Wireless Capsule Endoscopy to Diagnose Disorders of the Small Bowel, Esophagus, and Colon

Policy Number: 6.01.33  Last Review: 4/2019

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Wireless Capsule Endoscopy as a Diagnostic Technique in Disorders of the Small Bowel, Esophagus, and Colon when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Wireless capsule endoscopy of the small bowel may be considered medically necessary for the following indications:
- 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.
- In patients with an established diagnosis of Crohn 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.
- Suspected small bowel bleeding, as evidenced by prior inconclusive upper and lower gastrointestinal endoscopic studies performed during the current episode of illness.
- For surveillance of the small bowel in patients with hereditary GI polyposis syndromes, including familial adenomatous polyposis and Peutz-Jeghers syndrome.

When Policy Topic is not covered
Other indications of wireless capsule endoscopy are considered investigational, including but not limited to:
- Evaluation of the extent of involvement of known Crohn’s disease or ulcerative colitis
- Evaluation of the esophagus, in patients with gastroesophageal reflux (GERD) or other esophageal pathologies
- Evaluation of other gastrointestinal diseases 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
- Evaluation of the colon including, but not limited to, detection of colonic polyps or colon cancer.
- Initial evaluation of patients with acute upper GI bleeding

The patency capsule is considered investigational, including use to evaluate patency of the gastrointestinal tract before wireless capsule endoscopy.

**Considerations**

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.” (Van Gossum 2001)

**Description of Procedure or Service**

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals: With suspected small bowel bleeding</td>
<td>Interventions of interest are: Wireless capsule endoscopy</td>
<td>Comparators of interest are: Standard workup for gastrointestinal bleeding without capsule endoscopy</td>
<td>Relevant outcomes include: Test validity, Other test performance measures, Symptoms, Change in disease status</td>
</tr>
<tr>
<td>Individuals: With suspected Crohn disease</td>
<td>Interventions of interest are: Wireless capsule endoscopy</td>
<td>Comparators of interest are: Ileocolonoscopy, Barium small bowel follow-through, Computed tomography enterography, Magnetic resonance enterography</td>
<td>Relevant outcomes include: Test validity, Other test performance measures, Symptoms, Change in disease status</td>
</tr>
<tr>
<td>Individuals: With suspected celiac disease</td>
<td>Interventions of interest are: Wireless capsule endoscopy</td>
<td>Comparators of interest are: Endoscopy with biopsy</td>
<td>Relevant outcomes include: Test validity, Other test performance measures, Symptoms, Change in disease status</td>
</tr>
<tr>
<td>Individuals: With unexplained chronic abdominal pain</td>
<td>Interventions of interest are: Wireless capsule endoscopy</td>
<td>Comparators of interest are: Standard workup for abdominal pain without capsule endoscopy</td>
<td>Relevant outcomes include: Test validity, Other test performance measures, Symptoms, Change in disease status</td>
</tr>
<tr>
<td>Individuals: With an established diagnosis of Crohn disease</td>
<td>Interventions of interest are: Wireless capsule endoscopy</td>
<td>Comparators of interest are: Ileocolonoscopy, Barium small bowel follow-through, Computed tomography enterography, Magnetic resonance enterography</td>
<td>Relevant outcomes include: Test validity, Other test performance measures, Symptoms, Change in disease status</td>
</tr>
</tbody>
</table>
The wireless capsule endoscopy (CE) uses a device to visualize portions of the bowel that are not accessible via upper or lower endoscopy, primarily the small bowel. 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 images interpreted.
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 accuracy and 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 suspected small bowel Crohn disease (CD) who receive wireless CE, the evidence includes case series. Relevant outcomes are test accuracy and test validity, other test performance measures, symptoms, and change in disease status. Although the test performance characteristics and diagnostic yields of the capsule for these indications 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 accuracy and test validity, other test performance measures, symptoms, and change in disease status. The diagnostic characteristics of CE are inadequate enough 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 accuracy and 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 accuracy and 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 compared 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 accuracy and 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 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.

For individuals who have esophageal disorders who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test accuracy and 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 polyposis syndromes who receive wireless CE, the evidence includes case series and diagnostic accuracy studies. Relevant outcomes are test accuracy and 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 accuracy and validity, and other test performance measures, symptoms, and change in disease status. Systematic reviews of studies of its diagnostic performance for this purpose 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 accuracy and validity, and other test performance measures, symptoms, change in disease status, and resource utilization. The use of CE in the emergency department setting for suspected upper GI bleeding is based on efficiency (avoiding hospitalization, avoiding immediate endoscopy). Further 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 accuracy and 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 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. 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 accuracy and 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.

Background
Wireless Capsule Endoscopy
Wireless capsule endoscopy (CE) 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 by 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 gastrointestinal (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 disease. There is no single criterion standard diagnostic test for Crohn disease; rather, diagnosis is based on a constellation of findings. 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>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Year</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>PillCam™</td>
<td>Given® Imaging</td>
<td>2001</td>
<td>Detection of abnormalities in the small bowel and visualization of the small bowel mucosa</td>
</tr>
<tr>
<td>Given AGILE™ patency</td>
<td>Given® Imaging</td>
<td>2006</td>
<td>Verification of adequate patency of the GI tract before administration of the PillCam into patients with known or suspected strictures</td>
</tr>
<tr>
<td>PillCam™ ESO2 Capsule</td>
<td>Given® Imaging</td>
<td>2007</td>
<td>Visualization of the esophageal mucosa</td>
</tr>
<tr>
<td>Olympus Capsule Endoscope System</td>
<td>Olympus Medical Systems</td>
<td>2007</td>
<td>Visualization of the small intestine mucosa</td>
</tr>
<tr>
<td>PillCam™ COLON</td>
<td>Given® Imaging</td>
<td>2014</td>
<td>Visualization of the colon in patients who have had an incomplete colonoscopy due to a technical impossibility and not incomplete evacuation</td>
</tr>
<tr>
<td>PillCam™ COLON 2</td>
<td>Given® Imaging</td>
<td>2016</td>
<td>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</td>
</tr>
</tbody>
</table>

GI: gastrointestinal.

In 2001, the PillCam™ Given® Diagnostic Imaging System (Given Imaging) was cleared for marketing by 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." In 2003, after a supplemental 510(k) premarket notification, 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 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 (PillCam™ ESO2 Capsule) was cleared by FDA in June 2007.

In 2007, the Olympus Capsule Endoscopy System was cleared for marketing by FDA through the 510(k) process for “visualization of the small intestine mucosa.” More recent versions of both 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 cleared by FDA through the 510(k) process. This system is an accessory to the PillCam™ video capsule and, according to FDA, 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.

**Rationale**

This evidence review was created in February 2002 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed 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 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

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

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall Diagnostic Yieldª</th>
<th>Diagnostic Yield of Patients With IDAᵇ</th>
<th>R², %</th>
<th>Diagnostic Yield, n (%)ᶜ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koulaouzidis et al (2012)²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N</td>
<td>1960</td>
<td>264</td>
<td>66.6  (61.0 to 72.3)</td>
<td>78.8</td>
</tr>
<tr>
<td>Pooled effect (95% CI), %</td>
<td>47 (42 to 52)</td>
<td>66.6 (61.0 to 72.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI: confidence interval; IDA: iron-deficient anemia.
ª Per-patient analysis.
b From 4 studies (n=264 patients; 13.47% of total).
c 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leung et al (2012)³</td>
<td>China</td>
<td>1</td>
<td>2005-2007</td>
<td>Consecutive adults with active overt obscure GI bleeding</td>
<td>30 randomized to CE</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Diagnostic Yield (95% CI), %ª</th>
<th>Rebleeding Rates (95% CI), %</th>
<th>Hospitalization Rate, n (%)</th>
<th>Transfusion Rate, n (%)</th>
<th>Mean Follow-Up (SD), mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leung et al (2012)³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CE</td>
<td>53.3 (36.1 to 69.8)</td>
<td>16.7 (7.3 to 33.6)</td>
<td>5 (16.7)</td>
<td>3 (10)</td>
<td>48.5 (20.9)</td>
</tr>
<tr>
<td>Angiography</td>
<td>20 (9.5 to 37.3)</td>
<td>33.3 (19.2 to 51.2)</td>
<td>5 (16.7)</td>
<td>3 (10)</td>
<td></td>
</tr>
</tbody>
</table>
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.

\( a \) 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Population(^a)</th>
<th>Intervention(^b)</th>
<th>Comparator(^c)</th>
<th>Outcomes(^d)</th>
<th>Duration of Follow-Up(^e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leung et al (2012)(^3)</td>
<td>2. It is possible patients with a moderate bleeding would not undergo angiography in clinical setting 4. Patients with overt but nonmassive bleeding may not be ideal for CE or angiography</td>
<td>2. A criterion standard is lacking for evaluation of obscure GI bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.

\(^a\) 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.

\(^b\) Intervention key: 1. Classification thresholds not defined; 2. Version used unclear; 3. Not intervention of interest.

\(^c\) 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.

\(^d\) 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).

\(^e\) 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

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

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.


\(^b\) Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

\(^c\) Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

\(^d\) 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).

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

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

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

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Locating Bleeding With CE, %</th>
<th>Diagnostic Yield for Positive Lesions, %</th>
<th>PPV of CE, %</th>
<th>NPV of CE %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity^a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hartmann et al (2005)</td>
<td>CE and intraoperative endoscopy</td>
<td>95</td>
<td>75</td>
<td>Both procedures: 76.6</td>
<td>95</td>
</tr>
<tr>
<td>Pennazio (2004)</td>
<td>CE and PE</td>
<td>89</td>
<td>95</td>
<td>67 (95% CI, 54 to 80)</td>
<td>97</td>
</tr>
</tbody>
</table>

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

^a 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 Disease
The purpose of wireless CE for patients with suspected Crohn 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 diseases 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N (Range)</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi et al (2017)a</td>
<td>2002-2013</td>
<td>24</td>
<td>Patients with suspected or established CD</td>
<td>NR</td>
<td>RCT, nonrandomized, and diagnostic accuracy studies</td>
</tr>
</tbody>
</table>

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

a 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

<table>
<thead>
<tr>
<th>Study</th>
<th>CE vs SBFTa</th>
<th>CE vs ECb</th>
<th>CE vs CTEb</th>
<th>CE vs MREb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi et al (2017)a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>94</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnostic yield, %</td>
<td>66 vs 21.3</td>
<td>75.7 vs 29.4</td>
<td>72.5 vs 22.5</td>
<td>85.7 vs 100</td>
</tr>
<tr>
<td>Weighted incremental</td>
<td>0.44 (0.29 to</td>
<td>0.50 (0.21 to</td>
<td>0.36 (0.18 to</td>
<td>-0.16 (-0.63 to</td>
</tr>
<tr>
<td>T² , %</td>
<td>30</td>
<td>52</td>
<td>68</td>
<td>44</td>
</tr>
<tr>
<td>yield (95% CI)</td>
<td>0.59</td>
<td>0.79</td>
<td>0.90</td>
<td>0.32</td>
</tr>
</tbody>
</table>

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

a From 4 studies (3 included in meta-analysis).
b 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. 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). 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. 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. 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. 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. 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 Disease**

**Clinical Context and Test Purpose**
The purpose of wireless CE for patients who have established diagnosis of Crohn disease is to inform management decisions based on disease status.

The question addressed in this evidence review is: Does the use of wireless CE is 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. 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. 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 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. 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**

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

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**

<table>
<thead>
<tr>
<th>Study</th>
<th>Active Colonic Inflammation, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
<th>Correlation Between Colon CE and Colonoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Disease Severity</td>
<td>Extent of Inflammation</td>
</tr>
<tr>
<td>Shi et al (2017)</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>N</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Mucosal inflammation (MES &gt;0)</td>
<td>97</td>
<td>94-95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----</td>
<td>-------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M-to-S inflammation (MES &gt;1)</td>
<td>94</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postinflammatory polyps</td>
<td>100</td>
<td>91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICC (95% CI)</td>
<td></td>
<td>0.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.46 to 0.81)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.64</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.38 to 0.78)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

San Juan-Acosta et al (2014)<sup>16</sup>.

<table>
<thead>
<tr>
<th>CE vs colonoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease activity</td>
</tr>
<tr>
<td>Disease extent</td>
</tr>
<tr>
<td>( \kappa ) (95% CI)</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Oliva et al (2014)<sup>17</sup>.

<table>
<thead>
<tr>
<th>Oliva et al (2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
</tr>
<tr>
<td>% (95% CI)</td>
</tr>
</tbody>
</table>

Sung et al (2012)<sup>18</sup>.

<table>
<thead>
<tr>
<th>Sung et al (2012)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
</tr>
<tr>
<td>% (95% CI)</td>
</tr>
</tbody>
</table>

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%. 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%. 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. 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. 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). 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. 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. 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N (Range)</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR: not reported.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Study</th>
<th>CE, %</th>
<th>Likelihood Ratios</th>
<th>Diagnostic Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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 is 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. 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

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Active Bleeding or Endoscopic Findings, n</th>
<th>Hospitalization, n</th>
<th>Mortality, n</th>
<th>GBS Score</th>
<th>Agreement Between CE and EGD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sung et al (2016)²⁸</td>
<td>“Coffee ground” material: 2</td>
<td>68</td>
<td>68</td>
<td>68</td>
<td>68</td>
</tr>
<tr>
<td>CE</td>
<td>Peptic ulcer with Forrest 1b stigmata: 2</td>
<td>7</td>
<td>0</td>
<td>6 patients: 0</td>
<td></td>
</tr>
</tbody>
</table>

²⁸ Sung et al (2016) reported on a retrospective RCT to evaluate the use of CE in the emergency department for patients with suspected upper GI bleeding. 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.
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

<table>
<thead>
<tr>
<th>Study</th>
<th>Populationa</th>
<th>Interventionb</th>
<th>Comparatorc</th>
<th>Outcomesd</th>
<th>Duration of Follow-Upc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sung et al (2016)28,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gutkin et al (2013)29,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

a 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.

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

c 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.

d 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 discomorts and inconvenience of venipuncture or noninvasive tests).

e 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Selectiona</th>
<th>Blindingb</th>
<th>Delivery of Testc</th>
<th>Selective Reportingd</th>
<th>Data Completenesse</th>
<th>Statisticalf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sung et al (2016)28,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. As a feasibility study, confidence intervals and p
The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

- **Selection key:** 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).
- **Blinding key:** 1. Not blinded to results of reference or other comparator tests.
- **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.
- **Selective Reporting key:** 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
- **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.
- **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. 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. 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>N (Range)</th>
<th>Design</th>
<th>Outcome</th>
</tr>
</thead>
</table>

CCE: colon capsule endoscopy.

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

<table>
<thead>
<tr>
<th>Random-Effects Model</th>
<th>Trials</th>
<th>N</th>
<th>Outcomes</th>
<th>Effect Size</th>
<th>95% CI</th>
<th>I², %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NR</td>
<td>Diagnostic accuracy for ≥10 mm polyps</td>
<td>Sens=80.0% Spec=96.2% PLR=18.6 NLR=0.22 DOR=90.4</td>
<td>66% to 90.3% 94.0% to 97.6% 12.0 to 28.2 0.13 to 0.34 44 to 163</td>
<td>53.4 31.3</td>
</tr>
<tr>
<td>For ≥10 mm polyps</td>
<td>10</td>
<td>NR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>NR</td>
<td>Diagnostic accuracy for ≥6 mm polyps using 1st-generation CCE</td>
<td>Sens=58% Spec=85.7% PLR=3.7 NLR=0.51 DOR=7.4</td>
<td>44% to 70% 80.2% to 90.0%</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random-Effects Model</td>
<td>Trials</td>
<td>N</td>
<td>Outcomes</td>
<td>Effect Size</td>
<td>95% CI</td>
<td>$I^2$, %</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------</td>
<td>---</td>
<td>----------</td>
<td>-------------</td>
<td>--------</td>
<td>---------</td>
</tr>
<tr>
<td>For ≥6 mm polyps</td>
<td>6</td>
<td>NR</td>
<td>Diagnostic accuracy for ≥6 mm polyps using 2nd-generation CCE</td>
<td>Sens=86% Spec=88.1% PLR=7.9 NLR=0.16 DOR=50.5</td>
<td>82% to 89% 74.2% to 95.0% 3.7 to 16.1 0.12 to 0.21 20.3 to 107.0</td>
<td>0</td>
</tr>
<tr>
<td>For ≥10 mm polyps</td>
<td>3</td>
<td>NR</td>
<td>Diagnostic accuracy for ≥6 mm polyps using 1st-generation CCE</td>
<td>Sens=54% Spec=97.4% PLR=NR NLR=NR DOR=NR</td>
<td>29% to 77% 96.0% to 98.3%</td>
<td>76.2</td>
</tr>
<tr>
<td>For ≥10 mm polyps</td>
<td>6</td>
<td>NR</td>
<td>Diagnostic accuracy for ≥6 mm polyps using 2nd-generation CCE</td>
<td>Sens=88% Spec=95.3% PLR=NR NLR=NR DOR=NR</td>
<td>81% to 91% 91.5% to 97.5%</td>
<td>0</td>
</tr>
</tbody>
</table>

Adapted from Spada et al (2016). 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. 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%).

**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. 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. 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. These patients often had significant findings on CE. 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.

**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 avoiding 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.

**SUPPLEMENTAL INFORMATION**

**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 (see Table 22).41

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

**Celiac disease**  
Recommend against CE in patients with suspected celiac disease  
Recommend for CE in patients with celiac disease and unexplained symptoms despite treatment and appropriate investigations  

**Gastrointestinal bleeding**  
Recommend for CE in patients with documented overt gastrointestinal bleeding (excluding hematemesis) and negative colonoscopy and high-quality esophagogastrroduodenoscopy  
Recommend for CE in patients with an overt, obscure bleeding episode  
Recommend for endoscopy, colonoscopy and/or CE in patients with prior negative CE who have repeated obscure bleeding  

CD: Crohn 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.\(^{42}\) 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 disease (CD; strong recommendation, moderate level of evidence).

ACG issued guidelines in 2009 on the management of CD in adults.\(^{43}\) 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).\(^{44}\) These guidelines made the following statements related to video CE (see Table 23).
Table 23. Recommendations on Diagnosis and Management of Small Bowel Bleeding

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>SOR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>“… 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”</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>“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”</td>
<td>Strong</td>
<td>High</td>
</tr>
</tbody>
</table>

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. 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

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>QOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.”</td>
<td>Moderate</td>
</tr>
<tr>
<td>“We suggest DAE or push enteroscopy if VCE is unavailable or nondiagnostic in patients with overt small bowel bleeding.”</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

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:

“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. 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.
Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage
determination, coverage decisions are left to the discretion of local Medicare
carriers.

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

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01371591a</td>
<td>Pilot Study to Investigate the Use of Wireless Capsule Endoscopy for EmergencyDepartment Patients With Suspected Acute Upper Gastrointestinal Bleeding</td>
<td>100</td>
<td>Aug 2018 (ongoing)</td>
</tr>
<tr>
<td>NCT03291743</td>
<td>The Biologic Onset of Crohn’s Disease: A Screening Study in First Degree Relatives</td>
<td>144</td>
<td>Feb 2020</td>
</tr>
<tr>
<td>NCT03241368a</td>
<td>Multicenter, Prospective, Randomized Study Comparing PillCam® Crohn’s Capsule Endoscopy to Ileocolonoscopy (IC) Plus MRE for Detection of Active CD in the Small Bowel and Colon in Subjects With Known CD and Mucosal Disease</td>
<td>352</td>
<td>Aug 2020</td>
</tr>
<tr>
<td><strong>Unpublished</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02754661a</td>
<td>Multicenter, Prospective, Randomized Study Comparing the Diagnostic Yield of Colon Capsule Endoscopy Versus Computed Tomographic Colonography in a Screening Population</td>
<td>320</td>
<td>Aug 2018 (completed)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
a Denotes industry-sponsored or cosponsored trial.

References


Billing Coding/Physician Documentation Information

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>91110</td>
<td>Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), esophagus through ileum, with physician interpretation and report</td>
</tr>
<tr>
<td>91111</td>
<td>Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), esophagus with physician interpretation and report</td>
</tr>
<tr>
<td>91112</td>
<td>Gastrointestinal transit and pressure measurement, stomach through colon, wireless capsule, with interpretation and report</td>
</tr>
<tr>
<td>0355T</td>
<td>Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), colon, with interpretation and report</td>
</tr>
</tbody>
</table>

ICD-10 Codes:

- D13.2- D13.39: Benign neoplasm of other and unspecified parts of the small intestine code range
- K50.00-K50.919: Crohn’s disease (regional enteritis) code range
- K92.0-K92.2: Hematemesis and gastrointestinal hemorrhage, unspecified code range
- K92.2: Phakomatoses, not elsewhere classified (includes Peutz-Jeghers syndrome) code range
- Q85.0-Q85.9: Phakomatoses, not elsewhere classified (includes Peutz-Jeghers syndrome) code range

Additional Policy Key Words

N/A

Policy Implementation/Update Information

- **4/1/03**: New policy. Added to Medical section, considered medically necessary to investigate obscure bleeding.
- **4/1/04**: Policy statement revised to include the initial diagnosis in patients with suspected Crohn’s disease as medically necessary; also revised to include its use as a technique to evaluate other gastrointestinal diseases not presenting with gastrointestinal bleeding, including, but not limited to celiac sprue, irritable bowel syndrome, small bowel neoplasm or intestinal polyposis syndrome as investigational.
- **4/1/05**: No policy statement changes.
- **7/1/05**: Policy statement revised to include wireless capsule endoscopy of the esophagus as investigational.
- **4/1/06**: No policy statement changes.
- **4/1/07**: Policy statement revised to include hereditary GI polyposis syndromes, including familial adenomatous polyposis and Peutz-Jeghers syndrome as medically necessary indications.
- **4/1/08**: No policy statement changes.
- **4/1/09**: Policy statement revised to indicate that the patency capsule system is
considered investigational.

4/1/10 Policy statement revised to clarify that evaluation of the colon is investigational.

4/1/11 No policy statement changes.
4/1/12 No policy statement changes.
4/1/13 No policy statement changes; coding updated.
4/1/14 Added ulcerative colitis, acute GI bleeding and Lynch Syndrome to investigational policy statement.
11/1/14 Added portal hypertensive enteropathy and unexplained chronic abdominal pain to the investigational policy statement; Added a statement indicating wireless capsule endoscopy may be medically necessary, in patients with an established diagnosis of Crohn disease, for 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. New CPT code 0355T

4/1/15 No policy statement changes.
4/1/16 No policy statement changes.
4/1/17 Minor change to policy statement to change “Obscure gastrointestinal bleeding” to “Suspected small bowel bleeding;” policy statements otherwise unchanged. Title changed to “Wireless Capsule Endoscopy to Diagnose Disorders of the Small Bowel, Esophagus, and Colon”.
4/1/18 No policy statement changes.
4/1/19 No policy statement changes.

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.