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Abstract

Background

Small-bowel capsule endoscopy is a tool used to visualize the small bowel to identify the location of bleeds in obscure gastrointestinal bleeding (OGIB). Capsule endoscopy is currently funded in Ontario in cases where there has been a failure to identify a source of bleeding via conventional diagnostic procedures. In Ontario, capsule endoscopy is a diagnostic option for patients whose findings on esophagogastroduodenoscopy, colonoscopy, and push enteroscopy have been negative (i.e., the source of bleeding was not found).

Objectives

This economic analysis aims to estimate the budget impact of different rates of capsule endoscopy use as a complement to push enteroscopy procedures in patients aged 18 years and older.

Data Sources

Population-based administrative databases for Ontario were used to identify patients receiving push enteroscopy and small-bowel capsule endoscopy in the fiscal years 2008 to 2012.

Review Methods

A systematic literature search was performed to identify economic evaluations of capsule endoscopy for the investigation of OGIB. Studies were assessed for their methodological quality and their applicability to the Ontarian setting. An original budget impact analysis was performed using data from Ontarian administrative sources and published literature. The budget impact was estimated for different levels of use of capsule endoscopy as a complement to push enteroscopy due to the uncertain clinical utility of the capsule based on current clinical evidence. The analysis was conducted from the provincial public payer perspective.

Results

With varying rates of capsule endoscopy use, the budgetary impact spans from savings of $510,000,[1] when no (0%) push enteroscopy procedures are complemented with capsule endoscopy, to $2,036,000, when all (100%) push enteroscopy procedures are complemented with capsule endoscopy. A scenario where 50% of push enteroscopy procedures are complemented with capsule endoscopy (expected use based on expert opinion) would result in additional expenditure of about $763,000.

Limitations

In the literature on OGIB, estimates of rebleeding rates after endoscopic procedures or spontaneous cessation rates are unreliable, with a lack of data. Rough estimates from expert consultation can provide an indication of expected additional use of capsule endoscopy; however, a wide range of capsule uses was explored.

[1]All currency is in 2014 Canadian dollars unless otherwise indicated.

Conclusions

The budgetary impact in the first year in Ontario of capsule endoscopy use to complement push enteroscopy procedures ranges from $510,000 in savings to an additional expenditure of $2,036,000 (at 0% and 100% push enteroscopy procedures complemented, respectively). The expected scenario of 50% of push enteroscopy procedures likely to benefit from the use of capsule endoscopy, based on expert opinion, would result in additional expenditures of $763,000 in the first year.

Plain Language Summary

Small-bowel capsule endoscopy (CE) is a diagnostic test to investigate obscure gastrointestinal bleeding (OGIB) when the source of bleeding is suspected to be the small bowel. This procedure is performed after upper gastrointestinal (GI) bleeding has been ruled out through an esophagogastroduodenoscopy and lower GI bleeding has been ruled out through colonoscopy. After these procedures have been performed, they are sometimes repeated; then a push enteroscopy (PE) is performed, which explores the upper GI tract and a small portion of the small bowel.

Health Quality Ontario was asked to investigate the appropriate use of CE and its economic impact on the health care system. The evidence-based analysis (reported separately) looked at the usefulness of CE compared with PE, finding there was very low GRADE evidence that it had increased accuracy in locating the source of bleeding.

Our economic analysis explored the costs associated with different rates of CE use to complement PE, compared with current use where it complements about 20% of PE procedures. We estimated that CE currently costs Ontario about $510,000[2] a year, whereas investigation of OGIB with PE and CE combined totals $2.1 million annually. The budgetary impact for Ontario in the first year of small-bowel CE use to complement PE ranges from a savings of $510,000 (if 0% of PEs were complemented; i.e., if the technology were delisted and its current use eliminated) to an additional expenditure of $2,036,000 (if 100% of PEs were complemented). In the scenario where 50% of PE procedures would be complemented (the expected proportion of patients expected to benefit from CE, based on expert opinion), the estimated cost would be an additional $763,000 in the first year of implementation. The impact on government spending was estimated for a wide range of rates of CE complementing PE procedures. The estimates of changes in government spending are for 1 year only and do not include any changes in costs and savings over the long term.

[2]All currency is in 2014 Canadian dollars unless otherwise indicated.

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List of Abbreviations

CCI	Canadian Classification of Health Interventions
CE	Capsule endoscopy
DBE	Double-balloon enteroscopy
GI	Gastrointestinal
ICER	Incremental cost-effectiveness ratio
ICES	Institute for Clinical and Evaluative Sciences
LYG	Life-year gained
OCCI	Ontario Case Costing Initiative
OGIB	Obscure gastrointestinal bleeding
OHIP	Ontario Health Insurance Plan
PE	Push enteroscopy
QALY	Quality-adjusted life-year

Background

The Programs for the Assessment of Technology in Health (PATH) Research Institute was commissioned by Health Quality Ontario to evaluate the cost-effectiveness and predict the costs and effects of small bowel capsule endoscopy for obscure gastrointestinal bleeding. Published economic evaluations are reviewed, and the structure and inputs of the economic model used to estimate cost-effectiveness are summarized. The results of the economic analyses are presented for the small bowel capsule endoscopy versus push enteroscopy, and the budget impact of implementing each intervention is estimated.

Health Quality Ontario conducts full evidence-based analyses, including economic analyses, of health technologies being considered for use in Ontario. These analyses are then presented to the Ontario Health Technology Advisory Committee, whose mandate it is to examine proposed health technologies in the context of available evidence and existing clinical practice, and to provide advice and recommendations to Ontario health care practitioners, the broader health care system, and the Ontario Ministry of Health and Long-Term Care.

DISCLAIMER: Health Quality Ontario uses a standardized costing method for its economic analyses. The main cost categories and associated methods of retrieval from the province's perspective are described below.

Hospital costs: Ontario Case Costing Initiative cost data are used for in-hospital stay, emergency department visit, and day procedure costs for the designated International Classification of Diseases diagnosis codes and Canadian Classification of Health Interventions procedure codes. Adjustments may be required to reflect accuracy in the estimated costs of the diagnoses and procedures under consideration. Due to difficulties in estimating indirect costs in hospitals associated with a particular diagnosis or procedure, Health Quality Ontario normally defaults to a consideration of direct treatment costs only.

Non-hospital costs: These include physician services costs obtained from the Ontario Schedule of Physician Benefits, laboratory fees from the Ontario Schedule of Laboratory Fees, drug costs from the Ontario Drug Benefit Formulary, and device costs from the perspective of local health care institutions whenever possible, or from the device manufacturer.

Discounting: For cost-effectiveness analyses, a discount rate of 5% is applied (to both costs and effects/QALYs), as recommended by economic guidelines.

Downstream costs: All reported downstream costs are based on assumptions of population trends (i.e., incidence, prevalence, and mortality rates), time horizon, resource utilization, patient compliance, health care patterns, market trends (i.e., rates of intervention uptake or trends in current programs in place in the province), and estimates of funding and prices. These may or may not be realized by the Ontario health care system or individual institutions and are often based on evidence from the medical literature, standard listing references, and educated hypotheses from expert panels. In cases where a deviation from this standard is used, an explanation is offered as to the reasons, the assumptions, and the revised approach.

The economic analysis represents ***an estimate only***, based on the assumptions and costing methods explicitly stated above. These estimates will change if different assumptions and costing methods are applied to the analysis.

NOTE: Numbers may be rounded to the nearest decimal point, as they may be reported from an Excel spreadsheet.

Objective of Analysis

The objective of this analysis was to determine the cost and budgetary impact of the use of different levels of capsule endoscopy (CE) as a diagnostic tool complementary to push enteroscopy (PE) in patients with obscure gastrointestinal bleeding (OGIB) from the perspective of the Ontario Ministry of Health and Long-Term Care.

Clinical Need and Target Population

Obscure Gastrointestinal Bleeding

Obscure gastrointestinal bleeding (OGIB) is defined as persistent or recurrent bleeding associated with negative findings on upper and lower gastrointestinal (GI) evaluations (i.e., the source of bleeding was not found). Obscure gastrointestinal bleeding can be further classified into obscure overt and obscure occult bleeding, depending on the presence or absence of clinically evident bleeding. (1) Overt OGIB is defined as visible GI bleeding (e.g., melena or hematochezia) and can be categorized as active (i.e., there is evidence of ongoing bleeding) or inactive bleeding. Occult OGIB occurs when there is a positive finding on a fecal occult blood test or an unexplained iron deficiency anemia suspected to be caused by GI blood loss. (2)

Prevalence and Incidence

Gastrointestinal bleeding is a common clinical presentation, with about 100 episodes per 100,000 persons per year. (3) Obscure gastrointestinal bleeding represents about 5% of all cases of GI bleeding, with the small bowel as the presumed source. This has led to the use of the new term "mid-gastrointestinal bleeding" to describe bleeding that occurs between the papilla and the ileocecal valve. (4)

Obscure gastrointestinal bleeding can arise from any lesion throughout the GI tract, although a majority of instances commonly arise in the small bowel. (5) The etiology of bleeding in the small bowel is varied and dependent on the age of the patient. (1)

Interventions Under Evaluation

The diagnosis and management of patients with OGIB is particularly challenging due to the length and complex loops of the small intestine. (6) Indeed, the presenting symptoms can help direct the appropriate interventions. Hematemesis indicates upper GI bleeding, whereas melena can indicate bleeding occurring anywhere from the nose to the large bowel. Hematochezia suggests either a lower GI bleed or a fast upper GI bleed.

For this analysis, the intervention of interest is CE for the identification of bleeding in patients with a suspected small-bowel bleed. Small-bowel CE has also been used in studies to monitor or diagnose Crohn's disease, with related economic models. Expert consultation revealed that small-bowel CE is used sparingly for the indication of Crohn's disease (about 1/100 capsules); thus, this analysis focuses on the indication of OGIB specifically, regardless of the cause of presentation.

Capsule endoscopy was first introduced by Given Imaging Ltd. (Yokneam, Israel) in 2001. Since that time, a third-generation product has been licensed and 4 other manufacturers now produce small-bowel CE devices (Table 1). The introduction of CE has allowed for the visualization of the entire GI tract. It is a relatively simple and noninvasive test, provided the patient can swallow the capsule. (7) The primary limitation is that the technology is purely diagnostic and offers no therapeutic benefit such as obtaining biopsies or administering therapy, besides directing further therapeutic measures.

Table 1: Small-Bowel Endoscopy Capsules Licensed for Use in Canada

Company Name	Licence No.	Date Issued	Class	Device Name
CapsoVision, Inc.	89763	2012-09-26	2	CapsoCam
Chongqing Jinshan Science & Technology (Group) Co., Ltd.	86038	2011-05-06	2	OMOM Smart Capsule
Given Imaging Ltd.	69804	2005-11-25	2	PillCam SB
Given Imaging Ltd.	69804	2007-06-18	2	PillCam SB2
Given Imaging Ltd.	69804	2013-03-13	2	PillCam SB3
IntroMedic Co., Ltd.	77649	2008-07-23	2	MiroCam Capsule Endoscope
IntroMedic Co., Ltd.	86466	2011-06-29	2	MiroCam Capsule Endoscope
Olympus Medical Systems Corp.	75207	2009-05-05	2	Capsule Endoscope System

In general, a CE system consists of 4 main parts: a disposable capsule, an image recorder, a portable real-time monitor, and a computer workstation. The capsule is swallowed and is propelled through the GI tract via bowel peristalsis. The capsule contains a video camera, a light source, a radio transmitter, and batteries. The various capsules differ in size, frame rate, and field of view. Once the capsule is swallowed by a patient, it begins to acquire images and transmit them to the sensor array attached to the patient's abdomen; this sensor array subsequently sends the data to the recorder (worn as a belt around the patient's waist). The data are then downloaded to a computer workstation, and the images are evaluated by a physician, using computer software. Each manufacturer provides its own software to process the data downloaded from the data recorder.

During CE, the patient is allowed to resume normal activities. The capsule is excreted usually after 8 to 72 hours, although occasionally excretion can take longer. Three of the available capsules use radio-frequency technology to transmit data, whereas the MiroCam capsule (IntroMedic Co., Ltd., Seoul, Korea) transmits data through a field generated by electrodes on the capsule and the direct contact between cellular tissue or bodily fluid and the electrodes attached to the human body. For all models except the CapsoCam capsule (CapsoVision, Inc., Silicon Valley, California), the capsule is discarded after excretion. The CapsoCam capsule does not generate or transfer radio-frequency signals, and all the data are stored onboard the capsule. Therefore, the patient is not required to wear any external devices or wires but is required to retrieve the capsule for data extraction.

In patients with dysphagia, gastroparesis, or known or suspected anatomical abnormalities that would preclude the safe ingestion of the capsule, the capsule can be placed into the stomach or small bowel. These delivery methods include overtubes to deliver the capsule into the stomach, and standard polypectomy snares and nets to deliver the capsule into the duodenum. (8) A capsule endoscope delivery device (US Endoscopy, Mentor, Ohio) can also be used; in this case, a disposable sheath is preloaded through the working channel of a standard endoscope and allows the activated video capsule endoscope to be delivered directly to the desired anatomical area.

A patency capsule is also available (Agile Patency System, Given Imaging) and is used to identify patients at high risk of capsule retention. This is a nonvideo capsule composed of lactose and barium that dissolves within 30 to 100 hours of entering the GI tract. Timer plugs on the capsule facilitate the controlled disintegration of the capsule body. The capsule contains a radio-frequency identification tag that can be used to determine the capsule location.

Contraindications for the use of CE include known bowel strictures or swallowing disorders and a history of bowel obstruction. Recent abdominal surgery is also a relative contraindication. (9)

Deep Enteroscopy

1. Push enteroscopy involves the oral insertion of a long dedicated enteroscope and allows for the examination of the upper GI tract up to the proximal jejunum, about 50 to 100 cm distal to the ligament of Treitz. (5) It is performed as an outpatient procedure under general or conscious sedation.
2. Balloon-assisted enteroscopy allows for the examination of the entire small bowel for both diagnostic and therapeutic purposes. The procedure involves the use of a special enteroscope and an overtube, both of which have balloons at the distal end. The system using 2 balloons is called double-balloon enteroscopy (DBE), and the system using a single balloon is called single-balloon enteroscopy. The enteroscope is advanced in short stages through the small bowel through alternating steps of inflating and deflating the balloons, alternating the insertion of the enteroscope and overtube, and pulling back the enteroscope and overtube. By repeating this series of push and pull, a longer distance in the small bowel can be traversed compared with conventional endoscopy techniques. Access is either from the foregut (antegrade) or colon (retrograde). Both routes need to be combined in order to allow for complete enteroscopy of the small bowel. (10) The procedure requires sedation and can take several hours. It can be used to obtain tissue biopsies for histological analysis, and can also provide other therapeutic options such as hemostasis of bleeding, polypectomy, balloon dilation, and foreign-body extraction. In addition, this procedure can be used to mark pathology with India ink to direct later surgery. (10)

Ontario Context

The Ontario Ministry of Health and Long-Term Care currently funds the time for a clinician to interpret the results of CE, as funded through Ontario Health Insurance Plan (OHIP) fee code G332. Funding is provided only when the procedure is rendered for the purpose of identifying GI bleeding of obscure origin when all appropriate conventional techniques have failed to identify a source. (11) There are some instances where the use of the technology occurs outside of this definition (e.g., the examination of the small bowel with no evidence of bleeding, or the monitoring of Crohn's disease in cases without unidentified bleeding), but these are not funded through the Ministry of Health and Long-Term Care.

A clinical pathway to assess OGIB in Ontario has not been formalized; although, through discussions with experts, a standard of practice followed by physicians in Ontario was described. Upon presentation with OGIB, a patient undergoes both an esophagogastroduodenoscopy to rule out the upper GI tract as the cause of bleeding and a colonoscopy to rule out the lower GI tract as the source. With continuation of symptoms, patients may undergo a repeat of either or both procedures and then proceed to PE to investigate the upper portion of the small bowel. Patients with negative findings on PE and a continuation of symptoms are considered for CE so that the small bowel can be better visualized. If CE produces negative findings and bleeding continues, patients are referred for DBE. Alternatively, patients may be referred directly for DBE if PE produces negative findings and symptoms continue.

For this reason, the budget impact of the rates at which CE complements PE findings are investigated.

Economic Analysis

Research Questions

What are the costs and budgetary impact of different rates of CE use for the diagnosis of obscure small-bowel bleeding, acting as a diagnostic tool complementary to PE, from the perspective of the Ontario Ministry of Health and Long-Term Care?

Economic Literature Review

Research Methods

Literature Search

Search Strategy

An economic literature search was performed on December 9, 2013, using Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE, Ovid Embase, Wiley's Cochrane Library (Issue 4 of 4 Oct 2013), and HEED, for studies published from January 1, 1998, to November 27, 2013. (Appendix 1 provides details of the search strategies.)

Titles and abstracts were reviewed by a single reviewer, and the full texts of all potential relevant articles were retrieved. The reference lists of all full-text articles were also reviewed to identify any additional studies that may not have been identified in the original search.

Inclusion Criteria

- English-language full-text publications
- articles published between January 1, 1998, and December 9, 2013
- full economic evaluations: cost-utility analyses, cost-effectiveness analyses, cost-benefit analyses
- cost-minimization studies
- economic evaluations reporting incremental cost-effectiveness ratios (ICERs) (i.e., cost per quality-adjusted life-year [QALY]/life-years gained [LYGs] or cost per event avoided)
- studies in patients with GI bleeding
- studies including CE

Exclusion Criteria

- studies relating to Crohn's disease
- narrative reviews
- editorials
- studies in pediatric populations
- abstracts, posters, reviews, letters/editorials, foreign language publications, unpublished studies

Results of Economic Literature Review

A total of 219 citations were identified in the database search, and 210 articles were excluded after the title and abstract review. Retrieval of the full texts of the remaining 9 articles was attempted, with 7

articles being collected for a more detailed review. After reviewing the full texts, we found that 4 articles met the inclusion criteria. A review of the reference lists did not result in any other potential articles.

The only cost-utility analysis identified through the systematic review was an American study by Gerson and Kamal, which used a model to compare no therapy, PE, intraoperative enteroscopy, angiography, DBE, and capsule-directed DBE in a population represented by a base-case patient: a 50-year-old man with a 6-month history of recurrent melena and associated iron-deficiency anemia. (12) In this scenario, the patient had prior normal findings on upper endoscopic examination, a colonoscopy, and a small-bowel series. In the CE arm, the patient would only proceed to DBE if he had persistent obscure bleeding after the CE investigation. The analysis was performed from the perspective of a third-party payer over a 1-year time horizon by using 1-month cycles for probabilities of hemorrhage, bleeding cessation, and alterations in health-related quality of life (because of a lack of data for rebleeding and bleeding cessation). The no-therapy arm (supportive blood transfusions only) was the least expensive and least effective treatment (average cost $532,[3] with 0.870 QALYs). The initial DBE arm cost $4,207 and was associated with 0.942 QALYs, compared with the capsule-directed DBE arm, which cost $4,309 and was associated with 0.942 QALYs. All other treatment arms cost more than the DBE arm and were less effective (except for PE, which was less expensive but less effective). The ICER (ratio comparing costs and effectiveness for the base case arm with the most effective arm) was $20,833 per QALY gained. The authors concluded that an initial DBE would be a cost-effective approach, but that capsule-directed DBE "might be preferred" because of the decreased use of endoscopic resources and fewer related complications.

Marmo et al performed a cost-effectiveness analysis to assess the CE examination versus "other diagnostic procedures" in patients with OGIB. (13) This study was based upon an Italian nationwide retrospective cohort study in patients with OGIB observed from January 2003 to October 2005 in 9 Italian hospitals. Patients were subjected to 2 alternative diagnostic pathways: 1 including CE and 1 not including CE (but including PE, small-bowel follow-through, enteroclysis, upper GI endoscopy, colonoscopy, computed tomography, angiography, magnetic resonance imaging, ultrasonography, scintigraphy, and intraoperative enteroscopy). The results of CE were compared with those of other procedures performed during the same admission or, if not applicable, over a time span that included the preceding or the following 3 months. This study showed significant superiority of CE over the other diagnostic procedures in terms of both diagnostic efficacy and cost savings, with a reduction in the median cost per single diagnosis of €1,738.07. The authors also suggested that CE should be used early, as the first-line diagnostic test after negative findings on upper GI endoscopy and total colonoscopy.

Somsouk and colleagues performed a cost-minimization analysis from the perspective of a US third-party payer. (14) This study compared initial small-bowel follow-through, enteroclysis, PE, CE, and DBE for a hypothetical cohort of patients who had experienced recurrent and refractory occult GI bleeding and in whom upper endoscopy and ileocolonoscopy had produced negative findings. Costs were determined via a treatment pathway with the medically refractory disease modelled with 2 separate end points: 1 in which treatment or definitive diagnosis was necessary, and 1 in which visual diagnosis was sufficient to suspend testing. The authors found that the least costly strategy was initial DBE in the evaluation of subjects with OGIB, with a cost of $3,824 per patient. Initial CE cost an incremental $440, whereas the other strategies were more expensive than CE. The authors concluded that CE and deep enteroscopy are cost-effective interventions compared with the previously available tests for small-bowel imaging and therapy. Furthermore, the authors concluded that CE appears to be preferred as the initial test when considering the overall endoscopic workload and if DBE were to be performed only if CE demonstrated positive

[3] All currency is in 2014 Canadian dollars unless otherwise indicated.

findings. The authors also noted that CE is preferred if the capacity of DBE is insufficient to meet demand, as its prolonged procedure time, fixed cost of capital investment, and technical skill required are likely to keep its capacity low, making CE a viable initial test in OGIB.

Albert et al performed a cost-minimization study comparing initial CE versus initial DBE to detect small-bowel bleeding as applied to a retrospectively collected cohort of patients, from the perspective of a German third-party payer. (15) The scenarios explored were diagnostic CE plus directed therapeutic DBE (on positive findings in the CE), and/or unidirectional diagnostic plus therapeutic DBE. For each of the 2 scenarios, the frequency of investigations per annum at which cost per procedure equalized was determined. The break-even point for the first scenario was 100 procedures per year; for the second, it was 70 procedures per year. Personnel cost, procedure time, procedures per year, and rate of therapeutic enteroscopy all had major influences on the procedure cost. In the studied patient cohort, the "CE-first" and the "DBE-first" strategies produced procedural costs of €830 and €1,076 per patient to obtain a diagnosis and €1,042 versus €1,181 to achieve therapeutic enteroscopy, respectively. The authors concluded that the cost of CE is more robust with respect to the impact of frequency and length of procedure to cost, and that a strategy incorporating CE seems to therefore minimize costs.

Budget Impact Analysis

Several economic evaluations identified in the literature review addressed OGIB investigation with CE, but no studies were relevant to the Ontarian context given the different treatment pathways and uncertain clinical utility as determined through the clinical evidence-based analysis (reported separately). Given these limitations, a budget impact analysis was performed to investigate the effect of varying the proportion of PE procedures that are complemented with small-bowel CE.

Research Methods

Types of Analyses

A descriptive cost analysis and a budget impact analysis were conducted to estimate the 1-year costs associated with an increased uptake of small-bowel CE as a follow-up diagnostic procedure after PE. A range of rates of CE use to complement PE were examined due to the difficulty in establishing the eligible patient population.

Perspective

The analysis was conducted from the perspective of the Ontario Ministry of Health and Long-Term Care.

Target Population and Database

The target population for this economic analysis was patients aged 18 years and older with OGIB who had received negative findings on upper and lower GI investigations through esophagogastroduodenoscopy and colonoscopy and were undergoing a PE procedure.

The potential number of patients eligible for the small-bowel CE was estimated via 2 methods: assumptions on the success of PE and rebleeding rates from a variety of lesions, derived from inputs in economic evaluations identified through the literature search (12); and estimates obtained through expert consultation. Table 2 presents the prevalence of various types of sources of bleeds, the proportion detected by PE procedures, rebleeding rates for detected and undetected sources, and calculated rebleeding rates and a total estimate, with combined estimates from Gerson and Kamal, based on a number of different trial results. (12) This shows an estimated 38% of patients being eligible for the small-bowel CE after PE, whereas expert opinion was that in practice about 50% of patients would be deemed eligible, based on the prevalence of common lesions and perceived clinical utility of CE. The

budget impact of a range of percentages of those eligible for small-bowel CE post-PE was explored, with 50% taken as the base case.

Table 2: Estimated Number of Patients Post–Push Enteroscopy Who Are Eligible for Capsule Endoscopy Based on Rebleeding Rates from Literature

Source of Bleed	Prevalence	Amount Detected by PE (16-38)	Rebleeds Post-PE	Rebleeds without Endoscopic Intervention	Calculated Total Proportion of Rebleeds
Angiodysplasia	0.40 (12)	0.18	0.20 (39, 40)	0.55 (33, 39, 40)	0.1948
Malignancy	0.05 (12)	0.02	—	0.90 (40)	—
Ulcerations	0.20 (12)	0.04	0.10 (41-43)	0.25 (40)	0.0488
Other	0.20 (12)	0.03	0.25 (44-47)	0.50 (39, 40)	0.0985
Missed lesions on upper and lower GI investigations	0.15 (48-50)	0.75 (12)	0.1875*	0.4625*	0.0244
Total					**0.3805**

Abbreviations: GI, gastrointestinal; PE, push enteroscopy.

*Parameters were not specified in Gerson and Kamal (12); thus weighted averages for angiodysplasia, malignancy, ulcerations, and other types of lesions were calculated.

The numbers of PE and CE procedures performed were derived from the Discharge Abstract Database and Same-day Surgery Database housed at the Institute for Clinical and Evaluative Sciences (ICES). ICES is an independent non-profit research organization that acts as a large repository for annually updated, de-identified, individual-level health administrative data. Disease-based cohorts can be created using health administrative case definitions that link hospital inpatient and outpatient care, physician claims, and drug benefits data over time. Data were captured from 2008 to 2012, which are the most recent data available.

Cohort Definition

All adult Ontarian residents in the database were included in the annual procedural counts. Individuals were excluded if they were aged 18 years or younger or if they were ineligible for OHIP coverage. The codes used for the collection of resource use are provided in Table 3; these were confirmed through expert consultation. Professional fee codes were identified through the Ontario Schedule of Benefits, (11) and Canadian Classification of Health Interventions (CCI) codes were from the Canadian Institute for Health Information. (51) It is important to note that the OHIP fee code used to identify patients undergoing a PE procedure (i.e., Z584) is also used as a professional fee code for the procedure (expert panel members, personal communication, March 2014). For this reason, the number of DBE procedures (identified through its Canadian Institute for Health Information International Statistical Classification of Diseases and Related Health Problems, 10th Revision [ICD-10] code) has been subtracted from the total number of procedures billed under OHIP fee code Z584. Although PE also has a CCI code to identify procedures, the indication is broad, capturing procedures other than the investigation of small-bowel bleeding.

Table 3: CCI and OHIP Fee Codes Used to Determine Number of Procedures

Procedure	OHIP Fee Code Used	CCI Code Used
Small-bowel capsule endoscopy	G332	3.OZ.94.AY
Double-balloon enteroscopy	—	2.NK.70-BA-BL 2.NK.71.BA-BL
Push enteroscopy	Z584	—

Resource Use

Using the fee codes and algorithm for calculating the net number of procedures for each diagnostic and therapeutic tool as described above, the numbers of procedures were captured through ICES and are presented in Table 4. The data presented are from 2008 to 2012, the most recent data available. Current use demonstrates that 491 small-bowel CE procedures were performed to complement the 2,451 PE procedures, resulting in a rate of 20% of PE procedures complemented by CE.

Table 4: Use of Procedures to Investigate Obscure Gastrointestinal Bleeding, Ontario, 2008 to 2012

Procedure	2008	2009	2010	2011	2012
Small-bowel capsule endoscopy	199	300	284	302	491
Push enteroscopy	1,982	3,547	2,680	2,420	2,451

Canadian Costs

The costs of PE and CE were calculated by incorporating costs from a number of sources: the cost of CE itself, obtained from the manufacturers; professional fees associated with the procedures; and the direct costs captured through the Ontario Case Costing Initiative (OCCI) database. These direct costs include direct medical costs (i.e., procedure, pathology, physician, nursing, diagnostic imaging, pharmacy, and laboratory costs) and hospital overhead costs (e.g., administration, finance, human resources, and plant operations).

One important component of the costs of PE and CE are those associated with complications due to the procedures. In the head-to-head comparison studies of PE and CE identified through the clinical evidence-based analysis, there were no adverse events reported for PE, whereas a 1.4% retention rate was reported for CE in a systematic review on CE complications. (52) According to this review, 12.5% of patients underwent a DBE procedure to retrieve the capsule, and 58.7% of patients underwent a surgical procedure; in the remaining cases, the capsules were excreted naturally or the results were not reported. The cost of capsule retrieval via surgical means was taken from a recent economic evaluation of small-bowel CE for the indication of Crohn's disease. Once converted to Canadian dollars and adjusted for inflation, the resulting estimate is $10,374.85 for capsule retrieval through surgical means. (53) The cost of DBE was determined in consultation with expert panel members, who aided in the identification of related professional fees and proper coding for obtaining direct costs from the OCCI database (see Appendix 2 for more detail). The cost of DBE is $1,409.37 (Table 5). The codes used to determine the cost of DBE were confirmed through expert consultation and include OHIP fee code A418, the code for partial assessment by a gastroenterologist; OHIP fee code Z459, the code used for PE and also DBE procedures (expert consultation); direct costs identified through OCCI; anesthesia consultation; and 6 basic units and 6 time units for the procedure. The costs related to complications are presented in Table 5.

Table 5: Average Cost of Capsule Retention

Complication	Rate (%)	Cost ($CAD)	Reference
Endoscopic retrieval (DBE)	**12.5**		
Direct costs (OCCI)		596.00	(54)
OSB A418—gastroenterologist consultation		38.05	(11)
OSB Z584—small-bowel push enteroscopy		185.15	(11)
OSB A015—anesthesia consultation		106.90	(11)
Anesthesia—6 basic units and 6 time units		180.12	(11)
Disposables—overtube and balloon		384	(55)
Total DBE costs		**1,490.37**	
Surgical retrieval	58.7	10,374.85	(53)
Spontaneous expulsion/other	28.8	0	
Average cost retention		**6,276.33**	

Abbreviations: DBE, double-balloon enteroscopy; OCCI, Ontario Case Costing Initiative.

Incorporating the rate of complications and weighted costs, the total cost of CE was calculated based on the 1.4% complication rate. Table 6 presents the components of and final total weighted cost of small-bowel CE, $1,038.67.

Table 6: Total Average Weighted Cost of Capsule Endoscopy

Cost	Value ($CAD)	Proportion of Patients (%)	Weighted Cost ($CAD)
Capsule endoscopy	964.30	98.6	950.80
Capsule retention	6,276.33	1.4	87.87
Total weighted average cost			**1,038.67**

Sensitivity Analysis

Rate of Capsule Endoscopy Complementing Push Enteroscopy

The rate at which CE is used to complement PE procedures is the key variable in determining the budgetary impact. This impact was explored from 0% of PEs being complemented by CE (i.e., the funding for CE is eliminated) to 100% (i.e., each PE procedure would be followed by CE, to demonstrate the absolute maximum additional expenditure that could be expected).

Complication-Related Costs

The first factor related to cost that was examined was the complication rate. In the clinical studies identified in the clinical evidence-based analysis, the highest capsule retention rate reported was 6% (56); although technical failure (i.e., the capsule does not transmit images due to any of a number of factors such as premature death of the battery, problems with transmission, or other causes) was not reported for small-bowel CE, the rate of technical failure of the colon capsule (3.7%) was taken as a possible surrogate

as the technology is similar and the same manufacturer has a large market presence in Ontario (data are reported separately in a clinical evidence-based evaluation). (57-60) The cost of technical failure includes the cost of 1 capsule and 1 interpretation fee, with direct costs and consultation with a gastroenterologist charged twice.

The rate of capsule retrieval via surgery was also explored. From a systematic review, the base case used a rate of 58.7% for patients undergoing surgery to retrieve the capsule. (52) The effect of all patients receiving surgery was also explored by increasing this rate to 100%.

Finally, the effect of variations of the price of the capsule itself on the budget impact was explored. As the manufacturer incorporates the cost of workstations, sensor belts, and proprietary software into the average cost of the capsule, this could increase or decrease depending on diffusion and individual contracts. The impact of a fluctuation of price of 15% was tested.

Results of Budget Impact Analysis

The total 1-year cost associated with CE complementing PE procedures for all possible proportions of patients is shown in Table 7. The cost ranges from a savings of $510,000, for a scenario where 0% of PEs are complemented with CE, up to an additional expenditure of $2,035,800, in the scenario where 100% of PEs are complemented with CE. According to ICES data, CE is currently used to complement 20% of PE procedures (bolded row).

Table 7: Sensitivity Analysis—Capsule Endoscopy Uptake Rate

Proportion of PEs Complemented With CE (%)	Current Expenditure for CE ($CAD)	Scenario CE Expenditure ($CAD)	Budget Impact ($CAD)
0	510,000	—	(510,000)
10	510,000	254,600	(255,400)
20	**510,000**	**510,000**	—
30	510,000	763,700	253,700
40	510,000	1,018,300	508,300
50	510,000	1,272,900	762,900
60	510,000	1,527,500	1,017,500
70	510,000	1,782,000	1,272,000
80	510,000	2,036,600	1,526,600
90	510,000	2,291,200	1,781,200
100	510,000	2,545,800	2,035,800

Sensitivity Analysis

Sensitivity analyses were performed around cost-related variables for 2 scenarios: the current use of small-bowel CE at 20% of PEs being complemented (Table 8); and the expected utilization if all patients anticipated to benefit from CE were given the treatment (i.e., 50% of PEs being complemented) (see Table 8).

Table 8: Sensitivity Analyses—Cost-Related Parameters

For Scenario at Current Expenditure—20% of PE Procedures Complemented With CE			
Variable	**Base Case Value**	**Sensitivity Analysis Value**	**Budget Impact**
Base case			N/A
Complication			
Capsule retention	1.4%	6%	$123,300
Technical failure	0%	3.7%	
Percentage of retentions resolved surgically	58.7%	100%	$27,300
Cost of device			
+15%	$600	$690	$42,700
−15%		$510	($44,300)

For Scenario With 50% of PE Procedures Complemented With CE			
Variable	**Base Case Value**	**Sensitivity Analysis Value**	**Budget Impact**
Base case			$762,900
Complication			
Capsule retention	1.4%	6%	$949,000
Technical failure	0%	3.7%	
Percentage of retentions resolved surgically	58.7%	100%	$805,000
Cost of device			
+15%	$600	$690	$828,100
−15%		$510	$697,700

Abbreviations: CE, capsule endoscopy; N/A, not available; PE, push enteroscopy.

Conclusions

Push enteroscopy is used in about 2,451 cases annually in Ontario for the investigation of OGIB. Of these, about 20% are currently complemented by CE in an attempt to visualize the small bowel to identify the source of obscure bleeding, resulting in about $510,000 spent on CE. This analysis explored the changes in expenditure by the Ministry of Health and Long-Term Care if the proportion of PE procedures complemented with CE varied over the entire possible range of values. The results ranged from a budgetary impact of $510,000 savings if 0% of PEs were complemented with CE to additional expenditure of about $2.1 million if 100% of PE procedures were complemented. Based on expert opinion that about 50% of PE procedures would likely benefit from a follow-up CE (based on the type and prevalence of common lesions), the expected budgetary impact was estimated to be about $763,000.

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Appendices

Appendix 1: Literature Search Strategies

1. Database(s): Embase <1996 to 2013 December 06>, Ovid MEDLINE(R) In-Process and Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:

#	Searches	Results
1	exp Gastrointestinal Hemorrhage/	88696
2	Inflammatory Bowel Diseases/ use pmez	13810
3	exp Intestine, Small/ use pmez	140097
4	exp Crohn Disease/	72253
5	Colon Crohn Disease/ use emefd	1222
6	exp Small Intestine/ use emefd	60090
7	(crohn* or OGIB or ((GI or gastrointestin* or gastro-intestin* or small bowel? or (small adj3 intestin*)) adj2 (bleed* or blood or lesion* or h?emorrhag* or rebleed*))).ti,ab.	110782
8	or/1-7	384419
9	exp Capsule Endoscopy/	6191
10	exp Capsule Endoscopes/ use pmez	340
11	exp Capsule Endoscope/ use emefd	584
12	(((capsule* or videocapsule* or wireless*) adj2 (endoscop* or enteroscop*)) or pillcam* or pill cam* or (capsule* adj2 (wireless* or camera* or video* or disposable* or ingestible* or m2a or olympus)) or videocapsule* or endo?capsule* or WCE or (given adj (imaging or diagnostic*)) or mirocam or capsocam or intromedic or omom).ti,ab,dv.	8015
13	or/9-12	9546
14	*Economics/ use pmez	10567
15	*Economics, Medical/ use pmez or *Economics, Pharmaceutical/ use pmez	6571
16	exp "Costs and Cost Analysis"/ use pmez	183771
17	exp Models, Economic/ use pmez	10416
18	Markov Chains/ use pmez or Monte Carlo Method/ use pmez	29632
19	Quality-Adjusted Life Years/ use pmez	7362
20	*Economic Aspect/ use emefd	4358
21	Health Economics/ use emefd	15558
22	exp Health Care Cost/ use emefd	168782
23	exp Economic Evaluation/ use emefd	174159
24	exp Pharmacoeconomics/ use emefd	134989
25	(econom* or cost or costly or costing or costed or price or prices or pricing or priced or discount or discounts or discounted or discounting or expenditure or expenditures or budget* or afford* or pharmacoeconomic* or pharmaco-economic*).ti,ab.	1025851

26	(cost* adj1 (util* or effective* or efficac* or benefit* or consequence* or analy* or minimi* or saving* or breakdown or lowering or estimate* or variable* or allocation or control or illness or sharing or life or lives or affordabl* or instrument* or technolog* or day* or fee or fees or charge or charges)).ti,ab.	222805
27	(decision adj1 (tree* or analy* or model*)).ti,ab.	21965
28	((value or values or valuation) adj2 (money or monetary or life or lives or costs)).ti,ab.	6923
29	(qoly or qolys or hrqol or qaly or qalys or qale or qales).ti,ab.	31399
30	(sensitivity analys*s or "willingness to pay" or quality-adjusted life year* or quality adjusted life year* or quality-adjusted life expectanc* or quality adjusted life expectanc*).ti,ab.	48107
31	(unit-cost or unit-costs or markov).ti,ab.	30300
32	or/14-31	1436011
33	8 and 13 and 32	303
34	limit 33 to english language	278
35	limit 34 to yr="1998 -Current"	278
36	remove duplicates from 35	222

2. Database(s): The Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Gastrointestinal Hemorrhage] explode all trees	1732
#2	MeSH descriptor: [Inflammatory Bowel Diseases] this term only	225
#3	MeSH descriptor: [Intestine, Small] explode all trees	1568
#4	MeSH descriptor: [Crohn Disease] this term only	903
#5	crohn* or OGIB or (GI or gastrointestin* or gastro-intestin* or small bowel? or (small near/3 intestin*)) near/2 (bleed* or blood or lesion* or h?emorrhag* or rebleed*):ti,ab,kw (Word variations have been searched)	2498
#6	#1 or #2 or #3 or #4 or #5	5328
#7	MeSH descriptor: [Capsule Endoscopy] explode all trees	96
#8	MeSH descriptor: [Capsule Endoscopes] this term only	21
#9	((capsule* or videocapsule* or wireless*) near/2 (endoscop* or enteroscop*)) or pillcam* or "pill cam" or (capsule* near/2 (wireless* or camera* or video* or disposable* or ingestible* or m2a or olympus)) or videocapsule* or endo?capsule* or WCE or (given next (imaging or diagnostic*)) or mirocam or capsocam or intromedic or omom:ti,ab,kw (Word variations have been searched)	193
#10	#7 or #8 or #9	193
#11	#6 and #10 from 1998 to 2013, in Technology Assessments and Economic Evaluations	24[a]

[a] 5 potentially relevant results from HTA & NHSEED combined (0+5)

3. Database(s): HEED

((capsule* OR videocapsule* OR wireless*) AND (endoscop* OR enteroscop*)) OR pillcam*

11 potentially relevant results

Appendix 2: Additional Costing

Intervention	Resource Item	Cost ($CAD)	Reference/Comments
Colonoscopy			
	Partial assessment	38.05	OSB A418—partial assessment (gastroenterology), consultation and visits, as suggested by expert panel (11)
	Direct costs	297.00	OCCI data using CCI code 2.NM.BA-BJ (54)
	Professional fee	103.90	OSB Z497/Z499/Z492/Z496/Z494/Z498/Z495/Z491,Z555 and E740 (11)
	Average cost	**438.95**	
Double-balloon enteroscopy			
	Partial assessment	38.05	OSB A418 (11)
	Professional fee	185.15	OSB Z584—small-bowel push enteroscopy—expert panel indicated this fee is also charged for double-balloon enteroscopy (11)
	Anesthesia consultation	106.90	OSB A015 (11)
	Anesthesia (6 basic units and 6 time units)	180.12	OSB (11)
	Disposables—overtube and balloon	384.00	Alberta Health (55)
	Direct costs	596.00	OCCI using codes 2.NK.70.BC and 2.NK.70.BD (54)
	Average cost	**1,490.37**	

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