

## Medical Policy



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### Title: **Wireless Capsule Endoscopy to Diagnose Disorders of the Small Bowel, Esophagus, and Colon**

#### **Professional**

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Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected small bowel bleeding	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Standard workup for gastrointestinal bleeding without capsule endoscopy	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status

<b>Populations</b>	<b>Interventions</b>	<b>Comparators</b>	<b>Outcomes</b>
Individuals: • With suspected Crohn’s disease	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Ileocolonoscopy • Small bowel follow-through • Computed tomography enterography • Magnetic resonance enterography	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With suspected celiac disease	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Endoscopy with biopsy	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With unexplained chronic abdominal pain	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Standard workup for abdominal pain without capsule endoscopy	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With an established diagnosis of Crohn’s disease	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Ileocolonoscopy • Small bowel follow-through • Computed tomography enterography • Magnetic resonance enterography	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With ulcerative colitis	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Optical colonoscopy	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With esophageal disorders	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Endoscopy	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With hereditary gastrointestinal polyposis syndromes	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Ileocolonoscopy • Small bowel follow-through • Computed tomography enterography • Magnetic resonance enterography	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With portal hypertensive enteropathy	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Endoscopy	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With acute upper gastrointestinal tract bleeding	Interventions of interest are: • Wireless capsule endoscopy	Comparators of interest are: • Standard workup for gastrointestinal bleeding without capsule endoscopy	Relevant outcomes include: • Test validity • Other test performance measures • Symptoms

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>Who are screened for colon cancer</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Wireless capsule endoscopy</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Optical colonoscopy</li> </ul>	<ul style="list-style-type: none"> <li>Hospitalizations</li> <li>Resource utilization</li> </ul> Relevant outcomes include: <ul style="list-style-type: none"> <li>Overall survival</li> <li>Disease-specific survival</li> <li>Test validity</li> <li>Other test performance measures</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>Who are scheduled to undergo capsule endoscopy for known or suspected small bowel stricture</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>Patency capsule</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>Capsule endoscopy without patency capsule</li> <li>Alternative workup without capsule endoscopy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>Test validity</li> <li>Other test performance measures</li> <li>Symptoms</li> <li>Change in disease status</li> </ul>

**DESCRIPTION**

The wireless capsule endoscopy (CE) uses a noninvasive device to visualize segments of the gastrointestinal tract. Patients swallow a capsule that records images of the intestinal mucosa as it passes through the gastrointestinal (GI) tract. The capsule is collected after being excreted and the images interpreted.

**OBJECTIVE**

The objective of this policy is to determine whether the use of wireless capsule endoscopy improves the net health outcome for patients with suspected or established gastrointestinal disorders.

**BACKGROUND**

**Wireless Capsule Endoscopy**

Wireless capsule endoscopy is performed using the PillCam Given Diagnostic Imaging System (previously called M2A, which is a disposable imaging capsule manufactured by Given Imaging. The capsule measures 11 X 30 mm and contains video imaging, self-illumination, and image transmission modules, as well as a battery supply that lasts up to 8 hours. The indwelling camera takes images at a rate of 2 frames per second as peristalsis carries the capsule through the GI tract. The average transit time from ingestion to evacuation is 24 hours. The device uses wireless radio transmission to send the images to a receiving recorder device that the patient wears around the waist. This receiving device also contains localizing antennae sensors that can roughly gauge where the image was taken over the abdomen. Images are then downloaded onto a workstation for viewing and processing.

CE has been proposed as a method for identifying Crohn’s disease. There is no single criterion standard diagnostic test for Crohn’s disease; rather, diagnosis is based on a constellation of findings.<sup>1</sup> Thus it is difficult to determine the diagnostic characteristics

of various tests used to diagnose the condition and difficult to determine a single comparator diagnostic test to CE.

### REGULATORY STATUS

Table 1 summarizes various wireless CE devices with clearance by the U.S. Food and Drug Administration (FDA).

**Table 1.** Wireless Capsule Endoscopy Devices Cleared by the Food and Drug Administration

Device	Manufacturer	Year	Indication
PillCam™	Given® Imaging	2001	Detection of abnormalities in the small bowel and visualization of the small bowel mucosa
Given AGILE™ patency system	Given® Imaging	2006	Verification of adequate patency of the GI tract before administration of the PillCam into patients with known or suspected strictures
PillCam™ ESO2 Capsule	Given® Imaging	2007	Visualization of the esophageal mucosa
Olympus Capsule Endoscope System	Olympus Medical Systems	2007	Visualization of the small intestine mucosa
PillCam™ COLON	Given® Imaging	2014	Visualization of the colon in patients who have had an incomplete colonoscopy due to a technical impossibility and not incomplete evacuation
PillCam™ COLON 2	Given® Imaging	2016	Detection of colon polyps in patients after an incomplete colonoscopy and a complete evaluation of the colon was not technically possible, and for detection of colon polyps in patients with evidence of GI bleeding of lower GI origin with major risks for colonoscopy or moderate sedation

GI: gastrointestinal.

On August 1, 2001, the PillCam™ Given® Diagnostic Imaging System (Given Imaging) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. FDA clearance provides for the capsule's use "along with – not as a replacement for – other endoscopic and radiologic evaluations of the small bowel." FDA clarified that the "capsule was not studied in the large intestine." On July 1, 2003, a supplemental 510(k) premarket notification was cleared, and the labeled indications were modified by removing the "adjunctive" use qualification: "the Given® Diagnostic System is intended for visualization of the small bowel mucosa. It may be used as a tool in the detection of abnormalities of the small bowel."

In November 2004, the device received FDA clearance for the following labeled indication: "the Given® Diagnostic System with the PillCam™ ESO Capsule is intended for the visualization of esophageal mucosa." A new model was cleared by FDA in June 2007, the PillCam ESO2 Capsule.

In September 2007, the Olympus Capsule Endoscope System was cleared for marketing by FDA through the 510(k) process for "visualization of the small intestine mucosa." More recent versions of both these systems also incorporate a blood indicator feature to assist with rapid screening of intestinal lesions with bleeding potential.

In 2006, the Given AGILE™ patency system was also cleared by FDA through the 510(k) process. This system is an accessory to the PillCam™ video capsule and, according to FDA material, is intended to verify adequate patency of the GI tract before administration of the PillCam™ into patients with known or suspected strictures. This capsule is of similar size to the endoscopy capsule but made of lactose and barium and dissolves within 30 to 100 hours of entering the GI tract. It carries a tracer material that can be detected by a scanning device. Excretion of the intact capsule without symptoms (abdominal pain or obstruction) is reported to predict the uncomplicated passage of the wireless capsule.

In 2014, PillCam™ COLON was cleared for marketing by FDA through a de novo 510(k) classification. The new classification applies to devices with low to moderate risk that have no predicate on the market. PillCam™ COLON is intended to visualize the colon in patients who have had an incomplete colonoscopy due to a technical impossibility and not incomplete evacuation.

In 2016, the PillCam™ COLON 2 Capsule Endoscopy System was cleared by FDA through the 510(k) process for the detection of colon polyps in patients after an incomplete colonoscopy with adequate preparation, and a complete evaluation of the colon was not technically possible, and for detection of colon polyps in patients with evidence of GI bleeding of lower GI origin in patients with major risks for colonoscopy or moderate sedation, but who could tolerate a colonoscopy and moderate sedation in the event that a clinically significant colon abnormality was identified on capsule endoscopy.

FDA Product Code: NEZ.

## **POLICY**

- A. Wireless capsule endoscopy of the small bowel may be considered **medically necessary** for the following indications:
1. Initial diagnosis in patients with suspected Crohn's disease without evidence of disease on conventional diagnostic tests such as small bowel follow-through and upper and lower endoscopy.
  2. In patients with an established diagnosis of Crohn's disease, when there are unexpected change(s) in the course of disease or response to treatment, suggesting the initial diagnosis may be incorrect and reexamination may be indicated.

3. Obscure gastrointestinal bleeding suspected of being of small bowel origin, as evidenced by prior inconclusive upper and lower gastrointestinal (GI) endoscopic studies performed during the current episode of illness.
  4. For surveillance of the small bowel in patients with hereditary GI polyposis syndromes, including familial adenomatous polyposis and Peutz-Jeghers syndrome.
- B. Other indications for wireless capsule endoscopy are considered **experimental / investigational**, including, but not limited to:
1. Evaluation of the extent of involvement of known Crohn's disease or ulcerative colitis.
  2. Evaluation of the esophagus, in patients with gastroesophageal reflux or other esophageal pathologies.
  3. Evaluation of other gastrointestinal diseases and conditions not presenting with GI bleeding, including, but not limited to, celiac sprue, irritable bowel syndrome, Lynch syndrome (risk for hereditary nonpolyposis colorectal cancer), portal hypertensive enteropathy, small bowel neoplasm, and unexplained chronic abdominal pain.
  4. Evaluation of the colon, including, but not limited to, detection of colonic polyps or colon cancer.
  5. Initial evaluation of patients with acute upper GI bleeding.
- C. The patency capsule is considered **experimental / investigational**, including use to evaluate patency of the gastrointestinal tract before wireless capsule endoscopy.

### **Policy Guidelines**

Obscure GI bleeding is defined as "recurrent or persistent iron-deficiency anemia, positive fecal occult blood test, or visible bleeding with no bleeding source found at original endoscopy."

### **RATIONALE**

The most recent literature review was conducted through September 7, 2018.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome.

That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

## **Suspected Small Bowel Bleeding**

### Clinical Context and Test Purpose

The purpose of wireless capsule endoscopy (CE) for patients who have suspected small bowel bleeding is to confirm a diagnosis and inform a decision to proceed to appropriate treatment.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with suspected small bowel bleeding?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is patients with suspected small bowel bleeding. Suspected small bowel bleeding, previously referred to as obscure gastrointestinal (GI) tract bleeding, is defined as bleeding from the GI tract that persists or recurs without an obvious etiology after imaging with upper and lower endoscopy and radiologic evaluation of the small bowel. Recurrent or persistent iron-deficiency anemia, positive fecal occult blood test, or visible bleeding with no bleeding source found at original endoscopy are other indicators of obscure GI tract bleeding. Examples of etiologies for small bowel bleeding include angiodysplasia, tumor, medication induced, infections, Crohn's disease (CD), Meckel diverticulum, Zollinger-Ellison syndrome, vasculitis, radiation enteritis, jejunal diverticula, and chronic mesenteric ischemia.

### Interventions

The intervention of interest is wireless CE.

### Comparators

The following practice is currently being used to diagnose small bowel bleeding: a standard workup without wireless CE and, with or without direct endoscopic procedures or specialized GI imaging. A "true" reference standard for suspected small bowel bleeding is difficult or impossible to achieve, because the bleeding source may resolve and invasive techniques (eg, surgery) cannot be justifiably used.

### Outcomes

The outcomes of interest for diagnostic accuracy include test validity (ie, sensitivity, specificity). The primary outcomes of interest are symptoms and disease status that would change due to patient management decisions following wireless CE.

Timing

Wireless CE would be performed prior to surgical exploration if conventional endoscopy has been inconclusive. Follow-up for further diagnostic evaluation and surveillance for recurrence of symptoms would be immediate to weeks if no etiology is identified. Follow-up of weeks to months would be based on the disease condition identified by CE.

Setting

Patients with suspected small bowel bleeding are actively managed by gastroenterologists and primary care providers in an outpatient setting.

Study Selection Criteria

Below are selection criteria for studies to assess whether a test is clinically valid. These will be applied to all of the indications reviewed in this policy.

- The study population represents the population of interest. Eligibility and selection are described.
- The test is compared with a credible reference standard.
- If the test is intended to replace or be an adjunct to an existing test; it should also be compared with that test.
- Studies should report sensitivity, specificity, and predictive values. Studies that completely report true- and false-positive results are ideal. Studies reporting other measures (eg, receiver operator curve, area under the receiver operator curve, c-statistic, likelihood ratios) may be included but are less informative.
- Studies should also report reclassification of diagnostic or risk category.

Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Systematic Reviews

Tables 2 and 3 summarize the characteristics and results of selected systematic reviews, which have evaluated a number of case series that compared the diagnostic accuracy of CE with alternative procedures such as intraoperative endoscopy or mesenteric angiography.

**Table 2.** Characteristics of Systematic Reviews Evaluating CE for Iron-Deficient Anemia

Study	Dates	Trials	Participants	N (Range)	Design	QUADAS Assessment of Included Trials
Koulaouzidi et al (2012) <sup>2</sup>	2004-2011	24	Patients with iron-deficiency anemia who had SBCE and at last 1 lower and upper GI endoscopy prior to CE	1960 (35-652)	Observational	Low-to-moderate quality

CE: capsule endoscopy; SBCE: small bowel capsule endoscopy.

**Table 3.** Results of Systematic Reviews Evaluating CE for Iron-Deficient Anemia

Study	Overall Diagnostic Yield <sup>a</sup>	Diagnostic Yield of Patients With IDA <sup>b</sup>	I <sup>2</sup> , %	Diagnostic Yield, n (%) <sup>c</sup>
Koulaouzidis et al (2012) <sup>2</sup>				
Total N	1960	264		<ul style="list-style-type: none"> <li>• Angioectasias: 293 (45.9)</li> <li>• Inflammatory lesions: 126 (19.7)</li> <li>• Polyp/mass lesions: 42 (6.6)</li> <li>• Not classified: 177 (27.7)</li> </ul>
Pooled effect (95% CI), %	47 (42 to 52)	66.6 (61.0 to 72.3)	78.8	
p			<0.001	

CI: confidence interval; IDA: iron-deficient anemia.

<sup>a</sup> Per-patient analysis.

<sup>b</sup> From 4 studies (n=264 patients; 13.47% of total).

<sup>c</sup> Patients with positive SBCE findings.

**Randomized Controlled Trials**

A small RCT compared CE with mesenteric angiography in patients with acute melena or hematochezia. While CE had a higher diagnostic yield, secondary outcomes such as transfusion, hospitalization, and mortality did not differ significantly between groups. Tables 4 and 5 summarize the characteristics and results of selected RCTs.

**Table 4.** Characteristics of RCT Evaluating CE for Obscure GI Bleeding

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Leung et al (2012) <sup>3</sup>	China	1	2005-2007	Consecutive adults with active overt obscure GI bleeding	30 randomized to CE	30 randomized to mesenteric angiography

CE: capsule endoscopy; GI: gastrointestinal; RCT: randomized controlled trial.

**Table 5.** Results of RCT Evaluating CE for Obscure GI Bleeding

Study	Diagnostic Yield (95% CI), % <sup>a</sup>	Rebleeding Rates (95% CI), %	Hospitalization Rate, n (%)	Transfusion Rate, n (%)	Mean Follow-Up (SD), mo
Leung et al (2012) <sup>3</sup>					
CE	53.3 (36.1 to 69.8)	16.7 (7.3 to 33.6)	5 (16.7)	3 (10)	48.5 (20.9)
Angiography	20 (9.5 to 37.3)	33.3 (19.2 to 51.2)	5 (16.7)	3 (10)	
Difference	33.3 (8.9 to 52.8)	16.7 (-5.3 to 36.8)			
p	0.016	0.23	1.0	1.0	

CI: confidence interval; CE: capsule endoscopy; GI: gastrointestinal; RCT: randomized controlled trial; SD: standard deviation.

<sup>a</sup> Percentage identified with high probability of bleeding.

The purpose of the gaps tables (see Tables 6 and 7) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

**Table 6.** Relevance Gaps of RCT Evaluating CE for Obscure GI Bleeding

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
Leung et al (2012) <sup>3</sup>	2. It is possible patients with a moderate bleeding would		2. A criterion standard is lacking for		

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
	not undergo angiography in clinical setting 4. Patients with overt but nonmassive bleeding may not be ideal for CE or angiography		evaluation of obscure GI bleeding		

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment. CE: capsule endoscopy; GI: gastrointestinal; RCT: randomized controlled trial.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

<sup>b</sup> Intervention key: 1. Classification thresholds not defined; 2. Version used unclear; 3. Not intervention of interest.

<sup>c</sup> Comparator key: 1. Classification thresholds not defined; 2. Not compared to credible reference standard; 3. Not compared to other tests in use for same purpose.

<sup>d</sup> Outcomes key: 1. Study does not directly assess a key health outcome; 2. Evidence chain or decision model not explicated; 3. Key clinical validity outcomes not reported (sensitivity, specificity and predictive values); 4. Reclassification of diagnostic or risk categories not reported; 5. Adverse events of the test not described (excluding minor discomforts and inconvenience of venipuncture or noninvasive tests).

<sup>e</sup> Follow-Up key: 1. Follow-up duration not sufficient with respect to natural history of disease (true positives, true negatives, false positives, false negatives cannot be determined).

**Table 7. Study Design and Conduct Gaps of RCT Evaluating CE for Obscure GI Bleeding**

Study	Allocation <sup>a</sup>	Blinding <sup>b</sup>	Selective Reporting <sup>d</sup>	Follow-Up <sup>e</sup>	Power <sup>d</sup>	Statistical <sup>f</sup>
Leung et al (2012) <sup>3</sup>					3. Study underpowered to detect significant difference in clinical outcome	

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment. CE: capsule endoscopy; RCT: randomized controlled trial.

<sup>a</sup> Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

<sup>b</sup> Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

<sup>c</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

<sup>d</sup> Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

<sup>e</sup> Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

<sup>f</sup> Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

**Case Series**

Tables 8 and 9 summarize the characteristics and results of selected case series.

**Table 8. Characteristics of Case Series Evaluating CE for Obscure GI Bleeding**

Study	Country	Participants	Treatment Delivery	Follow-Up (Range), mo
Hartmann et al (2005) <sup>4</sup>	Germany	47 patients >18 y with obscure GI bleeding	Patients received CE and criterion standard, intraoperative endoscopy	NR
Pennazio et al (2004) <sup>5</sup>	Italy	100 patients ≥18 y with obscure GI bleeding	51 patients received CE and PE before or after the procedure	Mean: 18 (5-25)

CE: capsule endoscopy; GI: gastrointestinal; NR: not reported; PE: push enteroscopy.

**Table 9.** Results of Case Series Evaluating CE for Obscure GI Bleeding

Study	Treatment	Locating Bleeding With CE, %		Diagnostic Yield for Positive Lesions, %	PPV of CE, %	NPV of CE %
		Sensitivity	Specificity <sup>a</sup>			
Hartmann et al (2005) <sup>4</sup>	CE and intraoperative endoscopy	95	75	Both procedures: 76.6	95	86
Pennazio (2004) <sup>5</sup>	CE and PE	89	95	67 (95% CI, 54 to 80)	97	82.6

CE: capsule endoscopy; PPV: positive predictive value; NPV: negative predictive value; PE: push enteroscopy; CI: confidence interval

<sup>a</sup>CE results confirmed by intraoperative endoscopy or other reference standard.

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility. Based on evidence that CE isolates the source of bleeding at least as well as other diagnostic tools and that few diagnostic options are available to patients with suspected small bowel bleeding, a chain of evidence can be constructed to support the clinical utility of CE for this indication.

### *Section Summary: Suspected Small Bowel Bleeding*

A small RCT compared CE with mesenteric angiography in patients with acute melena or hematochezia. While CE had a higher diagnostic yield, secondary outcomes such as transfusion, hospitalization, and mortality did not differ significantly between groups. A large number of uncontrolled studies have evaluated the use of CE in the evaluation of patients with suspected small bowel bleeding. These studies have consistently reported that a substantial proportion of patients receive a definitive diagnosis following this test when there are few other diagnostic options. A meta-analysis of 24 studies estimated that the diagnostic yield in this patient population was approximately half of the included patients and was higher in patients with documented iron-deficiency anemia. CE appears to locate the source of bleeding at least as well as other diagnostic methods and direct treatment to the source of bleeding.

## **Suspected Crohn's Disease**

### Clinical Context and Test Purpose

The purpose of wireless CE for patients with suspected Crohn's disease (CD) is to confirm a diagnosis and inform a decision to proceed to appropriate treatment.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with suspected CD?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is individuals with suspected CD. CD is one of the 2 types of inflammatory bowel disease (IBD), Crohn's disease can involve the entire GI tract and is characterized by transmural inflammation.

### Interventions

The test being considered is wireless CE.

### Comparators

The following tests are currently being used to diagnose CD: ileocolonoscopy, barium small bowel follow-through, computed tomography enterography (CTE), magnetic resonance enterography (MRE).

### Outcomes

The general outcomes of interest are test validity, other test performance measures, symptoms, and change in disease status.

### Timing

The diagnosis of CD requires confirmatory imaging when the disease is prominent on the differential diagnosis list. The imaging study would be performed and promptly followed by appropriate treatment. CD is a chronic condition requiring long-term follow-up.

### Setting

Patients with suspected CD are actively managed by gastroenterologists and primary care providers in an outpatient setting.

### Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist.

This evidence review focuses on the clinical validity and clinical utility.

### Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Results from a meta-analysis by Choi et al (2017), which compared CE with various modalities for diagnosing CD, are summarized in Tables 10 and 11. The reference standards varied for the selected studies, so quantitative data were not synthesized for diagnostic accuracy. In the pooled analysis, in patients with suspected CD, the sensitivity of CE ranged from 89.6% to 92.0% and the specificity was 100%.

**Table 10.** Characteristics of Systematic Reviews Assessing the Diagnostic Yield of CE vs Other Modalities<sup>a</sup>

Study	Dates	Trials	Participants	N (Range)	Design
Choi et al (2017) <sup>6</sup>	2002-2013	24	Patients with suspected or established CD	NR	RCT, nonrandomized, and diagnostic accuracy studies

CD: Crohn's disease; CE: capsule endoscopy; NR: not reported; RCT: randomized controlled trial.

<sup>a</sup> Other modalities include small bowel follow-through, enteroclysis, computed tomography enterography, and magnetic resonance enterography.

**Table 11.** Results of Systematic Reviews Assessing the Diagnostic Yield of CE vs Other Modalities

Study	CE vs SBFT <sup>a</sup>	CE vs EC <sup>b</sup>	CE vs CTE <sup>b</sup>	CE vs MRE <sup>b</sup>
Choi et al (2017) <sup>6</sup>				
N	94			
Diagnostic yield, %	66 vs 21.3	75.7 vs 29.4	72.5 vs 22.5	85.7 vs 100
Weighted incremental yield (95% CI)	0.44 (0.29 to 0.59)	0.50 (0.21 to 0.79)	0.36 (0.18 to 0.90)	-0.16 (-0.63 to 0.32)
<i>I</i> <sup>2</sup> , %	30	52	68	44

CE: capsule endoscopy; CI: confidence interval; CTE: computed tomography enterography; EC: enteroclysis; MRE: magnetic resonance enterography; SBFT: small bowel follow-through.

<sup>a</sup> From 4 studies (3 included in meta-analysis).

<sup>b</sup> From 2 studies.

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Based on evidence that CE can provide a diagnosis of CD when other tests cannot, a chain of evidence can be constructed to support the clinical utility of CE for this indication.

*Section Summary: Suspected CD*

For patients with suspected CD who cannot be diagnosed by other modalities, CE can confirm the diagnosis in a substantial number of patients. The diagnostic yield in the available studies varied but is likely superior to alternative tests such as CTE or MRE scanning.

**Suspected Celiac Disease**

Clinical Context and Test Purpose

The purpose of wireless CE for patients who have suspected celiac disease is to confirm a diagnosis and inform a decision to proceed to appropriate treatment.

The question addressed in this evidence review is: Does use of CE endoscopy improve the net health outcome in patients with suspected celiac disease?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with suspected celiac disease. Celiac disease, or gluten-sensitive enteropathy, is an immune-mediated condition of the small intestine. Serologic markers of the disease have good sensitivity and specificity in triaging patients to endoscopy.

Interventions

The test being considered is wireless CE. CE has been evaluated as an alternative method of diagnosing celiac disease, assessing the extent of disease, and in the evaluation of celiac disease unresponsive to treatment.

Comparators

The following test is currently being used to diagnose celiac disease: endoscopy with biopsy. The criterion standard for diagnosis of celiac disease is obtained through small bowel biopsies obtained during endoscopy.

Outcomes

The general outcomes of interest are test validity, other test performance measures, symptoms, and change in disease status.

Timing

The diagnosis of celiac disease requires confirmatory imaging when the disease is prominent on the differential diagnosis list. The imaging study would be performed and promptly followed by appropriate treatment. Celiac disease is a chronic condition requiring long-term follow-up.

Setting

Patients with suspected celiac disease are actively managed by gastroenterologists and primary care providers in an outpatient setting.

Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and

unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

### Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

### Systematic Reviews

A meta-analysis by El-Matary et al (2009) compared the diagnostic performance of CE with a reference standard of duodenal biopsy.<sup>7</sup> The pooled analysis of 3 studies showed a sensitivity of 83% and a specificity of 98%. Another meta-analysis by Rokkas and Niv (2012) also compared the diagnostic performance of CE with biopsy, summarizing 6 studies (total N=166 subjects).<sup>8</sup> The overall pooled sensitivity was 89%, and the specificity was 95%.

CE detected involvement of intestines beyond the duodenum; however, the clinical significance of detecting the extent of celiac disease is uncertain. Given the less than 90% sensitivity of CE for celiac disease, it does not appear to be an adequate alternative method of making an initial diagnosis.

### Nonrandomized Studies

In a study by Kurien et al (2013), 62 patients with an equivocal diagnosis of celiac disease and 69 patients with the confirmed celiac disease who were unresponsive to standard treatment were evaluated with CE.<sup>9</sup> Results were combined with human leukocyte antigen typing and response to gluten challenge, with the final diagnosis made by 3 expert physicians who received the information from all 3 sources. The main outcome was the increase in diagnostic yield after CE combined with the other tests. The diagnostic yield was greatest in cases with antibody negative villous atrophy where a diagnosis of celiac disease was made in 9 (28%) of 32 patients. In 8 (12%) of the 69 nonresponsive celiac disease patients, CE identified 2 cases of enteropathy-associated lymphoma, 4 type 1 refractory disease cases, 1 fibroepithelial polyp, and 1 case of ulcerative jejunitis. This study was limited by the small sample size and use of other tests in conjunction with CE to ascertain a final diagnosis.

The role of CE in nonresponsive celiac disease has been evaluated in only a few studies. One case series by Culliford et al (2005) evaluated 47 patients with complicated celiac disease and found unexpected additional findings in 60% of patients, most of which were ulcerations.<sup>10</sup> However, the definition of "complicated" celiac disease included other factors such as evidence of blood loss, itself an indication for CE. The impact on patient management and outcomes is unclear.

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of wireless CE for diagnosing celiac disease has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

### Section Summary: Suspected Celiac Disease

In cases where the diagnosis of celiac disease is equivocal, CE can sometimes reveal morphologic changes in the small bowel consistent with celiac disease. However, it is unlikely that the appearance of small bowel on CE is itself sufficient to make a definitive diagnosis of celiac disease. Small bowel biopsy, celiac serologies, and human leukocyte antigen typing remain the standard tests for confirming celiac disease and have a higher sensitivity and specificity for this purpose. Case series of patients with unresponsive celiac disease undergoing CE have shown some yield of actionable diagnoses that have the potential to improve patient outcomes. Larger studies are needed to better determine the diagnostic yield of CE in these patients.

## **Unexplained Chronic Abdominal Pain**

### Clinical Context and Test Purpose

The purpose of wireless CE for patients who have unexplained chronic abdominal pain is to confirm a diagnosis and inform a decision to proceed to appropriate treatment.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with unexplained chronic abdominal pain?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is individuals with unexplained chronic abdominal pain.

### Interventions

The test being considered is wireless CE.

### Comparators

The following practice is currently being used to diagnose chronic abdominal pain: standard workup for abdominal pain without CE.

### Outcomes

The general outcomes of interest are test validity, other test performance measures, symptoms, and change in disease status.

### Timing

The diagnosis of chronic abdominal pain is often one of exclusion after a comprehensive clinical evaluation including empirical treatment. Imaging studies are used during initial and follow-up evaluations. Continued follow-up would be based on a definitive or working diagnosis, which would typically occur over weeks to months.

### Setting

Patients with unexplained chronic abdominal pain are actively managed by gastroenterologists and primary care providers in an outpatient setting.

### Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

### Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

### Systematic Reviews

Xue et al (2015) reported on a systematic review of 21 studies (total N=1520 patients) evaluating CE for unexplained chronic abdominal pain.<sup>11</sup> The pooled diagnostic yield was 20.9% (95% CI, 15.9% to 25.9%). The most commonly identified findings were inflammatory lesions (78.3%) and tumors (9.0%). Studies in the review were highly heterogeneous. Limitations in interpreting the findings included retrospective study designs, different durations of abdominal pain, and use of different tests before CE.

### Case Series

In a study not included in the systematic review, Yang et al (2014) reported on a case series evaluating 243 patients with CE for unexplained chronic abdominal pain.<sup>12</sup> The diagnostic yield of CE was 23.0%. Identified findings included 19 (7.8%) patients with CD, 15 (6.2%) with enteritis, 11 (4.5%) with idiopathic intestinal lymphangiectasia, 5 (2.1%) with uncinariasis, 5 (2.1%) with abnormal transit time and other findings (eg, small bowel tumor, ascariasis, anaphylactoid purpura).

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of wireless CE for diagnosing unexplained chronic abdominal pain has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

### *Section Summary: Unexplained Chronic Abdominal Pain*

While CE diagnosed unexplained chronic abdominal pain in a proportion of patients reported in retrospective studies, the sequence and chronology of testing and treatment recommended before CE needs to be defined to determine whether CE had utility to diagnose the condition.

## **Established Crohn's Disease**

### Clinical Context and Test Purpose

The purpose of wireless CE for patients who have established diagnosis of Crohn's disease is to inform management decisions based on disease status.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients diagnosed with CD?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is patients with CD.

### Interventions

The intervention of interest is wireless CE.

### Comparators

The following test is currently being used to monitor CD: ileocolonoscopy, barium small bowel follow-through, CTE, and MRE.

An international consensus statement indicated that radiographic imaging should take precedence over CE because of the capability to detect obstructive strictures as well as extraluminal and transmural disease.<sup>1</sup> The consensus statement identified some studies in which CE had a higher percentage of positive findings than alternative tests in patients with established CD, but it is not clear how these findings correlated with either symptoms or outcomes of the therapeutic intervention. A 2013 European consensus statement indicated MRE or CTE is usually preferred to CE in patients with known CD patients.<sup>13</sup> The 2013 consensus also

indicated CE should be limited in patients with CD to the evaluation of unexplained symptoms, unexplained iron-deficiency, or obscure GI bleeding after other investigations are inconclusive.

### Outcomes

The beneficial outcome of a true test result, if correctly classified as low disease activity, is avoidance of endoscopy and unnecessary medications.

### Timing

Wireless CE would be performed to monitor patients with CD.

### Setting

Patients with an established diagnosis of Crohn's disease are actively managed by gastroenterologists and primary care providers in an outpatient setting.

### Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist.

This evidence review focuses on the clinical validity and clinical utility.

### Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Kopylov et al (2017) published a systematic review of studies evaluating use of CE for CD.<sup>14</sup> Reviewers included prospective studies comparing CE with MRE and/or small bowel contrast ultrasound in patients who had suspected and/or established CD. In pooled analyses of the 11 studies that included patients with established CD, the diagnostic yield of CE was similar to that of MRE (odds ratio [OR], 1.88; 95% CI, 0.53 to 1.48;  $I^2=48\%$ ) and to ultrasound (OR=0.57; 95% CI, 0.27 to 1.20;  $I^2=67\%$ ).

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Based on evidence that CE has similar diagnostic yield as radiography when used to monitor CD and CE can be used when radiography cannot, a chain of evidence can be constructed to support the clinical utility of CE for this indication.

### *Section Summary: Established Diagnosis of CD*

A 2017 systematic review of 11 studies in patients with established CD found a similar diagnostic yield with CE compared with radiography. International consensus statements have suggested that radiographic imaging has advantages (eg, ability to detect obstructive strictures) and that CE should be limited to certain situations (eg, unexplained symptoms or other inconclusive investigations).

## **Ulcerative Colitis**

Ulcerative colitis is an inflammatory disease of the large intestine. CE has been proposed as an alternative method for assessing the extent and severity of disease activity in those with known ulcerative colitis.

### Clinical Context and Test Purpose

The purpose of wireless CE for patients who have ulcerative colitis is to inform management decisions based on disease status.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with ulcerative colitis?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is individuals with ulcerative colitis.

### Interventions

The test being considered is wireless CE.

### Comparators

The following test is currently being used to manage ulcerative colitis: optical colonoscopy.

### Outcomes

The general outcomes of interest are test validity, other test performance measures, symptoms, and change in disease status.

### Timing

Wireless CE would be performed to monitor patients after a confirmed diagnosis of ulcerative colitis.

**Setting**

Patients with ulcerative colitis are actively managed by gastroenterologists and primary care providers in an outpatient setting.

**Technically Reliable**

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

**Clinically Valid**

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

A number of prospective observational studies have evaluated the diagnostic accuracy of CE in patients with ulcerative colitis. Tables 12 and 13 summarize the characteristics and results of these studies.

**Table 12.** Characteristics of Observational Comparative Studies Assessing CE for UC

Study	Study Type	Country	Dates	Participants	Treatment	Follow-Up
Shi et al (2017) <sup>15</sup>	Single-center prospective observational	China	2014-2016	Patients 18-80 y with UC requiring colonoscopy	150 patients underwent CE-2 and colonoscopy	NR
San Juan-Acosta et al (2014) <sup>16</sup>	Single-blind prospective comparative	Spain	2010-2012	Patients 18-70 y with UC with flare in disease activity or due for CRC screening	23 underwent CE-1, 19 had CE-2; all followed by colonoscopy	NR
Oliva et al (2014) <sup>17</sup>	Prospective observational	Spain	2011-2012	Patients 6-18 y with a diagnosis at least 3 mo prior to enrollment	30 patients underwent CE-2, followed by colonoscopy	NR
Sung et al (2012) <sup>18</sup>	Prospective cohort	China and Singapore	2000-2008	Patients with suspected or known UC	100 patients underwent CE and same-day colonoscopy	NR

CE-1: first-generation capsule endoscopy CE-2: second-generation capsule endoscopy; CRC: colorectal cancer; NR: not reported; UC: ulcerative colitis.

**Table 13.** Results of Observational Comparative Studies Assessing CE for Ulcerative Colitis

Study	Active Colonic Inflammation, %		PPV, %	NPV, %	Correlation Between Colon CE and Colonoscopy	
	Sensitivity <sup>a</sup>	Specificity			Disease Severity	Extent of Inflammation
Shi et al (2017) <sup>15</sup>						
N	150	150	150		150	150
Mucosal inflammation (MES >0)	97			94-95		
M-to-S inflammation (MES >1)	94					
Postinflammatory polyps	100	91				

Study	Active Colonic Inflammation, %		PPV, %	NPV, %	Correlation Between Colon CE and Colonoscopy	
ICC (95% CI)					0.69 (0.46 to 0.81) <sup>a</sup>	0.64 (0.38 to 0.78) <sup>b</sup>
p					<0.001	<0.001
San Juan-Acosta et al (2014) <sup>16</sup>						
N	42	42	42		42	42
CE vs colonoscopy						
Disease activity	77.78	95.83	93.33	85.19		
Disease extent	68.75	96.15	91.67	83.33		
κ (95% CI)					0.79 (0.62 to 0.96)	0.71 (0.52 to 0.90)
Oliva et al (2014) <sup>17</sup>						
N	30	30	30			
% (95% CI)	96 (79 to 99)	100 (61 to 100)	100 (85 to 100)	85 (49 to 97)		
Sung et al (2012) <sup>18</sup>						
N	100	100	100			
% (95% CI)	89 (80 to 95)	75 (51 to 90)	93 (84 to 97)	65 (43 to 83)		

CE: capsule endoscopy; CI: confidence interval; ICC: intraclass correlation coefficient; MES: Mayo Endoscopic Subscore; M-to-S: moderate to severe; NPV: negative predictive value; PPV: positive predictive value.

<sup>a</sup> MES.

<sup>b</sup> Ulcerative Colitis Endoscopic Index of Severity.

In the study by San Juan-Acosta et al (2014), although the correspondence between the 2 methods was reasonably good, it is uncertain whether management changes based on one or the other test would result in similar or different patient outcomes.<sup>16</sup>

Oliva et al (2014) evaluated 30 patients with known ulcerative colitis with both CE and colonoscopy to assess disease activity.<sup>17</sup> The reference standard for disease activity was a Matts score greater than 6 as judged by colonoscopy. Although the 2 methods had a high concordance at this cutoff level of disease in this study, patient outcomes linked to these assessments of disease activity cannot be determined.

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility. Because the clinical validity of wireless CE for monitoring ulcerative colitis has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

### *Section Summary: Ulcerative Colitis*

Several diagnostic accuracy studies have compared CE with colonoscopy to assess disease activity in patients with ulcerative colitis. Two of 4 studies were small (ie, <50 patients) and thus data on diagnostic accuracy are limited. Because there are insufficient data on diagnostic accuracy, a chain of evidence on clinical utility cannot be constructed.

## **Esophageal Disorders**

### Clinical Context and Test Purpose

The purpose of wireless CE for patients who have esophageal disorders is to inform management decisions based on disease status.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with esophageal disorders?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is individuals with esophageal disorders. Gastrointestinal reflux disease and chronic sequelae such as Barrett esophagus may require diagnostic and surveillance interventions.

### Interventions

The test being considered is wireless CE. In the esophagus, the capsule camera has been proposed as a screening technique for Barrett esophagus associated with gastroesophageal reflux disease. Evaluation of the esophagus requires limited transit time, and it is estimated that the test takes 20 minutes to perform.

CE can visualize several types of esophageal conditions. It could substitute for traditional upper endoscopy for several indications and may have the advantage of comfort and convenience. However, interventional procedures and biopsies cannot be performed with CE. CE could triage patients for endoscopy if either the sensitivity or the specificity is high. Traditional endoscopy could then be performed on the appropriate group to determine false positives or false negatives, having spared the group with a high positive predictive value an endoscopy procedure.

### Comparators

The following test is currently being used to manage esophageal disorders: upper GI endoscopy.

### Outcomes

The general outcomes of interest are test validity, other test performance measures, symptoms, and change in disease status.

### Timing

Wireless CE would be performed to monitor patients after a confirmed diagnosis of an esophageal disorder.

### Setting

Patients with esophageal disorders are actively managed by gastroenterologists and primary care providers in an outpatient setting.

### Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

### Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Most studies have shown that CE has inferior diagnostic characteristics compared with traditional upper endoscopy for a variety of esophageal conditions. A meta-analysis by Guturu et al (2011) evaluated 9 studies comparing CE with traditional endoscopy for detecting esophageal varices and calculated a sensitivity of 83% and specificity of 85%.<sup>19</sup> A meta-analysis by Bhardwaj et al (2009) assessed 9 studies comparing CE with traditional endoscopy for detecting Barrett esophagus and reported a sensitivity of 77% and specificity of 86%.<sup>20</sup> Because of the lower sensitivity and specificity of that test, CE cannot substitute for traditional endoscopy nor can it be used to triage patients to endoscopy.

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of wireless CE for monitoring esophageal disorders has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

*Section Summary: Esophageal Disorders*

Other available modalities are superior to CE for monitoring esophageal disorders. The diagnostic characteristics of CE are inadequate to substitute for other modalities or to triage patients to other modalities.

**Hereditary GI Polyposis Syndromes**

Clinical Context and Test Purpose

The purpose of wireless CE for patients who have hereditary GI polyposis syndromes is to inform management decisions based on disease status.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with hereditary GI polyposis syndromes?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with hereditary GI polyposis syndromes, including Lynch syndrome and Peutz-Jeghers syndrome.

Interventions

The test being considered is wireless CE.

Comparators

The following tests and practices are currently being used to manage hereditary GI polyposis syndromes: ileocolonoscopy, barium small bowel follow-through, CTE, and MRE.

Outcomes

The general outcomes of interest are, test validity, other test performance measures, symptoms, and change in disease status.

Timing

Wireless CE would be performed to monitor patients after a confirmed diagnosis with hereditary GI polyposis syndromes.

Setting

Patients with hereditary GI polyposis syndromes are actively managed by gastroenterologists and primary care providers in an outpatient setting.

Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist.

This evidence review focuses on the clinical validity and clinical utility.

### Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Persons with familial adenomatous polyposis and Peutz-Jeghers syndrome are genetically at high risk of small bowel polyps and tumors. Urquhart et al (2014) compared CE with MRE in 20 patients with Peutz-Jeghers syndrome.<sup>21</sup> CE identified more polyps 10 mm or larger (47 polyps) than MRE (14 polyps;  $p=0.02$ ). However, subsequent balloon enteroscopy in 12 patients showed a poor correlation of findings between techniques, with a 100% positive predictive value of finding a polyp on balloon enteroscopy with MRE vs 60% for CE. A study by Brown et al (2006) in 19 patients showed a greater number of polyps identified with CE than with barium follow-through examinations.<sup>22</sup> Mata et al (2005) studied the role of CE in 24 patients with hereditary GI polyposis syndromes, including familial adenomatous polyposis ( $n=20$ ) or Peutz-Jeghers syndrome ( $n=4$ ).<sup>23</sup> Compared with barium studies using small bowel enteroclysis, CE identified 4 additional patients with small bowel polyps, which were subsequently removed with endoscopic polypectomy. Although these studies were small, they demonstrated that CE can identify additional lesions compared with other diagnostic methods in persons with disease syndromes at high risk for such lesions.

The lifetime risk of small bowel cancer in Lynch syndrome has been estimated at 5%. Although not extremely high, this risk is greatly increased compared with the general population. There are a few case series of the prevalence of neoplastic lesions in asymptomatic patients in patients with Lynch syndrome. Haanstra et al (2015), 200 patients with Lynch syndrome underwent CE.<sup>24</sup> Small bowel neoplasia was detected in the duodenum in 2 patients (1 adenocarcinoma, 1 adenoma). These lesions would have been in the reach of a gastroduodenoscope. In a smaller study by Saurin et al (2010), 35 asymptomatic patients with Lynch syndrome underwent colon CE.<sup>25</sup> Small bowel neoplasms were diagnosed in 3 (8.6%) patients (1 adenocarcinoma, 2 adenomas with low-grade dysplasia).

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of wireless CE for monitoring hereditary GI polyposis syndromes has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

*Section Summary: Hereditary GI Polyposis Syndromes*

Although studies have shown at least a low prevalence of small bowel neoplasms, these data are insufficient to determine whether evaluation with CE would improve patient outcomes. Additional data on the prevalence and natural history of small bowel polyps in Lynch syndrome patients are necessary. At this time, surveillance of the small bowel is not generally recommended as a routine intervention for patients with Lynch syndrome.

**Portal Hypertensive Enteropathy**

Patients with liver cirrhosis and portal hypertension can develop portal hypertensive enteropathy, which may lead to GI bleeding. CE has been considered as a diagnostic tool for portal hypertensive enteropathy.

Clinical Context and Test Purpose

The purpose of wireless CE for patients who have portal hypertensive enteropathy is to inform management decisions based on disease status.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with portal hypertensive enteropathy?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with portal hypertensive enteropathy.

Interventions

The test being considered is wireless CE.

Comparators

The following test is currently being used to manage portal hypertensive enteropathy: upper and lower endoscopy.

Outcomes

The general outcomes of interest are test validity, other test performance measures, symptoms, and change in disease status.

Timing

Wireless CE would be performed to monitor patients after a confirmed diagnosis with portal hypertensive enteropathy.

Setting

Patients with portal hypertensive enteropathy are actively managed by gastroenterologists and primary care providers in an outpatient setting.

**Clinically Valid**

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Several systematic reviews, including a Cochrane review, have been published. Tables 14 and 15 summarize the characteristics and results of select systematic reviews.

**Table 14.** Characteristics of Systematic Reviews Assessing CE for Portal Hypertensive Enteropathy

Study	Dates	Trials	Participants	N (Range)	Design
McCarty et al (2017) <sup>26</sup>	2005-2015	17	Patients with portal hypertension	1328 (8-330)	NR
Colli et al (2014) <sup>27</sup>	2005-2014	16	Adults with cirrhosis	936 (NR)	Cohort

NR: not reported.

**Table 15.** Results of Systematic Reviews Assessing CE for Portal Hypertensive Enteropathy

Study	CE, %		Likelihood Ratios		Diagnostic Accuracy	
	Sensitivity	Specificity	Positive	Negative	CE	Medium-to-Large Varices
McCarty et al (2017) <sup>26</sup>						
N	1328	1328	1328			
PE (95% CI), %	83 (76 to 89)	85 (75 to 91)	5.4 (3.3 to 9.0)	0.20 (0.14 to 0.28)	90 (88 to 93)	92 (90 to 94)
Studies with low risk of bias, n						
PE (95% CI), %	80 (81 to 88)	86 (68 to 94)			85 (81 to 88)	92 (89 to 94)
Colli et al (2014) <sup>27</sup>						
N	936	936	936			
PE (95% CI), %	84.8 (77.3 to 90.2)	84.3 (73.1 to 91.4)	5.4 (3.1 to 9.5)	0.18 (0.12 to 0.27)		
Studies with low risk of bias, n						
PE (95% CI), %	79.7 (73.1 to 85.0)	86.1 (64.5 to 95.5)	5.8 (2.1 to 16.1)	0.24 (0.18 to 0.31)		

CI: confidence interval; CE: capsule endoscopy; PE: pooled effect.

**Clinically Useful**

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

**Direct Evidence**

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of wireless CE for monitoring portal hypertensive enteropathy has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

### *Section Summary: Portal Hypertensive Enteropathy*

CE has been used to diagnose portal hypertensive enteropathy. Systematic reviews of studies of its diagnostic performance have reported limited sensitivity and specificity. Because neither the sensitivity nor the specificity was high for identifying esophageal varices, CE should not be used instead of esophagogastroduodenoscopy nor should it be used to triage patients to esophagogastroduodenoscopy. Based on these diagnostic characteristics, the test does not appear to have clinical utility.

## **Acute Upper GI Tract Bleeding**

### Clinical Context and Test Purpose

The purpose of wireless CE for patients who have acute upper GI tract bleeding is to inform management decisions based on disease status.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients with acute upper GI tract bleeding?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is patients with acute GI tract bleeding.

### Interventions

The intervention of interest is wireless CE.

### Comparators

The following practices are currently being used to manage acute upper GI tract bleeding: standard workup of acute bleeding without wireless CE and, with or without direct endoscopic procedures or specialized GI imaging.

### Outcomes

The primary outcomes of interest for clinical utility are symptoms and disease status that would change due to patient management decisions following wireless CE. Other outcomes of interest are avoidance of hospitalizations and reductions in resource utilization (eg, need for additional testing or procedures).

### Timing

Wireless CE would be performed as soon as possible after acute bleeding is identified. Wireless CE would be performed to monitor patients after a confirmed diagnosis with acute GI tract bleeding.

Setting

The test would be performed in in an urgent care or emergency department setting.

Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist.

This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Randomized Controlled Trials

Sung et al (2016) reported on a prospective RCT to evaluate the use of CE in the emergency department for patients with suspected upper GI bleeding.<sup>28</sup> CE was used to determine whether patients would be admitted to the hospital or sent home, vs an alternative strategy of admitting all patients. Eligible patients presented with signs and/or symptoms of acute upper GI bleeding but were without hemodynamic shock or conditions likely to preclude the use of the capsule endoscope. Seventy-one patients were randomized to CE in the emergency department (n=37), followed by monitoring for upper GI bleeding, or standard care (n=34), which included mandatory hospital admission. Seven CE patients with active bleeding or endoscopic findings were admitted, with the remainder discharged home. There were no deaths or morbid outcomes in either group, indicating that CE could result in equivalent patient outcomes with many patients safely avoiding emergency hospitalization.

Tables 16 and 17 summarize the characteristics and results of select RCTs.

**Table 16.** Characteristics of RCTs Assessing CE for Acute GI Tract Bleeding

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Sung et al (2016) <sup>28</sup>	China	NR	2013-2014	Patients presenting to ED with symptoms suggestive of UGIB	37 randomized to CE; admission determined by CE	34 randomized to SOC; admission determined by GBS
Gutkin et al (2013) <sup>29</sup>	U.S.	3	NR	Patients ≥18 y with history suggestive of acute UGIB ≤48 h prior to ED presentation	12 randomized to VCE prior to endoscopy	12 randomized to endoscopy

CE: capsule endoscopy; ED: emergency department; GBS: Glasgow Blatchford score; NR: not reported; RCT: randomized controlled trial; SOC: standard of care; UGIB: upper gastrointestinal bleeding; VCE: video capsule endoscopy.

**Table 17.** Results of RCTs Assessing CE for Acute GI Tract Bleeding

Study	Active Bleeding or Endoscopic Findings, n	Hospitalization, n	Mortality, n	GBS Score	Agreement Between CE and EGD
Sung et al (2016) <sup>28</sup>					

Study	Active Bleeding or Endoscopic Findings, n	Hospitalization, n	Mortality, n	GBS Score	Agreement Between CE and EGD
N	68	68	68	68	68
CE	<ul style="list-style-type: none"> <li>• “Coffee ground” material: 2</li> <li>• Peptic ulcer with Forrest Ib stigmata: 2</li> <li>• Forrest IIa: 2</li> <li>• Esophageal varix: 1</li> </ul>	7	0	<ul style="list-style-type: none"> <li>• 6 patients: 0</li> <li>• 3 patients: 1</li> <li>• 25 patients: ≥2</li> </ul>	
SOC	<ul style="list-style-type: none"> <li>• Peptic ulcer: 14</li> <li>• Duodenal ulcer: 12</li> <li>• Gastritis/duodenitis: 10</li> <li>• Gastric or duodenal erosions: 5</li> <li>• Mallory Weiss tear: 1</li> </ul>	34	0	<ul style="list-style-type: none"> <li>• No patients scored 0</li> <li>• 7 patients: 1</li> <li>• 27 patients: ≥2</li> </ul>	
Gutkin et al (2013) <sup>29</sup>					
N	24				24
VCE	8 (67.7%) had positive findings confirmed by endoscopy; for these patients, average Rockall score was 3; average Blatchford score was 13				VCE data identical to EGD results (p=1.0)

CE: capsule endoscopy; EGD: esophagogastroduodenoscopy; GBS: Glasgow Blatchford score; RCT: randomized controlled trial; RR: relative risk; SOC: standard of care; VCE: video capsule endoscopy.

The purpose of the gaps tables (see Tables 18 and 19) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

**Table 18.** Relevance Gaps

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
Sung et al (2016) <sup>28</sup>					
Gutkin et al (2013) <sup>29</sup>					

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

<sup>b</sup> Intervention key: 1. Classification thresholds not defined; 2. Version used unclear; 3. Not intervention of interest.

<sup>c</sup> Comparator key: 1. Classification thresholds not defined; 2. Not compared to credible reference standard; 3. Not compared to other tests in use for same purpose.

<sup>d</sup> Outcomes key: 1. Study does not directly assess a key health outcome; 2. Evidence chain or decision model not explicated; 3. Key clinical validity outcomes not reported (sensitivity, specificity and predictive values); 4. Reclassification of diagnostic or risk categories not reported; 5. Adverse events of the test not described (excluding minor discomforts and inconvenience of venipuncture or noninvasive tests).

<sup>e</sup> Follow-Up key: 1. Follow-up duration not sufficient with respect to natural history of disease (true positives, true negatives, false positives, false negatives cannot be determined).

**Table 19.** Study Design and Conduct Gaps

Study	Selection <sup>a</sup>	Blinding <sup>b</sup>	Delivery of Test <sup>c</sup>	Selective Reporting <sup>d</sup>	Data Completeness <sup>e</sup>	Statistical <sup>f</sup>
Sung et al (2016) <sup>28</sup>						3. As a feasibility study, confidence intervals and p

Study	Selection <sup>a</sup>	Blinding <sup>b</sup>	Delivery of Test <sup>c</sup>	Selective Reporting <sup>d</sup>	Data Completeness <sup>e</sup>	Statistical <sup>f</sup>
Gutkin et al (2013) <sup>29</sup>					2. Small sample size based on pilot/feasibility study	values were not reported

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).

<sup>b</sup> Blinding key: 1. Not blinded to results of reference or other comparator tests.

<sup>c</sup> Test Delivery key: 1. Timing of delivery of index or reference test not described; 2. Timing of index and comparator tests not same; 3. Procedure for interpreting tests not described; 4. Expertise of evaluators not described.

<sup>d</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

<sup>e</sup> Data Completeness key: 1. Inadequate description of indeterminate and missing samples; 2. High number of samples excluded; 3. High loss to follow-up or missing data.

<sup>f</sup> Statistical key: 1. Confidence intervals and/or p values not reported; 2. Comparison to other tests not reported.

### Cohort Studies

Two 2013 studies with small cohorts of patients (range, 49-83 patients) have reported on the use of CE before upper endoscopy for acute GI bleeding, to triage and/or risk-stratify patients in the emergency department or hospital.<sup>30,31</sup> These studies reported that CE provides useful information, such as identifying gross bleeding and inflammatory lesions in a substantial proportion of patients and in stratifying patients into high- or low-risk categories. However, the yield of CE in localizing the bleeding source was lower than for esophagogastroduodenoscopy, which is the standard initial evaluation for acute upper GI bleeding.

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of wireless CE for diagnosing acute upper GI tract bleeding has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

### *Section Summary: Acute Upper GI Tract Bleeding*

Use of CE in the emergency department setting for suspected upper GI bleeding is based on efficiency (avoiding hospitalization, avoiding immediate endoscopy). Controlled studies are needed to assess further the impact of CE on health outcomes compared with standard

management. Patients should be followed to their ultimate diagnosis to determine whether the use of CE vs other triage strategies or immediate endoscopy results in lower health care resource utilization.

## **Colon Cancer Screening**

### Clinical Context and Test Purpose

The purpose of wireless CE for patients who are being screened for colon cancer is to confirm a diagnosis and inform a decision to proceed to appropriate treatment.

The question addressed in this evidence review is: Does the use of wireless CE improve the net health outcome in patients undergoing colon cancer screening?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is patients who are undergoing colon cancer screening.

### Interventions

The intervention of interest is wireless CE.

### Comparators

The following test is currently being used to diagnose colon cancer: standard workup using optical colonoscopy.

### Outcomes

The outcomes of interest for diagnostic accuracy include test validity (ie, sensitivity, specificity). The primary outcomes of interest for clinical utility are overall mortality and disease-specific mortality from colon cancer.

### Timing

Wireless CE would be performed after an initial clinical examination. Though not completely standardized, follow-up for screening for colon cancer would be based on guidelines for asymptomatic screening or for follow-up of significant screening findings.

### Setting

Patients screened for colon cancer are actively managed by oncologists, gastroenterologists, radiologists, surgeons, and primary care providers in an outpatient setting.

### Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist.

This evidence review focuses on the clinical validity and clinical utility.

**Clinically Valid**

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Several studies have assessed the accuracy of CE for detecting colonic lesions. Spada et al (2016) reported on a systematic review and meta-analysis of the diagnostic accuracy of CE for detecting colorectal polyps with stratified results for first- and second-generation capsules.<sup>32</sup> Across the 14 eligible studies, the indications for endoscopy included colorectal cancer screening (n=1261 [47%]), postpolypectomy surveillance or family history of colorectal cancer (n=636 [24%]), symptoms suggestive of cancer and/or fecal occult blood test positivity (n=619 [23%]), positive imaging tests (n=136 [5%]), or other indication (24 [1%]). Characteristics of the systematic review and its main findings are summarized in Tables 20 and 21, respectively.

**Table 20.** Characteristics of Systematic Review Assessing CE for Colon Cancer Screening

Study	Dates	Trials	N (Range)	Design	Outcome
Spada et al (2016) <sup>32</sup>	2006-2015	14	2681 (40-884)	Diagnostic accuracy studies	Per-patient sensitivity of CCE for different categories of polyp size and for cancer

CCE: colon capsule endoscopy.

**Table 21.** Results of Systematic Review Assessing CE for Colon Cancer Screening

Random-Effects Model	Trials	N	Outcomes	Effect Size	95% CI	I <sup>2</sup> , %
For ≥10 mm polyps	10	NR	Diagnostic accuracy for ≥10 mm polyps	Sens=80.0 % Spec=96.2 % PLR=18.6 NLR=0.22 DOR=90.4	66% to 90.3% 94.0% to 97.6% 12.0 to 28.2 0.13 to 0.34 44 to 163	53.4 31.3
For ≥6 mm polyps	7	NR	Diagnostic accuracy for ≥6 mm polyps using 1st-generation CCE	Sens=58% Spec=85.7 % PLR=3.7 NLR=0.51 DOR=7.4	44% to 70% 80.2% to 90.0%	65
For ≥6 mm polyps	6	NR	Diagnostic accuracy for ≥6 mm polyps using 2nd-generation CCE	Sens=86% Spec=88.1 % PLR=7.9 NLR=0.16 DOR=50.5	82% to 89% 74.2% to 95.0% 3.7 to 16.1 0.12 to 0.21 20.3 to 107.0	0
For ≥10 mm polyps	3	NR	Diagnostic accuracy for ≥6 mm polyps using 1st-generation CCE	Sens=54% Spec=97.4 % PLR=NR NLR=NR DOR=NR	29% to 77% 96.0% to 98.3%	76.2 0
For ≥10 mm polyps	6	NR	Diagnostic accuracy for ≥6 mm polyps using 2nd-generation CCE	Sens=88% Spec=95.3 % PLR=NR NLR=NR DOR=NR	81% to 91% 91.5% to 97.5%	0 67

Adapted from Spada et al (2016).<sup>32</sup>

AUC: area under the curve; CCE: colon capsule endoscopy; CI: confidence interval; DOR: diagnostic odds ratio; NLR: negative likelihood ratio; NR: not reported; PLR: positive likelihood ratio; Sens: sensitivity; Spec: specificity.

There were no missed cancers (n=11) in the series using second-generation CE (per-patient sensitivity, 100%). In series using first-generation CE, 6 of 26 proven cancers were missed on CE (per-patient sensitivity, 77%).

### Prospective Studies

Other recent studies by Saito et al (2015), Morgan et al (2016), and Parodi (2018) have evaluated the diagnostic characteristics of CE, using subsequently performed colonoscopy as the reference standard.<sup>33-35</sup> In the Saito study, of 66 evaluable patients, per-patient sensitivity for detection of polyps was 94% (95% CI, 88.2% to 99.7%). In the Morgan study, for lesions 10 mm or larger, sensitivity of CE was 100% (95% CI, 56.1% to 100%), with a specificity of 93.0% (95% CI, 79.9% to 98.2%). For lesions 6 mm or larger, sensitivity was 93.3% (95% CI, 66.0% to 99.7%) and the specificity was 80.0% (95% CI, 62.5% to 90.9%). The Parodi study included 177 first-degree relatives of individuals with colorectal cancer and found, for lesions 6 mm or larger, a sensitivity of 91% (95% CI, 81% to 96%) and a specificity of 88% (95% CI, 81% to 93%).<sup>35</sup>

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of wireless CE for diagnosing colon cancer has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

### *Section Summary: Colon Cancer Screening*

Studies of diagnostic characteristics alone are insufficient evidence to determine the efficacy of CE for colon cancer screening. Because diagnostic performance is worse than standard colonoscopy, CE would need to be performed more frequently than standard colonoscopy to have comparable efficacy potentially. Without direct evidence of efficacy in a clinical trial of colon cancer screening using CE, modeling studies using established mathematical models of colon precursor incidence and progression to cancer could provide estimates of efficacy in preventing colon cancer mortality. Studies of CE in screening populations are necessary to determine the diagnostic characteristics of the test in this setting.

## **Known or Suspected Small Bowel Stricture**

### Clinical Context and Test Purpose

The purpose of the patency capsule for patients scheduled to undergo CE for known or suspected small bowel stricture is to confirm a diagnosis and inform a decision to proceed to CE.

The question addressed in this evidence review is: Does the use of a patency capsule improve the net health outcome in patients with known or suspected small bowel stricture?

The following PICOTS were used to select literature to inform this review.

### Patients

The relevant population of interest is individuals scheduled to undergo CE for known or suspected small bowel stricture. Contraindications to the use of CE include known or suspected obstruction or stricture, Zenker diverticulum, intestinal pseudo-obstruction, and motility disorders. Certain patients with known or suspected strictures of the small bowel may be at risk of retaining the capsule. Surgical removal may be necessary.

### Interventions

The test being considered is patency capsule as a technique to evaluate patients with known or suspected strictures before using wireless CE. The capsule could be to select patients for CE instead of assessing clinical risk factors.

The use of the patency capsule has some risk itself. Published studies are small and do not provide comparative data on the incremental value of this capsule over standard clinical evaluation. In some series, administration of the patency capsule has produced symptoms requiring hospitalization and even surgery. In European study, Spada et al (2007) reported on findings for 27 patients, 24 with CD.<sup>36</sup> In this study, 25 (92.6%) patients retrieved the patency capsule in their stools. Six patients complained of abdominal pain, four of whom excreted a nonintact capsule, and hospitalization was required in 1 patient due to the occlusive syndrome.

### Comparators

The following practices are currently being used to diagnose known or suspected small bowel stricture: CE without patency capsule and alternative workup without CE.

### Outcomes

The general outcomes of interest are test validity, symptoms, change in disease status, and treatment-related morbidity.

### Timing

Patency capsule use would occur before testing with the wireless CE.

### Setting

Patients who are scheduled to undergo patency capsule screening before wireless CE for known or suspected small bowel stricture are actively managed by oncologists, gastroenterologists, radiologists, surgeons, and primary care providers in an outpatient clinical setting.

### Technically Reliable

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist.

This evidence review focuses on the clinical validity and clinical utility.

### Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

In a series from Europe, Delvaux et al (2005) reported on findings in 22 patients with suspected intestinal stricture, 15 of whom had CD.<sup>37</sup> In this study, at 30 hours after ingestion, the patency capsule was detected in 17 (72.3%) patients. In all patients in whom the capsule was blocked in the small intestine, the stenosis had been suspected on CT scan or small bowel follow-through. In 3 patients, the delay in progression of the patency capsule led to cancellation of CE. In 3 patients, the patency capsule induced a symptomatic intestinal occlusion, which resolved spontaneously in one and required emergency surgery in two. The authors commented that the current technical development of the patency capsule limits its use in clinical practice, because it did not detect stenoses undiagnosed by CT or small bowel follow-through, and the start of dissolution at 40 hours after ingestion is too slow to prevent episodes of intestinal occlusion. They also commented that a careful interview eliciting the patient's history and symptoms remains the most useful indicator for suspicion of an intestinal stenosis.

Several studies have shown that patients who had uncomplicated passage of the patency capsule subsequently underwent uncomplicated CE.<sup>38-40</sup> These patients often had significant findings on CE.<sup>38,39</sup> However, it is difficult to determine whether CE findings in these patients improved their outcomes beyond any alternative testing regimen available. In one of these studies, 3 of 106 patients had severe adverse events, including 1 patient who required surgery.<sup>38</sup>

### Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

### Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs assessing the clinical utility of wireless CE for this indication were identified.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of the patency capsule for diagnosing known or suspected strictures has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

*Section Summary: Bowel Stricture*

The overall balance of harm and benefit of using the patency capsule cannot be determined from the existing studies.

## **SUMMARY OF EVIDENCE**

### Patients with Suspected GI Disorders

For individuals who have suspected small bowel bleeding (previously referred to as obscure GI bleeding) who receive wireless CE, the evidence includes numerous case series evaluating patients with a nondiagnostic standard workup. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. The evidence has demonstrated that CE can identify a bleeding source in a substantial number of patients who cannot be diagnosed by other methods, with a low incidence of adverse events. Because there are few other options for diagnosing obscure small bowel bleeding in patients with negative upper and lower endoscopy, this technique will likely improve health outcomes by directing specific treatment when a bleeding source is identified. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected small bowel CD who receive wireless CE, the evidence includes case series. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. Although the test performance characteristics and diagnostic yields of the capsule for this indication are uncertain, the diagnostic yields are as good as or better than other diagnostic options, and these data are likely to improve health outcomes by identifying some cases of CD and directing specific treatment. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have suspected celiac disease who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. The diagnostic characteristics of CE are inadequate to substitute for other modalities or to triage patients to other modalities. For other conditions (eg, determining the extent of CD), direct evidence of improved outcomes or a strong indirect chain of evidence to improved outcomes is lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have unexplained chronic abdominal pain who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. The diagnostic characteristics of CE are inadequate to substitute for other modalities or to triage patients to other modalities. For other conditions (eg, determining the extent of CD), direct evidence of improved outcomes or a strong chain of evidence to improved outcomes is lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

### Patients with Confirmed GI Disorders

For individuals who have an established diagnosis of CD who receive wireless CE, the evidence includes diagnostic accuracy studies and a systematic review. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. A 2017 systematic review of 11 studies in patients with established CD found a similar diagnostic yield with CE and with radiography. Because there is evidence that the diagnostic yields are as good as or better than other diagnostic options, there is indirect evidence that CE is likely to improve health outcomes by identifying some cases of CD and directing specific treatment. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have ulcerative colitis who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. Several diagnostic accuracy studies have compared CE with colonoscopy to assess disease activity in patients with ulcerative colitis. Two of 3 studies were small (ie, <50 patients) and thus data on diagnostic accuracy are limited. Direct evidence of improved outcomes and a strong chain of evidence to improved outcomes are lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have esophageal disorders who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. Other available modalities are superior to CE. The diagnostic characteristics of CE are inadequate to substitute for other modalities or to triage patients to other modalities. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have hereditary GI polyposis syndromes who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test validity, other test performance measures, symptoms, and change in disease status. The data are insufficient to determine whether evaluation with CE would improve patient outcomes. Further information on the prevalence and natural history of small bowel polyps in Lynch syndrome patients is necessary. At present, surveillance of the small bowel is not generally recommended as a routine intervention for patients with Lynch syndrome. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have portal hypertensive enteropathy who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test validity, and other test performance measures, symptoms, and change in disease status. Systematic reviews of studies of CE's diagnostic performance for this indicated have reported limited sensitivity and specificity. Due to insufficient data on diagnostic accuracy, a chain of evidence on clinical utility cannot be constructed. The evidence is insufficient to determine the effects of the technology on health outcomes.

### Acute Upper GI Bleeding

For individuals who have acute upper GI tract bleeding who receive wireless CE, the evidence includes a randomized controlled trial and several cohort studies. Relevant outcomes are test

validity, and other test performance measures, symptoms, hospitalizations, and resource utilization. The use of CE in the emergency department setting for suspected upper GI bleeding is intended to avoid unnecessary hospitalization or immediate endoscopy). Controlled studies are needed to assess further the impact of CE on health outcomes compared with standard management. The evidence is insufficient to determine the effects of the technology on health outcomes.

### Colon Cancer Screening

For individuals who are screened for colon cancer who receive wireless CE, the evidence includes diagnostic accuracy studies and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, test validity, and other test performance measures. Studies of CE in screening populations are necessary to determine the diagnostic characteristics of the test in this setting. Studies of diagnostic characteristics alone are insufficient evidence to determine the efficacy of CE for colon cancer screening. Because diagnostic performance is worse than standard colonoscopy, CE would need to be performed more frequently than standard colonoscopy to have comparable efficacy. Without direct evidence of efficacy in a clinical trial of colon cancer screening using CE, modeling studies using established mathematical models of colon precursor incidence and progression to cancer could provide estimates of efficacy in preventing colon cancer mortality. The evidence is insufficient to determine the effects of the technology on health outcomes.

### Patency Capsule for Patients with Bowel Stricture

For individuals who are scheduled to undergo CE for known or suspected small bowel stricture who receive a patency capsule, the evidence includes case series. Relevant outcomes are test validity, symptoms, change in disease status, and treatment-related morbidity, the available studies have reported that CE following a successful patency capsule test results in high rates of success with low rates of adverse events. The capsule is also associated with adverse events. Because of the lack of comparative data to other diagnostic strategies, it is not possible to determine whether the use of the patency capsule improves the net health outcome. The evidence is insufficient to determine the effects of the technology on health outcomes.

## **PRACTICE GUIDELINES AND POSITION STATEMENTS**

### **Canadian Association of Gastroenterology**

In 2017, the Canadian Association of Gastroenterology published guidelines on the use of video capsule endoscopy (CE), which included the following consensus recommendations (majority voting for recommendation) (see Table 22).<sup>41</sup>

**Table 22.** Recommendations on Use of Video CE

	<b>Recommendation</b>	<b>QOE</b>
<b>Crohn's disease</b>		
	Patients presenting with clinical features consistent with CD and negative ileocolonoscopy and imaging studies	Very low or low
	Patients with CD and clinical features not explained by negative ileocolonoscopy and imaging studies	Very low or low
	Patients with CD, when assessment of small-bowel mucosal healing is needed, and the area is beyond the reach of ileocolonoscopy	Very low or low
	Patients with suspected small bowel recurrence of CD after colectomy, undiagnosed by ileocolonoscopy and imaging studies	Very low or low
<b>Celiac disease</b>		

<b>Recommendation</b>	<b>QOE</b>
<b>Crohn's disease</b>	
Recommend against CE in patients with suspected celiac disease	Very low or low
Recommend for CE in patients with celiac disease and unexplained symptoms despite treatment and appropriate investigations	Very low or low
<b>Gastrointestinal bleeding</b>	
Recommend for CE in patients with documented overt gastrointestinal bleeding (excluding hematemesis) and negative colonoscopy and high-quality esophagogastroduodenoscopy	Very low or low
Recommend for CE in patients with an overt, obscure bleeding episode	Very low or low
Recommend for endoscopy, colonoscopy and/or CE in patients with prior negative CE who have repeated obscure bleeding	Very low or low

CD: Crohn's disease; CE: capsule endoscopy; QOE: quality of evidence (all consensus-based).

American College of Gastroenterology

In 2013, the American College of Gastroenterology (ACG) issued guidelines on the diagnosis and management of celiac disease.<sup>42</sup> The guidelines recommended that CE not be used for initial diagnosis, except for patients with positive celiac-specific serology who are unwilling or unable to undergo upper endoscopy with biopsy (strong recommendation, moderate level of evidence).

CE should be considered for the evaluation of small bowel mucosa in patients with complicated Crohn's disease (CD; strong recommendation, moderate level of evidence).

ACG issued guidelines in 2009 on the management of CD in adults.<sup>43</sup> The guidelines indicated that use of video CE had been assessed in a prospective blinded evaluation and was shown to be superior in its ability to detect small bowel pathology missed on small bowel radiographic studies and computed tomography radiographic examinations. However, because there is a risk of capsule retention in up to 13% of patients with CD, which could require surgical intervention, CE is considered to be a contraindication in patients with known small bowel strictures. It was recommended that radiographic studies such as computed tomography enterography, small bowel follow-through, or magnetic resonance imaging be done to assess for the presence of unsuspected bowel strictures before CE. A patency capsule may also be considered.

In 2015, ACG issued guidelines on the diagnosis and management of small bowel bleeding (including using "small bowel bleeding" to replace "obscure GI [gastrointestinal] bleeding," which should be reserved for patients in whom a source of bleeding cannot be identified anywhere in the GI tract).<sup>44</sup> These guidelines made the following statements related to video CE (see Table 23).

**Table 23.** Recommendations on Diagnosis and Management of Small Bowel Bleeding

<b>Recommendation</b>	<b>SOR</b>	<b>LOE</b>
"... VCE should be considered as a first-line procedure for SB evaluation after upper and lower GI sources have been excluded, including second-look endoscopy when indicated"	Strong	Moderate
"VCE should be performed before deep enteroscopy to increase diagnostic yield. Initial deep enteroscopy can be considered in cases of massive hemorrhage or when VCE is contraindicated"	Strong	High

LOE: level of evidence; SB: small bowel; SOR: strength of recommendation; VCE: video capsule endoscopy.

American Society of Gastrointestinal Endoscopy

In 2016, the American Society of Gastrointestinal Endoscopy released guidelines for the use of endoscopy in the management of suspected small bowel bleeding.<sup>45</sup> These guidelines made the following recommendations on capsule endoscopy (see Table 24).

**Table 24.** Recommendations on Use of Endoscopy to Manage Suspected Small Bowel Bleeding

Recommendation	QOE
We suggest VCE as the initial test for patients with overt or occult small-bowel bleeding. Positive VCE results should be followed with push enteroscopy if within reach or DAE."	Moderate
"We suggest DAE or push enteroscopy if VCE is unavailable or nondiagnostic in patients with overt small bowel bleeding."	Moderate

DAE: device-assisted enteroscopy; QOE: quality of evidence; VCE: video capsule endoscopy.

American Gastroenterological Association Institute

A 2007 position statement by American Gastroenterological Association Institute indicated the following on obscure GI bleeding and CE<sup>46</sup>:

"Evaluation of the patient with obscure bleeding is dependent on the extent of the bleeding and the age of the patient.

Patients with occult GI blood loss and no anemia most likely do not require evaluation beyond colonoscopy unless upper tract symptoms are present....

Patients with occult GI blood loss and iron deficiency anemia and negative workup on EGD [esophagogastroduodenoscopy] and colonoscopy need comprehensive evaluation, including capsule endoscopy to identify an intestinal bleeding lesion."

**U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS**

The U.S. Preventive Services Task Force published its most recent recommendations for colorectal cancer screening in 2016.<sup>47</sup> Colorectal cancer screening was recommended starting at age 50 years and continuing until age 75 years (A recommendation). Studies evaluating CE were not included in the evidence reviews in this report.

**ONGOING AND UNPUBLISHED CLINICAL TRIALS**

Some currently unpublished trials that might influence this review are listed in Table 25.

**Table 25.** Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<b>Ongoing</b>			
NCT01371591 <sup>a</sup>	Pilot Study to Investigate the Use of Wireless Capsule Endoscopy for Emergency Department Patients With Suspected Acute Upper Gastrointestinal Bleeding	100	Aug 2018 (ongoing)
NCT02754661 <sup>a</sup>	Evaluation the Efficacy of Colon Capsule Endoscopy (CCE) Versus Computed Tomographic Colonography (CTC) in the Identification of Colonic Polyps in a Screening Population. (TOPAZ)	320	Dec 2017
NCT01371591 <sup>a</sup>	Capsule Endoscopy for Hemorrhage in the Emergency Room (CHEER)	100	Aug 2018
NCT03241368 <sup>a</sup>	Clinical Study Comparing PillCam® Crohn's Capsule Endoscopy to Ileocolonoscopy (IC) Plus MRE for Detection of Active CD in	352	Aug 2020

NCT No.	Trial Name	Planned Enrollment	Completion Date
	the Small Bowel and Colon in Subjects With Known CD and Mucosal Disease (BLINK)		

NCT: national clinical trial.

<sup>a</sup> Denotes industry-sponsored or cosponsored trial.

## **CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

### CPT/HCPCS

- 91110 Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), esophagus through ileum, with physician interpretation and report
- 91111 Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), esophagus, with physician interpretation and report
- 0355T Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), colon, with interpretation and report

### ICD-10 Diagnoses

- D13.2 Benign neoplasm of duodenum
- D13.39 Benign neoplasm of other parts of small intestine
- K50.00 Crohn's disease of small intestine without complications
- K50.011 Crohn's disease of small intestine with rectal bleeding
- K50.012 Crohn's disease of small intestine with intestinal obstruction
- K50.013 Crohn's disease of small intestine with fistula
- K50.014 Crohn's disease of small intestine with abscess
- K50.018 Crohn's disease of small intestine with other complication
- K50.10 Crohn's disease of large intestine without complications
- K50.111 Crohn's disease of large intestine with rectal bleeding
- K50.112 Crohn's disease of large intestine with intestinal obstruction
- K50.113 Crohn's disease of large intestine with fistula
- K50.114 Crohn's disease of large intestine with abscess
- K50.118 Crohn's disease of large intestine with other complication
- K50.80 Crohn's disease of both small and large intestine without complications
- K50.811 Crohn's disease of both small and large intestine with rectal bleeding
- K50.812 Crohn's disease of both small and large intestine with intestinal obstruction
- K50.813 Crohn's disease of both small and large intestine with fistula
- K50.814 Crohn's disease of both small and large intestine with abscess
- K50.818 Crohn's disease of both small and large intestine with other complication
- K50.90 Crohn's disease, unspecified, without complications
- K50.911 Crohn's disease, unspecified, with rectal bleeding
- K50.912 Crohn's disease, unspecified, with intestinal obstruction
- K50.913 Crohn's disease, unspecified, with fistula

- K50.918 Crohn's disease, unspecified, with other complication
- K52.0 Gastroenteritis and colitis due to radiation
- K52.1 Toxic gastroenteritis and colitis
- K52.21 Food protein-induced enterocolitis syndrome
- K52.22 Food protein-induced enteropathy
- K52.29 Other allergic and dietetic gastroenteritis and colitis
- K52.3 Indeterminate colitis
- K52.831 Collagenous colitis
- K52.832 Lymphocytic colitis
- K52.838 Other microscopic colitis
- K52.839 Microscopic colitis, unspecified
- K52.89 Other specified noninfective gastroenteritis and colitis
- K52.9 Noninfective gastroenteritis and colitis, unspecified
- K92.0 Hematemesis
- K92.1 Melena
- K92.2 Gastrointestinal hemorrhage, unspecified
- Q85.8 Other phakomatoses, not elsewhere classified
- R10.0 Acute abdomen
- R10.11 Right upper quadrant pain
- R10.12 Left upper quadrant pain
- R10.13 Epigastric pain
- R10.2 Pelvic and perineal pain
- R10.31 Right lower quadrant pain
- R10.32 Left lower quadrant pain
- R10.33 Periumbilical pain
- R10.84 Generalized abdominal pain
- R19.7 Diarrhea, unspecified
- R50.2 Drug induced fever
- R50.9 Fever, unspecified
- R63.4 Abnormal weight loss

**REVISIONS**

06-29-2010	<p>Title was changed from: "Wireless Capsule Endoscopy"                  To: "Wireless Capsule Endoscopy as a Diagnostic Technique in Disorders of the Small Bowel, Esophagus, and Colon"</p> <p>Description Section was updated.</p> <p>In Policy Section:</p> <ul style="list-style-type: none"> <li>▪ Updated policy from:</li> </ul> <p>"1. Wireless capsular endoscopy is considered medically necessary as an adjunctive diagnostic imaging tool when all other modalities have failed to identify the source of bleeding (e.g., colonoscopy, and upper endoscopy, or panendoscopy) and the patient continues to require active medical or surgical treatment for:</p> <ul style="list-style-type: none"> <li>a. Clinically significant bleeding (i.e., drop in hemoglobin or progressive anemia) in chronic or acute obscure small intestinal bleeding.</li> <li>b. Abdominal pain, diarrhea, fever, elevated white blood cell count, elevated erythrocyte sedimentation rate, weight loss, or bleeding in the initial diagnosis with suspected Crohn's disease or Crohn's disease.</li> </ul>
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	<p>2. Wireless capsular endoscopy is considered investigational for all other indications, including but not limited to the study of the colon or stomach and investigating suspected diseases in the absence of bleeding."</p> <p>To:</p> <p>"A. Wireless capsule endoscopy of the small bowel may be considered medically necessary for the following indications:</p> <ol style="list-style-type: none"> <li>1. Initial diagnosis in patients with suspected Crohn's disease without evidence of disease on conventional diagnostic tests such as small-bowel follow-through (SBFT), and upper and lower endoscopy.</li> <li>2. Obscure gastrointestinal (GI) bleeding suspected of being of small bowel origin, as evidenced by prior inconclusive upper and lower gastrointestinal endoscopic studies.</li> <li>3. For surveillance of the small bowel in patients with hereditary GI polyposis syndromes, including familial adenomatous polyposis and Peutz-Jeghers syndrome.</li> </ol> <p>B. Other indications of wireless capsule endoscopy are considered experimental / investigational, including but not limited to:</p> <ol style="list-style-type: none"> <li>1. Evaluation of the extent of involvement of known Crohn's disease</li> <li>2. Evaluation of the esophagus, in patients with gastroesophageal reflux (GERD) or other esophageal pathologies</li> <li>3. Evaluation of other gastrointestinal diseases not presenting with GI bleeding including, but not limited to celiac sprue, irritable bowel syndrome, small bowel neoplasm</li> <li>4. Evaluation of the colon including, but not limited to, detection of colonic polyps or colon cancer.</li> </ol> <p>C. The patency capsule is considered experimental / investigational, including use to evaluate patency of the gastrointestinal tract before wireless capsule endoscopy."</p>
	Added Rationale Section
	In Coding Section: ▪ Added Diagnosis Codes: 211.2, 759.6
	Updated References
08-19-2011	Updated Rational section.
	Updated Reference section.
01-15-2013	In the Coding section: ▪ Added new CPT code: 91112 (Effective 01-01-2013)
	Added Medical Policy and Coding Disclaimers
01-10-2014	Updated Description section.
	In Policy section: ▪ In Item B, added "Initial evaluation of patients with acute GI bleeding."
	Updated Rationale section.
	In Coding section: ▪ Removed CPT code 91112 ▪ Added ICD-10 Diagnosis (Effective October 1, 2014)
	Updated Reference section.
12-11-2014	Updated Description section.
	In Policy section: ▪ In Item A, added "2. In patients with an established diagnosis of Crohn's disease, when there are unexpected change(s) in the course of disease or response to treatment, suggesting the initial diagnosis may be incorrect and re-examination may be indicated.

	<ul style="list-style-type: none"> <li>▪ In Item B, #1, added "or ulcerative colitis", to read, "Evaluation of the extent of involvement of known Crohn's disease or ulcerative colitis."</li> <li>▪ In Item B, #3, added "Lynch syndrome, portal hypertensive enteropathy," and "unexplained chronic abdominal pain." to read, "Evaluation of other gastrointestinal diseases not presenting with GI bleeding including, not but not limited, celiac sprue, irritable bowel syndrome, Lynch syndrome, portal hypertensive enteropathy, small bowel neoplasm, and unexplained chronic abdominal pain."</li> </ul>
	Added Policy Guidelines.
	Updated Rationale section.
	Updated Summary section.
	In Coding section:
	<ul style="list-style-type: none"> <li>▪ Added CPT code 0355T.</li> </ul>
	Updated References section.
11-24-2015	Updated Description section.
	In Policy section:
	<ul style="list-style-type: none"> <li>▪ In Item A 3, added "performed during the current episode of illness" to read, "Obscure gastrointestinal (GI) bleeding suspected of being of small bowel origin, as evidence by prior inconclusive upper and lower gastrointestinal endoscopic studies performed during the current episode of illness."</li> <li>▪ In Item B 3, added "and conditions" to read, "Evaluation of other gastrointestinal diseases and conditions not presenting with GI bleeding, including, but not limited to, celiac sprue, irritable bowel syndrome, Lynch syndrome, portal hypertensive enteropathy, small bowel neoplasm, and unexplained chronic abdominal pain."</li> </ul>
	Updated Rationale section.
	In Coding section:
	<ul style="list-style-type: none"> <li>▪ Added ICD-10 code Q85.8.</li> </ul>
	Updated References section.
10-01-2016	In Coding section:
	<ul style="list-style-type: none"> <li>▪ Added ICD-10 codes effective 10-01-2016: K52.21, K52.22, K52.29, K52.3, K52.831, K52.832, K52.838, K52.839</li> <li>▪ Termed ICD-10 code effective 09-30-2016: K52.2</li> </ul>
01-18-2017	Title of policy has been changed from "Wireless Capsule Endoscopy as a Diagnostic Technique in Disorders of the Small Bowel, Esophagus, and Colon."
	Updated Description section.
	Updated Rationale section.
	Updated References section.
01-30-2018	Updated Description section.
	In Policy section:
	<ul style="list-style-type: none"> <li>▪ In Item A 1, removed "(SBFT)" to read, "Initial diagnosis in patients with suspected Crohn's disease without evidence of disease on conventional diagnostic tests such as small bowel follow-through and upper and lower endoscopy."</li> <li>▪ Updated Policy Guidelines.</li> </ul>
	Updated Rationale section.
	In Coding section:
	<ul style="list-style-type: none"> <li>▪ Removed ICD-9 codes.</li> </ul>
	Updated References section.
01-04-2019	Updated Description section.
	In Policy section:
	<ul style="list-style-type: none"> <li>▪ In Item B, removed "of" and added "for" to read, "Other indications for wireless capsule endoscopy are considered experimental / investigational, including, but not limited to:"</li> </ul>

	<ul style="list-style-type: none"> <li>▪ In Item B 2, removed "(GERD)" to read, "Evaluation of the esophagus, in patients with gastroesophageal reflux or other esophageal pathologies."</li> <li>▪ In Item B 3, added "(risk for hereditary nonpolyposis colorectal cancer)" to read, "Evaluation of other gastrointestinal diseases and conditions not presenting with GI bleeding, including, but not limited to, celiac sprue, irritable bowel syndrome, Lynch syndrome (risk for hereditary nonpolyposis colorectal cancer), portal hypertensive enteropathy, small bowel neoplasm, and unexplained chronic abdominal pain."</li> <li>▪ In Item B 5, added "upper" to read, "Initial evaluation of patients with acute upper GI bleeding."</li> </ul>
	Updated Rationale section.
	Updated References section.

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