pinpont	N. Deaths due Leak	33	34	35	35	36	37	38	39	39	40	41	41	42	43	44	44	45	46	46	47	804
	Impact on Mortality	-24	-24	-25	-25	-26	-26	-27	-28	-28	-29	-29	-30	-30	-31	-31	-32	-32	-33	-33	-33	-575
	N. Complications	368	377	386	395	403	412	420	429	437	445	453	461	469	478	485	493	500	507	513	518	8946
	Impact on Complications	-263	-269	-276	-282	-288	-294	-300	-306	-312	-318	-324	-330	-335	-341	-347	-352	-357	-362	-366	-370	-6394
	N. Permanent stomas	170	174	178	182	185	189	193	197	200	204	207	211	215	218	221	225	228	231	234	236	4097
	Impact on Stomas	-72	-74	-76	-77	-79	-80	-82	-84	-85	-87	-88	-90	-91	-93	-94	-96	-97	-99	-100	-101	-1745
	Total Health Care Cost	135.3 M	138.7 M	142.1 M	145.6 M	148.8 M	152.1 M	155.4 M	158.7 M	161.8 M	164.9 M	168.1 M	171.2 M	174.4 M	177.6 M	180.5 M	183.5 M	186.3 M	188.9 M	191.3 M	193.4 M	3.3 B
	MSP Portion	28.6 M	29.3 M	29.9 M	30.6 M	31.3 M	32.0 M	32.6 M	33.3 M	33.9 M	34.5 M	35.2 M	35.8 M	36.4 M	37.1 M	37.7 M	38.3 M	38.8 M	39.3 M	39.8 M	40.2 M	694.5 M
	HA Portion	106.7 M	109.4 M	112.2 M	114.9 M	117.5 M	120.1 M	122.8 M	125.4 M	127.9 M	130.4 M	132.9 M	135.4 M	138.0 M	140.5 M	142.9 M	145.3 M	147.5 M	149.6 M	151.5 M	153.2 M	2.6 B
	Capital costs with acquisitions	[redacted]																				
	Capital costs with maintenance	[redacted]																				
	Total Health Care + Capital Costs	[redacted]																				
	Total Budget Impact compared to Status Quo	7.9 M	-14.7 M	-15.2 M	-15.6 M	-16.0 M	-16.5 M	-16.9 M	-17.3 M	-17.8 M	-18.2 M	3.6 M	-19.0 M	-19.4 M	-19.9 M	-20.2 M	-20.6 M	-21.0 M	-21.4 M	-21.7 M	-22.0 M	-322.0 M
	MSP Budget Impact	-1.8 M	-1.8 M	-1.8 M	-1.9 M	-1.9 M	-2.0 M	-2.0 M	-2.0 M	-2.1 M	-2.1 M	-2.2 M	-2.2 M	-2.2 M	-2.3 M	-2.3 M	-2.3 M	-2.4 M	-2.4 M	-2.4 M	-2.5 M	-42.7 M
	HA Budget Impact compared to Status Quo	9.7 M	-12.9 M	-13.3 M	-13.7 M	-14.1 M	-14.5 M	-14.9 M	-15.3 M	-15.7 M	-16.0 M	5.7 M	-16.8 M	-17.2 M	-17.6 M	-17.9 M	-18.3 M	-18.6 M	-19.0 M	-19.3 M	-19.5 M	-279.3 M
	ICGA Costs Disposables	[redacted]																				

	Total ICGA Costs (Disposables + Capital Costs)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Cost Avoided with Complications (Health System)	-18.7 M	-19.2 M	-19.7 M	-20.2 M	-20.7 M	-21.2 M	-21.7 M	-22.2 M	-22.7 M	-23.2 M	-23.7 M	-24.1 M	-24.6 M	-25.1 M	-25.6 M	-26.0 M	-26.5 M	-26.9 M	-27.2 M	-27.6 M	-466.9 M
	Cost Avoided with Complications (Health Authorities)	-16.9 M	-17.4 M	-17.9 M	-18.4 M	-18.8 M	-19.3 M	-19.7 M	-20.2 M	-20.6 M	-21.1 M	-21.5 M	-21.9 M	-22.4 M	-22.8 M	-23.3 M	-23.7 M	-24.1 M	-24.4 M	-24.8 M	-25.1 M	-424.2 M
ICGA in 80.9% of colorectal surgeries ICGA in 77.9% of colorectal surgeries 17 Spy Elite, 17 Spy Pinpoint	N. Deaths due Leak	38	39	40	41	42	43	44	45	45	46	47	48	49	50	51	51	52	53	53	54	931
	Impact on Mortality	-18	-19	-19	-20	-20	-21	-21	-21	-22	-22	-23	-23	-24	-24	-24	-25	-25	-25	-26	-26	-448
	N. Complications	426	436	447	457	467	477	486	496	506	515	524	534	543	553	562	571	579	587	594	600	10358
	Impact on Complications	-205	-210	-215	-220	-224	-229	-234	-239	-243	-248	-252	-257	-261	-266	-270	-274	-278	-282	-285	-289	-4982
	N. Permanent stomas	186	190	194	199	203	207	211	215	219	223	227	231	235	239	242	246	249	253	256	258	4483
	Impact on Stomas	-56	-58	-59	-60	-61	-63	-64	-65	-66	-68	-69	-70	-71	-72	-74	-75	-76	-77	-78	-78	-1359
	Total Health Care Cost	138.8 M	142.3 M	145.8 M	149.4 M	152.7 M	156.1 M	159.5 M	162.8 M	166.1 M	169.3 M	172.5 M	175.8 M	179.1 M	182.3 M	185.4 M	188.4 M	191.3 M	194.0 M	196.4 M	198.6 M	3.4 B
	MSP Portion	29.0 M	29.6 M	30.3 M	31.1 M	31.7 M	32.4 M	33.1 M	33.7 M	34.4 M	35.0 M	35.6 M	36.3 M	36.9 M	37.6 M	38.2 M	38.8 M	39.3 M	39.9 M	40.3 M	40.8 M	704.0 M
	HA Portion	109.8 M	112.6 M	115.5 M	118.3 M	121.0 M	123.7 M	126.4 M	129.1 M	131.7 M	134.3 M	136.9 M	139.5 M	142.1 M	144.8 M	147.2 M	149.6 M	152.0 M	154.1 M	156.1 M	157.9 M	2.7 B
	Capital costs with acquisitions	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Capital costs with maintenance	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Total Health Care + Capital Costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Total Budget Impact compared to Status Quo	-2.3 M	-12.0 M	-12.4 M	-12.7 M	-13.1 M	-13.4 M	-13.7 M	-14.1 M	-14.4 M	-14.7 M	-5.6 M	-15.4 M	-15.7 M	-16.0 M	-16.3 M	-16.7 M	-16.9 M	-17.2 M	-17.5 M	-17.7 M	-277.9 M
	MSP Budget Impact	-1.4 M	-1.4 M	-1.4 M	-1.5 M	-1.5 M	-1.5 M	-1.6 M	-1.6 M	-1.6 M	-1.7 M	-1.7 M	-1.7 M	-1.7 M	-1.8 M	-1.8 M	-1.8 M	-1.9 M	-1.9 M	-1.9 M	-1.9 M	-33.2 M
	HA Budget Impact compared to Status Quo	-902.8 K	-10.6 M	-10.9 M	-11.3 M	-11.6 M	-11.9 M	-12.2 M	-12.5 M	-12.8 M	-13.1 M	-4.0 M	-13.7 M	-14.0 M	-14.3 M	-14.5 M	-14.8 M	-15.1 M	-15.3 M	-15.6 M	-15.8 M	-244.7 M
	ICGA Costs Disposables	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Total ICGA Costs (Disposables + Capital Costs)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Cost Avoided with Complications (Health System)	-14.6 M	-15.0 M	-15.4 M	-15.8 M	-16.2 M	-16.5 M	-16.9 M	-17.3 M	-17.7 M	-18.1 M	-18.4 M	-18.8 M	-19.2 M	-19.6 M	-19.9 M	-20.3 M	-20.6 M	-20.9 M	-21.2 M	-21.5 M	-363.8 M
	Cost Avoided with Complications (Health Authorities)	-13.2 M	-13.6 M	-13.9 M	-14.3 M	-14.7 M	-15.0 M	-15.4 M	-15.7 M	-16.1 M	-16.4 M	-16.8 M	-17.1 M	-17.4 M	-17.8 M	-18.1 M	-18.4 M	-18.8 M	-19.0 M	-19.3 M	-19.6 M	-330.6 M