
Medical Policy



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***Current Policy Effective Date: 7/1/26**
(See policy history boxes for previous effective dates)

Title: Wireless Capsule Endoscopy for Gastrointestinal Disorders

Description

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

Medical Policy Statement

Wireless capsule endoscopy is **established** when criteria are met.

The use of a patency capsule (e.g., Given AGILE™) is **experimental/ investigational**. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Magnetic capsule endoscopy (e.g., NaviCam®) is **experimental/investigational**. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Inclusionary and Exclusionary Guidelines

Inclusions:

Wireless capsule endoscopy of the small bowel when **one** of the following are met:

- Initial diagnosis in individuals with suspected Crohn's disease without evidence of disease on conventional diagnostic tests such as CT enterography, MR enterography, small-bowel follow-through (SBFT) and upper and lower endoscopy.
- In individuals with an established diagnosis of Crohn's disease, when there are unexpected change(s) in the course of disease or response to treatment, suggesting the initial diagnosis may be incorrect and re-examination may be indicated.
- Evaluation for the extent of involvement and/or management of known Crohn's disease.
- 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 individuals with hereditary GI polyposis syndromes, including familial adenomatous polyposis and Peutz-Jeghers syndrome.

Exclusions:

Other indications for wireless capsule endoscopy including but not limited to:

- Evaluation for the extent of involvement and/or management of known ulcerative colitis.
- Evaluation of the esophagus, in individuals 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, 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 individuals with acute upper GI bleeding.
- Evaluation of individuals with evidence of lower GI bleeding who have major risks for colonoscopy or moderate sedation.
- Evaluation of individuals following incomplete colonoscopy.
- Use of wireless capsule for routine colorectal cancer screening, confirmation of lesions or pathology normally within the reach of upper or lower endoscopes.
- In individuals with known or suspected gastrointestinal obstruction, strictures or fistulas.

The patency capsule (e.g., Given AGILE™), including use to evaluate patency of the GI tract before wireless capsule endoscopy.

Magnetic capsule endoscopy (e.g., NaviCam®) for the evaluation of individuals with unexplained upper abdominal complaints and all other indications.

CPT/HCPCS Level II Codes

Established codes:

91110

Other codes (investigational, not medically necessary, etc.):

91111

91113

91299

0651T

Notes:

- *Code(s) may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.*
 - *Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.*
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Background

Health and Health Outcome Disparities in Certain Populations

Screening for colon cancer is suboptimal in the U.S., with only 68.8% of Americans age 50 to 75 years up-to-date with colorectal cancer screening as of 2018.¹ Additionally, screening rates vary considerably by race, ethnicity, and socioeconomic status in the U.S, with highest rates of screening occurring in White Americans (71.1%) and the lowest rates of screening among Hispanic Americans (56.1%). Black Americans (70.1%), American Indian/Native Americans (62.1%), and Asian Americans/Pacific Islanders (64.8%) have lower screening rates than White Americans. These disparities seem to be associated with limited access to care, a lack of knowledge on family history, and adverse social determinants of health.

As of 2018, the mortality rate for colorectal cancer had decreased by 53% among men and by 30% in women since 1990 and 1969, respectively.² However, colorectal cancer incidence and mortality rates vary between racial and ethnic groups. Between 2012 and 2016, reported incidence rates were highest in non-Hispanic Black individuals, accounting for 45.7 per 100,000 population, and lowest in Asian/Pacific Islander individuals, accounting for 30.0 per 100,000 population. The magnitude of disparity is more evident in mortality rates. Colorectal cancer death rates in non-Hispanic Black individuals (19.0 per 100,000 population) between 2013 and 2017 were nearly 40% higher than those in non-Hispanic White individuals (13.8 per 100,000) and twice that of Asian/Pacific Islander individuals (9.5 per 100,000). Disparities have been attributed to many socioeconomic and social determinants of health, including low median family income, higher prevalence of risk factors, and lower rates of screening and likelihood of timely follow-up.

WIRELESS CAPSULE ENDOSCOPY

Wireless capsule endoscopy (CE) is performed using disposable imaging video capsule. The capsule measures approximately 11 by 30 mm but vary by specific product and contain video imaging, self-illumination, and image transmission modules, as well as a battery supply that lasts at least 12 hours. The indwelling camera takes images as peristalsis carries the capsule through the gastrointestinal tract.

Magnetic Capsule Endoscopy

The U.S. Food and Drug Administration (FDA) approved a novel magnetically maneuvered CE system (NaviCam™; AnX Robotica, Inc.) in May 2020.³ This system consists of a single-use ingestible capsule and magnet linked to a physician-operated console. The capsule contains a camera that wirelessly captures images of the desired anatomy. The console allows the operator to control the motion and direction of the capsule, ensuring visualization of the entire stomach. The system is non-invasive, does not require sedation, and has a procedural time of approximately 15 to 20 minutes. The capsule leaves the body in 24 hours on average but may take as long as 2 weeks. The device is contraindicated for use in individuals with gastrointestinal obstruction, stenosis, fistula, or those with dysphagia. Other contraindications include individuals with cardiac pacemakers or other implantable electronic medical devices as well as pregnant women, those less than 22 years of age, and those with a body mass index of 38 or greater. Other magnetically controlled devices have since received approval, and the NaviCam Small Bowel Capsule is now AI-assisted.

Summary of Evidence

Individuals With Suspected GI Disorders

For individuals who have suspected small bowel bleeding (previously referred to as obscure gastrointestinal [GI] bleeding) who receive wireless capsule endoscopy (CE), the evidence includes numerous case series evaluating patients with a nondiagnostic standard workup and a randomized clinical trial (RCT). 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 an improvement in the net health outcome.

For individuals who have suspected small bowel Crohn's disease (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 Crohn's disease and directing specific treatment. The evidence is sufficient to determine that the technology results in an 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. The 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 (e.g., determining the extent of Crohn's disease), direct evidence of improved outcomes or a strong indirect chain of evidence to improved outcomes is lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 (e.g., determining the extent of Crohn's disease), direct evidence of improved outcomes or a strong chain of evidence to improved outcomes is lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Individuals With Confirmed Gastrointestinal Disorders

For individuals who have an established diagnosis of Crohn's disease who receive wireless CE, the evidence includes diagnostic accuracy studies, a systematic review, and a retrospective cohort study. 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 Crohn's disease 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 Crohn's disease and directing specific treatment. In addition, the retrospective cohort study demonstrated that CE is a useful tool for guiding therapeutic management in Crohn's disease patients both for treatment escalation and de-escalation. 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. The 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 (i.e., <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 that the technology results in an improvement in the net health outcome.

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 that the technology results in an improvement in the net health outcome.

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 that the technology results in an improvement in the net health outcome.

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, other test performance measures, symptoms, and change in disease status. Systematic reviews of studies of CE's diagnostic performance for this indication 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 that the technology results in an improvement in the net health outcome.

Acute Upper Gastrointestinal Bleeding

For individuals who have acute upper GI tract bleeding who receive wireless CE, the evidence includes RCTs and several cohort studies. Relevant outcomes are test validity, other test performance measures, symptoms, hospitalizations, and resource utilization. The use of CE in the emergency department setting for suspected upper GI bleeding is intended to avoid unnecessary hospitalization or immediate endoscopy. Controlled studies are needed to assess further the impact of CE on health outcomes compared with standard management. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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, test accuracy, 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 that the technology results in an improvement in the net health outcome.

Lower Gastrointestinal Tract Bleeding and Major Risks for Colonoscopy or Moderate Sedation

For individuals who are screened for colon polyps with evidence of lower GI tract bleeding and major risks for colonoscopy or moderate sedation who receive wireless CE, the evidence includes diagnostic accuracy studies. Relevant outcomes are test accuracy, test validity, other test performance measures, symptoms, change in disease status, and resource utilization. Studies of CE in the intended use population are necessary to determine the diagnostic characteristics of the test in the triage setting. Studies of diagnostic characteristics alone are insufficient evidence to determine the clinical utility of CE in this population, and no studies adequately assess the impact of findings on specific health outcomes or patient adherence. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Incomplete Colonoscopy

For individuals who are screened for colon polyps following an incomplete colonoscopy with adequate preparation who receive wireless CE, the evidence includes case series. Relevant outcomes are test accuracy, test validity, other test performance measures, symptoms, change in disease status, and resource utilization. Studies of CE compared to standard management with repeat colonoscopy in the intended use population are necessary to determine the diagnostic characteristics of the test in the triage setting. Studies of diagnostic characteristics alone are insufficient evidence to determine the clinical utility of CE in this population, and no studies adequately assess the impact of findings on specific health outcomes or patient adherence. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Patency Capsule for Individuals 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 that the technology results in an improvement in the net health outcome.

Magnetic Capsule Endoscopy for Individuals with Suspected Gastrointestinal Disorders

For individuals who have unexplained upper abdominal complaints who receive magnetic CE, the evidence includes diagnostic accuracy studies. Relevant outcomes are test validity, symptoms, change in disease status, and treatment-related morbidity. Studies evaluating the diagnostic characteristics of magnetic CE as compared to conventional gastroscopy in the target population have generally demonstrated similar accuracy, sensitivity, and specificity, with increases in patient preference and an acceptable safety profile with the magnetic CE approach. However, the diagnostic characteristics of magnetic CE are inadequate to substitute for other modalities or to triage patients to other modalities based on the current literature. Direct evidence of improved outcomes or a strong chain of evidence to improved outcomes is lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to individuals and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms. The following is a summary of the key literature to date.

Suspected Small Bowel Bleeding

Clinical Context and Test Purpose

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

Systematic Reviews

Tables 1 and 2 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 1. Characteristics of Systematic Reviews Evaluating Capsule Endoscopy for Iron-Deficient Anemia

Study	Dates	Trials	Participants	N (Range)	Design	QUADAS Assessment of Included Trials
Koulaouzidis et al (2012) ⁴	2004-2011	24	Patients with iron-deficiency anemia who had SBCE and at last 1 lower and upper GI endoscopy prior to CE	1960 (35-652)	Observational	Low-to-moderate quality

CE: capsule endoscopy; SBCE: small bowel capsule endoscopy QUADAS: Quality Assessment of Diagnostic Accuracy Studies; SBCE: small bowel capsule endoscopy.

Table 2. Results of Systematic Reviews Evaluating Capsule Endoscopy for Iron-Deficient Anemia

Study	Overall Diagnostic Yield ^a	Diagnostic Yield of Patients With IDA ^b	I^2 , %	Diagnostic Yield, n (%) ^c
Koulaouzidis et al (2012) ⁴				
Total N	1960	264		● Angioectasias: 293 (45.9) ● Inflammatory lesions: 126 (19.7) ● Polyp/mass lesions: 42 (6.6) ● Not classified: 177 (27.7)
Pooled effect (95% CI), %	47 (42 to 52)	66.6 (61.0 to 72.3)	78.8	
p			<.001	

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 individuals 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 3 and 4 summarize the characteristics and results of selected RCTs.

Table 3. Characteristics of RCT Evaluating Capsule Endoscopy for Obscure GI Bleeding

Study	Countries	Sites	Dates	Participants	Interventions
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					Active	Comparator
Leung et al (2012) ⁵	China	1	2005-2007	Consecutive adults with active overt obscure GI bleeding	30 randomized to CE	30 randomized to mesenteric angiography

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

Table 4. Results of RCT Evaluating Capsule Endoscopy for Obscure GI Bleeding

Study	Diagnostic Yield (95% CI), % ^a	Rebleeding Rates (95% CI), %	Hospitalization Rate, n (%)	Transfusion Rate, n (%)	Mean Follow-Up (SD), mo
Leung et al (2012) ⁵					
CE	53.3 (36.1 to 69.8)	16.7 (7.3 to 33.6)	5 (16.7)	3 (10)	48.5 (20.9)
Angiography	20 (9.5 to 37.3)	33.3 (19.2 to 51.2)	5 (16.7)	3 (10)	
Difference	33.3 (8.9 to 52.8)	16.7 (-5.3 to 36.8)			
p	.016	.23	1.0	1.0	

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

^a Percentage identified with a high probability of bleeding.

The purpose of the limitations tables (Tables 5 and 6) 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 5. Study Relevance Limitations of RCT Evaluating Capsule Endoscopy for Obscure GI Bleeding

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Duration of Follow-Up ^e
Leung et al (2012) ⁵	2. It is possible patients with moderate bleeding would not undergo angiography in clinical setting 4. Patients with overt but nonmassive bleeding may not be ideal for CE or angiography		2. A criterion standard is lacking for evaluation of obscure GI bleeding		

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

The study limitations 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 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 6. Study Design and Conduct Limitations of RCT Evaluating Capsule Endoscopy for Obscure GI Bleeding

Study	Allocation ^a	Blinding ^b	Selective Reporting ^d	Follow-Up ^e	Power ^d	Statistical ^f
Leung et al (2012) ⁵					3. Study underpowered to detect significant difference in clinical outcome	

GI: gastrointestinal; RCT: randomized controlled trial.

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

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

^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).

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

^f 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 7 and 8 summarize the characteristics and results of selected case series.

Table 7. Characteristics of Case Series Evaluating Capsule Endoscopy for Obscure GI Bleeding

Study	Country	Participants	Treatment Delivery	Follow-Up (Range), mo
Hartmann et al (2005) ⁶	Germany	47 patients >18 y with obscure GI bleeding	Patients received CE and criterion standard, intraoperative endoscopy	NR
Pennazio et al (2004) ⁷	Italy	100 patients ≥18 y with obscure GI bleeding	51 patients received CE and PE before or after the procedure	Mean: 18 (5-25)

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

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

Study	Treatment	Locating Bleeding With CE, %		Diagnostic Yield for Positive Lesions, %	PPV of CE, %	NPV of CE, %
		Sensitivity	Specificity ^a			
Hartmann et al (2005) ⁶	CE and intraoperative endoscopy	95	75	Both procedures: 76.6	95	86
Pennazio (2004) ⁷	CE and PE	89	95	67 (95% CI, 54 to 80)	97	82.6

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

^a CE results confirmed by intraoperative endoscopy or other reference standards.

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 individuals 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 individuals 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 individuals with suspected small bowel bleeding. These studies have consistently reported that a substantial proportion of individuals 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 individuals population was approximately half of the included individuals and was higher in individuals with documented iron-deficiency anemia. CE appears to locate the source of bleeding at least as well as other diagnostic methods and direct treatment to the source of bleeding.

Suspected Crohn's Disease

Clinical Context and Test Purpose

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

Review of Evidence

Systematic Reviews

Results from a meta-analysis by Choi et al (2017)⁸, which compared CE with various modalities for diagnosing CD, are summarized in Tables 9 and 10. 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 9. Characteristics of Systematic Reviews Assessing the Diagnostic Yield of Capsule Endoscopy versus Other Modalities^a

Study	Dates	Trials	Participants	N (Range)	Design
Choi et al (2017) ⁸	2002-2013	24	Patients with suspected or established CD	NR	RCT, nonrandomized, and diagnostic accuracy studies

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

^a Other modalities include small bowel follow-through, enteroclysis, computed tomography enterography, and magnetic resonance enterography.

Table 10. Results of Systematic Reviews Assessing the Diagnostic Yield of CE vs Other Modalities

Study	CE vs SBFT ^a	CE vs EC ^b	CE vs CTE ^b	CE vs MRE ^b
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Choi et al (2017) ⁸				
N	94			
Diagnostic yield, %	66 vs 21.3	75.7 vs 29.4	72.5 vs 22.5	85.7 vs 100
Weighted incremental yield (95% CI)	0.44 (0.29 to 0.59)	0.50 (0.21 to 0.79)	0.36 (0.18 to 0.90)	-0.16 (-0.63 to 0.32)
I^2 , %	30	52	68	44

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

^a From 4 studies (3 included in meta-analysis).

^b From 2 studies.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 Crohn's Disease

For individuals with suspected CD who cannot be diagnosed by other modalities, CE can confirm the diagnosis in a substantial number of individuals.

Suspected Celiac Disease

Clinical Context and Test Purpose

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

Review of Evidence

Systematic Reviews

A meta-analysis by El-Matary et al (2009) compared the diagnostic performance of CE with a reference standard of duodenal biopsy.⁹ The pooled analysis of three 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 (N=166 subjects).¹⁰ The overall pooled sensitivity was 89%, and the specificity was 95%.

Capsule endoscopy 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 confirmed celiac disease who were unresponsive to standard treatment were evaluated with CE.¹¹ Results were combined with human leukocyte antigen typing and response to gluten challenge, with the final diagnosis made by three 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.

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.¹² 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.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 individuals with unresponsive celiac disease undergoing CE have shown some yield of actionable diagnoses that have the potential to improve individual outcomes. Larger studies are needed to better determine the diagnostic yield of CE in these individuals.

Unexplained Chronic Abdominal Pain

Review of Evidence

Systematic Reviews

Xue et al (2015) reported on a systematic review of 21 studies (N=1520 patients) evaluating CE for unexplained chronic abdominal pain.¹³ 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.¹⁴ 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, and 5 (2.1%) with abnormal transit time and other findings (e.g., small bowel tumor, ascariasis, anaphylactoid purpura).

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 for unexplained chronic abdominal pain in a proportion of individuals reported in retrospective studies, the sequence and chronology of testing and treatment recommended before CE needs to be defined to determine whether CE had utility to diagnose the condition.

Established Crohn's Disease

Clinical Context and Test Purpose

The purpose of wireless CE for individuals who have an established diagnosis of CD is to inform management decisions based on disease status.

Review of Evidence

Systematic Reviews

Kopylov et al (2017) published a systematic review of studies evaluating use of CE for CD.¹⁵ 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; I²=48%) and to ultrasound (OR=0.57; 95% CI, 0.27 to 1.20; I²=67%).

Diagnostic Accuracy Studies

Bruining et al (2020) reported results from the multicenter, prospective BLINK trial comparing the diagnostic accuracy of CE compared to ileocolonoscopy (IC) and/or magnetic resonance enterography (MRE) in patients with established CD.¹⁶ The per-protocol analysis included 99/158 enrolled subjects with 16 patients tested by all 3 modalities. Major reasons for exclusion from analysis included patency failure or MRE stricture and major protocol violations. The reference standard was defined as the presence or absence of inflammation as designated by the modality-specific scoring system at prospective interpretation by expert central readers. In cases of discrepant findings for any bowel segment, all modalities were reviewed and resolved by a consensus panel consisting of 3 gastroenterologists. Overall sensitivity, specificity, PPV, and NPV for active enteric inflammation were 94% (95% CI, 86% to 98%), 74% (95% CI, 55% to 87%), 91% (95% CI, 82% to 96%), 83% (95% CI, 64% to 94%) for CE compared to 100% (95% CI, 95% to 100%), 22% (95% CI, 10% to 41%), 77% (95% CI, 68% to 85%), and 100% (95% CI, 54% to 100) for IC and/or MRE. Sensitivity of CE was significantly higher compared to MRE for enteric inflammation in the proximal small bowel (97% vs 71%, p=.021) and similar in the terminal ileum and colon (p=.500 to .625). Discrepant reads between the proximal small bowel, terminal ileum, and colon were 57%, 49%, and 81%, respectively. In the proximal small bowel, the majority consensus panel decision was agreement with CE.

Cohort Studies

A study by Elosua et al (2022) evaluated the therapeutic impact of CE in patients with established CD in this retrospective, single-center study.¹⁷ Therapeutic impact was defined as change in CD-related treatment recommended based on CE results and 305 patients (N=432 procedures) with established CD who underwent a CE procedure between January 2008 and December 2019 were included. Of the included CE procedures, 87.5% were deemed conclusive. Mild inflammation was detected in 41.6% of patients and moderate-to-severe activity was detected in 21.9% of patients. Management changes guided by CE procedures occurred in 51.3% of procedures, with 46.1% of procedures leading to treatment escalation and 5.3% of procedures leading to de-escalation. Disease activity demonstrated by CE results was correlated with therapeutic changes. Mucosal healing assessed via CE was the only independent factor that predicted therapy de-escalation (OR, 6.86; 95% CI, 1.42 to 33). The authors conclude that CE is a useful tool for guiding therapeutic management in CD patients both for treatment escalation and de-escalation.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 Crohn's Disease

A 2017 systematic review of 11 studies in individuals with established CD found a similar diagnostic yield with CE compared with radiography. A diagnostic accuracy study of CE compared with IC and/or MRE for the detection of active inflammatory CD in individuals with established CD found a comparable sensitivity, higher specificity and PPV, and lower NPV compared to IC and/or MRE. The authors concluded that CE is a reliable tool for assessing Crohn's disease mucosal activity and extent compared with more invasive methods. This study demonstrates high performance of the CE as compared to MRE and/or IC without the need for multiple tests in non-stricturing Crohn's disease. Differences may be attributed to high rates of discrepant reads between modalities and high consensus panel agreement with CE results in cases of discrepancy. A retrospective cohort study demonstrated therapeutic management changes (both escalation and de-escalation in treatment) can be made based on CE results.

Ulcerative Colitis

Clinical Context and Test Purpose

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

Review of Evidence

A number of prospective observational studies have evaluated the diagnostic accuracy of CE in patients with ulcerative colitis. Tables 11 and 12 summarize the characteristics and results of these studies.

Table 11. Characteristics of Observational Comparative Studies Assessing Capsule Endoscopy for Ulcerative Colitis

Study	Study Type	Country	Dates	Participants	Treatment	Follow-Up
Shi et al (2017) ¹⁸	Single-center prospective observational	China	2014-2016	Patients 18-80 y with UC requiring colonoscopy	150 patients underwent CE-2 and colonoscopy	NR
San Juan-Acosta et al (2014) ¹⁹	Single-blind prospective comparative	Spain	2010-2012	Patients 18-70 y with UC with flare in disease activity or due for CRC screening	23 underwent CE-1, 19 had CE-2; all followed by colonoscopy	NR
Oliva et al (2014) ²⁰	Prospective observational	Spain	2011-2012	Patients 6-18 y with a diagnosis at least 3 mo prior to enrollment	30 patients underwent CE-2, followed by colonoscopy	NR
Sung et al (2012) ²¹	Prospective cohort	China and Singapore	2000-2008	Patients with suspected or known UC	100 patients underwent CE and same-day colonoscopy	NR

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

Table 12. Results of Observational Comparative Studies Assessing Capsule Endoscopy for Ulcerative Colitis

Study	Active Colonic Inflammation, %		PPV, %	NPV, %	Correlation Between Colon CE and Colonoscopy	
	Sensitivity ^a	Specificity			Disease Severity	Extent of Inflammation
Shi et al (2017) ¹⁸						
N	150	150	150		150	150
Mucosal inflammation (MES >0)	97			94-95		
M-to-S inflammation (MES >1)	94					
Postinflammatory polyps	100	91				
ICC (95% CI)					0.69 (0.46 to 0.81) ^a	0.64 (0.38 to 0.78) ^b
p					<.001	<.001
San Juan-Acosta et al (2014) ¹⁹						
N	42	42	42		42	42
CE vs colonoscopy						
Disease activity	77.78	95.83	93.33	85.19		
Disease extent	68.75	96.15	91.67	83.33		
κ (95% CI)					0.79 (0.62 to 0.96)	0.71 (0.52 to 0.90)
Oliva et al (2014) ²⁰						
N	30	30	30			
% (95% CI)	96 (79 to 99)	100 (61 to 100)	100 (85 to 100)	85 (49 to 97)		
Sung et al (2012) ²¹						
N	100	100	100			
% (95% CI)	89 (80 to 95)	75 (51 to 90)	93 (84 to 97)	65 (43 to 83)		

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

^a MES.

^b 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 1 or the other test would result in similar or different patient outcomes.¹⁹

Oliva et al (2014) evaluated 30 patients with known ulcerative colitis with both CE and colonoscopy to assess disease activity.²⁰ The reference standard for disease activity was a Matts score greater than 6 as judged by colonoscopy. Although the 2 methods had high concordance at this cutoff level of disease in this study, patient outcomes linked to these assessments of disease activity cannot be determined.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 and colonoscopy to assess disease activity in individuals with ulcerative colitis. Two of 4 studies were small (i.e., <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 individuals who have esophageal disorders is to inform management decisions based on disease status.

Review of Evidence

Systematic Reviews

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%.²² An updated meta-analysis of CE in patients with esophageal varices by Usman et al (2025) evaluated 20 studies and found similar results to the previous study with a sensitivity of 81.2% and specificity of 86.2%.²³ 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%.²⁴ Because of the lower sensitivity and specificity of

that test, CE cannot substitute for traditional endoscopy nor can it be used to triage individuals to endoscopy.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 individuals to other modalities.

Hereditary Gastrointestinal Polyposis Syndromes

Clinical Context and Test Purpose

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

Review of Evidence

Persons with familial adenomatous polyposis and PJS are genetically at high-risk of small bowel polyps and tumors. Urquhart et al (2014) compared CE with MRE in 20 patients with PJS.²⁵ Capsule endoscopy identified more polyps 10 mm or larger (47 polyps) than MRE (14 polyps; $p=.02$). 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 versus 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.²⁶ Mata et al (2005) studied the role of CE in 24 patients with hereditary GI polyposis syndromes, including familial adenomatous polyposis ($n=20$) or PJS ($n=4$).²⁷ 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 with Lynch syndrome. Haanstra et al (2015) evaluated 200 patients with Lynch syndrome who underwent CE.²⁸ 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.²⁹ Small bowel neoplasms were diagnosed in 3 (8.6%) patients (1 adenocarcinoma, 2 adenomas with low-grade dysplasia).

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 Gastrointestinal 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 individuals outcomes. Additional data on the prevalence and natural history of small bowel polyps in Lynch syndrome individuals are necessary. At this time, surveillance of the small bowel is not generally recommended as a routine intervention for individuals with Lynch syndrome.

Portal Hypertensive Enteropathy

Clinical Context and Test Purpose

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

Review of Evidence

Systematic Reviews

Several systematic reviews, including a Cochrane review, have been published. Tables 13 and 14 summarize the characteristics and results of select systematic reviews.

Table 13. Characteristics of Systematic Reviews Assessing Capsule Endoscopy for Portal Hypertensive Enteropathy

Study	Dates	Trials	Participants	N (Range)	Design
McCarty et al (2017) ³⁰	2005-2015	17	Patients with portal hypertension	1328 (8-330)	NR

Colli et al (2014) ³¹	2005-2014	16	Adults with cirrhosis	936 (NR)	Cohort
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NR: not reported.

Table 14. Results of Systematic Reviews Assessing Capsule Endoscopy for Portal Hypertensive Enteropathy

Study	CE, %		Likelihood Ratios		Diagnostic Accuracy	
	Sensitivity	Specificity	Positive	Negative	CE	Medium-to-Large Varices
McCarty et al (2017) ³⁰						
N	1328	1328	1328			
PE (95% CI), %	83 (76 to 89)	85 (75 to 91)	5.4 (3.3 to 9.0)	0.20 (0.14 to 0.28)	90 (88 to 93)	92 (90 to 94)
Studies with low risk of bias, n						
PE (95% CI), %	80 (81 to 88)	86 (68 to 94)			85 (81 to 88)	92 (89 to 94)
Colli et al (2014) ³¹						
N	936	936	936			
PE (95% CI), %	84.8 (77.3 to 90.2)	84.3 (73.1 to 91.4)	5.4 (3.1 to 9.5)	0.18 (0.12 to 0.27)		
Studies with low risk of bias, n	396	396	396			
PE (95% CI), %	79.7 (73.1 to 85.0)	86.1 (64.5 to 95.5)	5.8 (2.1 to 16.1)	0.24 (0.18 to 0.31)		

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

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

Capsule endoscopy 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 individuals to esophagogastroduodenoscopy. Based on these diagnostic characteristics, the test does not appear to have clinical utility.

Acute Upper Gastrointestinal Tract Bleeding

Review of Evidence

Randomized Controlled Trials

Sung et al (2016) reported on a prospective randomized controlled trial to evaluate the use of CE in the emergency department for individuals with suspected upper GI bleeding.³² Capsule endoscopy was used to determine whether individuals would be admitted to the hospital or sent home, versus an alternative strategy of admitting all individuals. Eligible individuals 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 individuals 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 individuals 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 individuals safely avoiding emergency hospitalization.

Tables 15 and 16 summarize the characteristics and results of select RCTs.

Table 15. Characteristics of RCTs Assessing Capsule Endoscopy for Acute Gastrointestinal Tract Bleeding

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Sung et al (2016) ³²	China	NR	2013-2014	Patients presenting to ED with symptoms suggestive of UGIB	37 randomized to CE; admission determined by CE	34 randomized to SOC; admission determined by GBS
Gutkin et al (2013) ³³	U.S.	3	NR	Patients ≥18 y with history suggestive of acute UGIB ≤48 h prior to ED presentation	12 randomized to VCE prior to endoscopy	12 randomized to endoscopy

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

Table 16. Results of RCTs Assessing Capsule Endoscopy for Acute Gastrointestinal Tract Bleeding

Study	Active Bleeding or Endoscopic Findings, n	Hospitalization, n	Mortality, n	GBS Score	Agreement Between CE and EGD
Sung et al (2016) ³²					
N	68	68	68	68	68

CE	• “Coffee ground” material: 2 • Peptic ulcer with Forrest Ib stigmata: 2 • Forrest Iia: 2 • Esophageal varix: 1	7	0	• 6 patients: 0 • patients: 1 • 25 patients: ≥ 2	
SOC	• Peptic ulcer: 4 • Duodenal ulcer: 12 • Gastritis/duodenitis: 10 • Gastric or duodenal erosions: 5 • Mallory Weiss tear: 1	34	0	• No patients scored 0 • 7 patients: 1 • 27 patients: ≥ 2	
Gutkin et al (2013) ³³					
N	24				24
VCE	8 (67.7%) had positive findings confirmed by endoscopy; for these patients, average Rockall score was 3; average Blatchford score was 13				VCE data identical to EGD results (p=1.0)

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

The purpose of the limitations tables (Tables 17 and 18) 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 17. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Duration of Follow-Up ^e
Sung et al (2016) ³²					
Gutkin et al (2013) ³³					

The study limitations 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 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 18. Study Design and Conduct Limitations

Study	Selection ^a	Blinding ^b	Delivery of Test ^c	Selective Reporting ^d	Data Completeness ^e	Statistical ^f
Sung et al (2016) ³²						3. As a feasibility study, confidence intervals and p values were not reported
Gutkin et al (2013) ³³					2. Small sample size based on pilot/feasibility study	

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

^a Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).

^b Blinding key: 1. Not blinded to results of reference or other comparator tests.

^c 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.

^d Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^e 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.

^f Statistical key: 1. Confidence intervals and/or p values not reported; 2. Comparison with 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.^{34,35} These studies reported that CE provides useful information, such as identifying gross bleeding and inflammatory lesions in a substantial proportion of individuals and in stratifying individuals 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.

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 Gastrointestinal 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 further assess the impact of CE on health outcomes compared with standard management. Individuals should be followed to their ultimate diagnosis to determine whether use of CE versus other triage strategies or immediate endoscopy results in lower health care resource utilization.

Colon Cancer Screening

Review of Evidence

Systematic Reviews

Several studies have assessed the accuracy of CE for detection of 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.³⁶ 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 (n=24 [1%]). There were no missed cancers (n=11) in the series using second-generation CE (per-patient sensitivity, 100%). In series using the first-generation CE, 6 of 26 proven cancers were missed on CE (per-patient sensitivity, 77%).

Kjølhed et al (2020) reported on a systematic review and meta-analysis of the diagnostic accuracy of CE compared to colonoscopy with stratified results for polyps of any size, polyps $\geq$ 6mm, and polyps $\geq$ 10 mm.³⁷ Across analyzed patients in the 12 eligible studies, the indications for endoscopy included colorectal cancer screening or history of polyps or colorectal cancer (n=1200 [63.2%]), positive fecal immunochemical test (n=493 [26%]), first-degree relatives of patients with colorectal cancer (n=177 [9.3%]), or unspecified (n=28 [1.5%]). The rate of patients with an adequate bowel preparation ranged from 40% to 100%. The rates of complete CE transits ranged from 57% to 100%. The authors note that the relatively high rate of incomplete CE investigations limits the utility of CE in the colorectal cancer setting. All but 1 study was assessed to have a high risk of bias and applicability concerns for the reference standard.

Characteristics of the systematic reviews and their main findings are summarized in Tables 19 and 20, respectively.

Table 19. Characteristics of Systematic Review Assessing Capsule Endoscopy for Colon Cancer Screening

Study	Dates	Trials	N (Range)	Design	Outcome
Spada et al (2016) ³⁶	2006-2015	14	2681 (40-884)	Diagnostic accuracy studies	Per-patient sensitivity of CCE for different categories of polyp size and for cancer
Kjølhed et al (2020) ³⁷	2009-2020	12	2199 (20-884)	Diagnostic accuracy studies	Per-patient sensitivity of CCE for various polyp size thresholds

CCE: colon capsule endoscopy.

Table 20. Results of Systematic Review Assessing Capsule Endoscopy for Colon Cancer Screening

Random-Effects Model	Trials	N	Outcomes	Effect Size	95% CI	I^2 , %
Spada et al (2016) ³⁶						
For $\geq$ 10 mm polyps	10	NR	Diagnostic accuracy for $\geq$ 10 mm polyps	Sens=80.0% Spec=96.2% PLR=18.6 NLR=0.22 DOR=90.4	66% to 90.3%; 94.0% to 97.6% 12.0 to 28.2 0.13 to 0.34 44 to 163	53.4 31.3

For ≥6 mm polyps	7	NR	Diagnostic accuracy for ≥6 mm polyps using 1 st -generation CCE	Sens=58% Spec=85.7% PLR=3.7 NLR=0.51 DOR=7.4	44% to 70% 80.2% to 90.0%	65
For ≥6 mm polyps	6	NR	Diagnostic accuracy for ≥6 mm polyps using 2 nd -generation CCE	Sens=86% Spec=88.1% PLR=7.9 NLR=0.16 DOR=50.5	82% to 89% 74.2% to 95.0% 3.7 to 16.1 0.12 to 0.21 20.3 to 107.0	0
For ≥10 mm polyps	3	NR	Diagnostic accuracy for ≥6 mm polyps using 1 st -generation CCE	Sens=54% Spec=97.4% PLR=NR NLR=NR DOR=NR	29% to 77% 96.0% to 98.3%	76.2 0
For ≥10 mm polyps	6	NR	Diagnostic accuracy for ≥6 mm polyps using 2 nd -generation CCE	Sens=88% Spec=95.3% PLR=NR NLR=NR DOR=NR	81% to 91% 91.5% to 97.5%	0 67
Kjolhede et al (2020) ³⁷						
For polyps of any size	4	338	Diagnostic accuracy for polyps of any size	Sens=85% Spec=85% PLR=NR NLR=NR DOR=30.5	73% to 92% 70% to 93% 16.2 to 57.2	NR
For polyps ≥ 6 mm	6	1324	Diagnostic accuracy for polyps ≥ 6 mm	Sens=87% Spec=88% PLR=NR NLR=NR DOR=51.1	83% to 90% 75% to 95% 19.8 to 131.8	NR
For polyps ≥ 10 mm	7	1577	Diagnostic accuracy for polyps ≥ 10 mm	Sens=87% Spec=95% PLR=NR NLR=NR DOR=136.0	82% to 90% 92% to 97% 70.6 to 262.1	NR

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.

Prospective Studies

Other recent studies by Saito et al (2015), Morgan et al (2016), Parodi (2018), and Cash et al (2021) have evaluated the diagnostic characteristics of CE, using subsequently performed colonoscopy as the reference standard.^{38,39,40,41} Of note, the Cash et al (2021) study randomized patients to colon CE or CT colonography followed by optical colonoscopy.⁴¹ In the Saito et al (2015) study of 66 evaluable patients, per-patient sensitivity for the detection of polyps was 94% (95% CI, 88.2% to 99.7%). In the Morgan et al (2016) 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 (2018) 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%). In the Cash et al (2021) study, data from 286 patients revealed that the

proportion of enrollees with any polyp 6 mm or larger confirmed by subsequent blinded optical colonoscopy was 31.6% for colon CE versus 8.6% for CT colonography.⁴¹ The sensitivity and specificity of colon CE for polyps 6 mm or larger was 79.2% and 96.3%, respectively, while that of CT colonography was 26.8% and 98.9%. For polyps 10 mm or larger, the sensitivity and specificity of colon CE was 85.7% and 98.2% compared with 50% and 99.1% for CT colonography. The authors concluded that colon CE should be considered comparable or superior to CT colonography as a screening test; however, neither test was as effective as optical colonoscopy.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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. 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.

Lower Gastrointestinal Tract Bleeding and Major Risks for Colonoscopy or Moderate Sedation

Review of Evidence

Diagnostic Accuracy Studies

Several studies have evaluated the diagnostic characteristics of CE for the detection of colon polyps in patients with evidence of lower GI bleeding (e.g., hematochezia, positive fecal occult blood test [FOBT]). Study characteristics and results are described in Table 21 and 22.

Table 21. Study Characteristics of Clinical Validity

Study	Study Population	Reference Standard	Threshold for Positive Index Test	Timing of Reference and Index Tests	Blinding of Assessors	Comments

Kobaek-Larsen et al (2017) ⁴²	FOBT-positive individuals participating in a CRC screening program in Denmark (N=253; median age, 64 years)	OC adjusted by any findings from all follow-up procedures; repeat colonoscopy was offered for suspected missed polyps	Polyps >9 mm within $\pm 50\%$ of CE measure	OC performed 1 day after CE	Investigators were blinded to both CE and OC; in the case of a second endoscopy, investigator was unblinded to CE findings.	RS adjusted in 75 patients due to follow-up procedures; only 50% (126) had complete OC and CE
Rondonotti et al (2014) ⁴³	FOBT-positive individuals participating in a CRC screening program in Italy (N=54; age range, 50-69 years)	OC followed by colon segment re-inspection if double unblinding to CTC and CE results revealed a disparity	Polyps ≥ 6 mm	CTC and OC performed 15 days after CE	Initial blinding to CE and CTC results followed by double-unblinding and opportunity for re-inspection and adjustment of RS	4 patients excluded from analysis (consent withdrawal [2], endoscopist not blinded [2])
Eliakim et al (2009) ⁴⁴	Individuals with known or suspected colonic disease in Israel; 21% of patients had hematochezia or positive FOBT (N=104; mean age, 49.8 years)	OC	Polyps ≥ 6 mm and ≥ 10 mm within $\pm 50\%$ of CE measure	OC performed within 10 hours of CE	Investigators blinded to both OC and CE.	6 patients excluded from analysis (did not complete bowel prep [2], withdrawal [1], could not ingest capsule [1], capsule retention [1], technical failure [1])

CE: capsule endoscopy; CRC: colorectal cancer; CTC: computed tomography colonography; FOBT: fecal occult blood test; OC: optical colonoscopy; RS: reference standard.

Table 22. Study Results of Clinical Validity

Study	N	CE Completion Rate, % (95% CI)	Sensitivity, % (95% CI) ¹	Specificity, % (95% CI) ¹	PLR; NLR	Adverse Events
Kobaek-Larsen et al (2017) ⁴²						None related to OC or CE.
All patients; CE >9mm	253	54 (48 to 60)	87 (83 to 91)	92 (89 to 95)	NR	
Complete CE and OC; CE >9 mm	126	---	97 (94 to 100)	90 (85 to 95)	NR	
All patients; OC > 9 mm	253	90 (86 to 94)	88 (84 to 92)	100 (100)	NR	
Complete CE and OC; OC > 9 mm	126	---	89 (84 to 94)	100 (100)	NR	
Rondonotti et al (2014) ⁴³						None related to OC or CE. 10 cases of mild abdominal pain and 2 cases of significant pain during CTC.
CE ≥ 6 mm	50	100	88.2 (62.2 to 97.9)	87.8 (70.8 to 96.0)	3.75; 0.06	
CTC ≥ 6 mm	50	100	88.2 (62.2 to 97.9)	84.8 (67.3 to 94.3)	3.0; 0.07	

Eliakim et al (2009) ⁴⁴						1 capsule retention; 7 cases of mild-moderate headache, nausea, or vomiting related to CE bowel preparation.
CE ≥6 mm	98	NR	89 (70 to 97)	76 (72 to 78)	NR	
CE ≥10 mm	98	NR	88 (56 to 98)	89 (86 to 90)	NR	

CE: capsule endoscopy; CI: confidence interval; CTC: computed tomography colonography; NLR: negative likelihood ratio; NR: not reported; OC: optical colonoscopy; PLR: positive likelihood ratio.

1 Per-patient analysis.

Kobaek-Larsen et al (2017) reported on FOBT-positive individuals participating in a colorectal cancer screening program in Denmark.⁴² The reference standard consisted of optical colonoscopy (OC) adjusted by any findings from all additional follow-up procedures, including repeat endoscopy due to suspected missed polyps unblinded to CE results in 53 patients, repeated OC due to inadequate bowel preparation in 8 patients, and follow-up CT colonography in 14 patients. CE completion rate was significantly lower than OC ($p < .001$), with only 50% of patients ($n = 126$) having complete OC and CE investigations.

Rondonotti et al (2014) reported on FOBT-positive individuals participating in a colorectal cancer screening program in Italy.⁴³ Unblinded colonoscopy, integrating OC, CT Colonography, and CE results, was used as the reference standard. Investigations were completed in all patients with a PLR and NLR of 3.75 and 0.06 for CE, respectively.

Eliakim et al (2009) conducted a prospective, multicenter study evaluating CE compared to colonoscopy in individuals with known or suspected colonic disease.⁴⁴ Twenty-one percent of patients had hematochezia or positive FOBT. The majority of patients were referred for OC due to personal or family history of colorectal cancer or for colorectal cancer screening. Polyps of any size were detected in 44% of patients, with 53% identified as having adenomas. Overall colon cleanliness for CE was considered adequate in 78% of patients (95% CI, 68 to 86%).

Study relevance, design, and conduct limitations are described in Table 23 and 24.

Table 23. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Duration of Follow-Up ^e
Kobaek-Larsen et al (2017) ⁴²	4. Study did not specifically evaluate individuals with major risks for colonoscopy or moderate sedation.		2. Adjusted and/or unblinded reference standard not uniformly applied to all individuals.	1,3. Impact of findings on health outcomes not assessed. Predictive values not reported.	
Rondonotti et al (2014) ⁴³	4. Study did not specifically evaluate individuals with major risks for colonoscopy or moderate sedation.			1. Impact of findings on health outcomes not assessed.	

Eliakim et al (2009) ⁴⁴	4. Study did not specifically evaluate individuals with major risks for colonoscopy or moderate sedation; only 21% of subjects had evidence of lower gastrointestinal bleeding.			1,3. Impact of findings on health outcomes not assessed. Predictive values not reported.	
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The study limitations 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 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 24. Study Design and Conduct Limitations

Study	Selection ^a	Blinding ^b	Delivery of Test ^c	Selective Reporting ^d	Data Completeness ^e	Statistical ^f
Kobaek-Larsen et al (2017) ⁴²	1. Selection not described.	1. In case of second endoscopy for suspected missed polyps, endoscopist not blinded to results of CE.			1,3. Unclear how many complete investigations included patients with comparison to adjusted and/or unblinded reference standard. High loss due to low CE completion rate.	
Rondonotti et al (2014) ⁴³	1. Selection not described.	1. Endoscopist was unblinded to results of CE and CTC in event polyps were missed prior to segment reinspection.	2. CTC and OC performed 15 days later.			
Eliakim et al (2009) ⁴⁴	1. Selection not described.			1. Not registered.		

CE: capsule endoscopy; CTC: computed tomography colonography; OC: optical colonoscopy.

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

^a Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).

^b Blinding key: 1. Not blinded to results of reference or other comparator tests.

^c 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.

^d Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^e 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.

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

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 detecting colon polyps in this population has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

Section Summary: Lower Gastrointestinal Tract Bleeding and Major Risks for

Colonoscopy or Moderate Sedation

Studies evaluating the diagnostic characteristics of CE as a triage test have primarily involved colorectal cancer screening populations that have not specifically enrolled patients with major risks for OC or moderate sedation. The 3 studies identified have been heterogeneous in the timing of delivery of the reference standard, in the definition and blinding of the reference standard, and in the significant polyp size threshold determining a positive test result. Only 1 small study reported positive and negative likelihood ratios. Per-patient sensitivity and specificity ranged from 88 to 97% and 76 to 92%, respectively, and was generally reported with wide confidence intervals. While 1 study reported a higher sensitivity and specificity compared to OC versus the defined reference standard, a consistent reference standard was not applied to all patients and carried a low combined rate of complete OC and CE investigations (50%). No studies assessed the impact of study findings on specific health outcomes. Adherence to recommended follow-up diagnostic or therapeutic interventions in patients with major risks for colonoscopy or moderate sedation is unknown. Studies of CE in the intended use population are necessary to determine the diagnostic characteristics of the test in the triage setting.

Incomplete Colonoscopy

Review of Evidence

Case Series

Studies evaluating the diagnostic characteristics of CE compared to a reference standard for the detection of colon polyps in patients with an incomplete colonoscopy following adequate bowel preparation were not identified. Several prospective case series describing the diagnostic yield of CE following incomplete colonoscopy for various indications are summarized in Table 25. Study relevance, design, and conduct limitations are described in Table 26 and 27.

Table 25. Study Characteristics and Results

Study	Study Population	Indications for OC	Threshold for Significant Polyps	Timing of CE	Incremental CE Diagnostic Yield, n/N (%)	Complete Visualization of the Colon, n/N (%)	Comments
Hussey et al (2018) ⁴⁶	Patients aged ≥18 y who had an incomplete OC for reasons other than poor bowel preparation or suspected	NR	> 6mm or ≥ 3 polyps	Administered 90 min after IC	CE (any polyps): 19/50 (38) CE (significant polyps): 7/50 (14)	CE: 38/50 (76) CE + IC: 42/50 (84)	CCE Findings (n): normal (13), polyps (19; 7/19 significant), inflammation (1), diverticular disease (1),

	obstruction of the colonic lumen (N=50)				CE + IC (any diagnosis): 37/50 (74)		angiodysplasia (1), cancer (1). 7 patients with significant polyps were referred for polypectomy which detected 14 adenomas and hyperplastic polyps.
Baltes et al (2018) ⁴⁷	Patients aged ≥18 y who had an incomplete OC due to failure to reach the cecum or ileo-cecal anastomosis due to looping, bowel angulation, adhesions, and intolerance of sedation or inflammation (N=81)	CRC screening (22%), anemia (15%), irregular stool (12%), abdominal pain (12%), colitis (5%), other reasons (12%)	≥ 6mm or ≥ 3 polyps	Protocol A: next day CE (n=38) Protocol B: CE within 30 d (n=36)	CE (significant polyps): NR (24) CE + IC (significant polyps): 21/74 (28)	Protocol A: CE: 24/38 (63.3) CE + IC: 34/38 (89.5) Protocol B: CE: 24/36 (66.7) CE + IC: 35/36 (97.2)	Per protocol analysis: 74/81 due to 7 exclusions for technical failure Adverse events: 1 capsule retention; 1 case of nausea and vomiting due to prep
Nogales et al (2017) ⁵⁰	Patients aged ≥18 y who had an incomplete OC when cecal intubation was not achieved despite adequate bowel preparation (N=96)	NR	>6mm or > 3 polyps	Within 72 hours in 8 cases of suspected CRC. During the following week for all other patients.	CE (any diagnosis): 58/96 (60.4) CE (significant polyps): 25/96 (26)	CE: 69/96 (71.9) CE + IC: 89/96 (92.7)	CCE Findings (n): polyps (41; 25/41 significant), diverticula (11), colon cancer (2), angioectasia (2), solitary colonic ulcers (2). In 43/58 patients (44.8%) the new findings modified the therapeutic approach.
Negreanu et al (2013) ⁴⁸	Patients who are risk for CRC who 1) refused (n=37) or failed prior OC (n=30), or 2) were unable to undergo OC because of anesthetic risk and co-morbidities (n=3) (N=70)	Abnormal transit (8), abdominal pain (4), anemia or overt bleeding (22), weight loss (1), average and high risk CRC screening (29), abnormal imaging or tumor markers (6)	>6 mm or ≥ 3 polyps	NR	CE (relevant lesions): 23/67 (34) [95% CI, 21.6 to 44.1] CE (significant polyps): 15/67 (22)	CE: 51/67 (76.1)	Exclusions: technical failures (3) CCE Findings (n): polyps >6mm (5), ≥ 3 polyps (10), multiple colonic angiomias (2), newly discovered Crohn disease (1), radiation enteritis (1), diverticulosis (17), ulcerative colitis and inflammatory pseudopolyps (1), <6 mm polyp (1). 17/23 patients with relevant lesions agreed to therapeutic interventions. 1 clinical failure (ulcerated rectal tumor) who refused OC following

							incomplete CE was reported. Adverse events: capsule impaction and retention (5)
Pioche et al (2012) ⁴⁹	Patients with an indication for OC per the recommendations of the French National Authority for Health, including symptoms or screening who had 1) colonoscopy failure due to difficult sigmoid loop or adhesions not related to stenosis or inadequate bowel cleansing (n=77) or 2) contraindication to OC with anesthesia due to cardiovascular or respiratory disease (n=30) (N=107)	Abnormal transit (14), abdominal pain (22), anemia or overt bleeding (30), weight loss (2), CRC screening (39)	>5 mm or ≥ 3 polyps	NR	CE (significant polyps, screening): 12/39 (30.8) [95% CI, 22.1 to 39.5] CE (any lesions explaining symptoms): 16/68 (23.5) CE (significant polyps not explaining symptoms): 8/68 (11.8) CE (any significant diagnosis): 36/107 (33.6) [95% CI, 24.7 to 42.5]	CE: 89/107 (83.2) [95% CI, 76.1 to 90.3]	CCE Findings (n): significant polyps (20), insignificant polyps (2), diverticulosis (6), telangiectasia (1), lesions explaining symptoms (16) Adverse events: capsule retention (6) Management: Screening group (12) (endoscopic treatments [6], follow-up [5], refusal [1]); Negative findings (9/64) (OC – normal findings or nonsignificant lesions [5], adenomas [1]; CTC – normal findings [3]); Symptomatic group (24) (medical treatments [8], colectomy [1], endoscopic APC [1], follow-up [6], endoscopic treatments [7], refusal [1])

APC: Argon plasma coagulation; CCE: colon capsule endoscopy; CE: capsule endoscopy; CI: confidence interval; CRC: colorectal cancer; IC: incomplete colonoscopy; NR: not reported; OC: optical colonoscopy.

Table 26. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Duration of Follow-Up ^e
Hussey et al (2018) ⁴⁶	2,3. Original indications for OC not reported.		2. Not compared to a reference standard.	1,3. Impact of findings on health outcomes not assessed. Clinical validity outcomes cannot be assessed.	1.No follow-up with reference standard.
Baltes et al (2018) ⁴⁷	1. It is not clear whether detection of polyps was the primary goal of CE for symptomatic patients.		2. Not compared to a reference standard.	1,3. Impact of findings on health outcomes not assessed. Clinical validity outcomes cannot be assessed.	1.No follow-up with reference standard.

Nogales et al (2017) ⁵⁰	2,3. Original indications for OC not reported.		2. Not compared to a reference standard.	1,3. Impact of findings on health outcomes not assessed. Clinical validity outcomes cannot be assessed.	1.No follow-up with reference standard.
Negreanu et al (2013) ⁴⁸	1,4. It is not clear whether detection of polyps was the primary goal of CE for symptomatic patients. Only a small subset of study patients reported IC.		2. Not compared to a reference standard.	1,3. Impact of findings on health outcomes not assessed. Clinical validity outcomes cannot be assessed.	1.No follow-up with reference standard.
Pioche et al (2012) ⁴⁹	1,4. It is not clear whether detection of polyps was the primary goal of CE for symptomatic patients. Only a subset of study patients reported IC.		2. Not compared to a reference standard.	1,3. Impact of findings on health outcomes not assessed. Clinical validity outcomes cannot be assessed.	No follow-up with reference standard.

CE: capsule endoscopy; IC: incomplete colonoscopy; OC: optical colonoscopy.

The study limitations 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 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 27. Study Design and Conduct Limitations

Study	Selection ^a	Blinding ^b	Delivery of Test ^c	Selective Reporting ^d	Data Completeness ^e	Statistical ^f
Hussey et al (2018) ⁴⁶	1. Selection not described.	1. No comparison to reference standard.		1.Not registered.		2. Comparison to other tests not reported.
Baltes et al (2018) ⁴⁷	1. Selection not described.	1.No comparison to reference standard.		1.Not registered.		2. Comparison to other tests not reported.
Nogales et al (2017) ⁵⁰		1.No comparison to reference standard.		1.Not registered.		2. Comparison to other tests not reported.
Negreanu et al (2013) ⁴⁸	1. Selection not described.	1.No comparison to reference standard.	1. Timing of CE not described.	1. Not registered.		2. Comparison to other tests not reported.
Pioche et al (2012) ⁴⁹	1. Selection not described.	1.No comparison to reference standard.	1. Timing of CE not described.	1. Not registered.		2. Comparison to other tests not reported.

CE: capsule endoscopy.

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

^a Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).

^b Blinding key: 1. Not blinded to results of reference or other comparator tests.

^c 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.

^d Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^e 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.

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

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 detecting colon polyps in this population has not been established, a chain of evidence supporting the test's clinical utility for this indication cannot be constructed.

Section Summary: Incomplete Colonoscopy

No studies evaluating the diagnostic characteristics of CE compared to a reference standard for the detection of colon polyps in patients with an incomplete colonoscopy following adequate bowel preparation were identified. Case series describing the incremental diagnostic yield of CE varied in their reporting of original indications for OC and inclusion of symptomatic and/or screening patients. It is unclear whether the primary goal of CE was the detection of colon polyps in symptomatic patients, as these lesions were reported as not explaining symptoms in 1 study. Successful CE completion rates were low (range, 63.3% to 83.2%) with 3/5 studies reporting full visualization of the colon for combined CE and incomplete colonoscopy IC in 84% to 97.2% of patients. Given the variable prevalence of significant and actionable findings for patients with mixed indications for colonoscopy, the diagnostic yield is insufficient to determine the clinical validity of the test. No studies assessed the impact of study findings on specific health outcomes. Information on adherence to recommended follow-up diagnostic or therapeutic interventions in patients with incomplete colonoscopies are limited, with several refusals and clinical failures reported. Studies of CE compared to standard management with repeat colonoscopy in the intended use population are necessary to determine the diagnostic characteristics of the test in the triage setting.

Known or Suspected Small Bowel Stricture

Review of Evidence

Case Series

In a series from Europe, Delvaux et al (2005) reported on findings in 22 patients with suspected intestinal stricture, 15 of whom had CD.⁵² 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 the cancellation of CE. In 3 patients, the patency capsule induced a symptomatic intestinal

occlusion, which resolved spontaneously in 1 and required emergency surgery in 2. 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 an uncomplicated passage of the patency capsule subsequently underwent uncomplicated CE.^{53,54,55} These patients often had significant findings on CE.^{53,54} However, it is difficult to determine whether CE findings in these patients improved their outcomes beyond any alternative testing regimen available. In 1 of these studies, 3 of 106 patients had severe adverse events, including 1 patient who required surgery.⁵³

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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: Known or Suspected Small Bowel Stricture

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

Unexplained Upper Abdominal Complaints

Review of Evidence

Diagnostic Accuracy Studies

Denzer et al (2015) prospectively evaluated a magnetically guided gastric capsule as compared to conventional gastroscopy in 189 patients with upper abdominal complaints (e.g., upper abdominal pain and/or anemia) from 2 French centers.⁵⁶ In this study, capsule gastroscopy was performed initially followed by conventional gastroscopy, with a maximum delay of 1 day but a minimum delay of 4 hours. For conventional gastroscopy, the examination was performed blinded initially. If results of the magnetic capsule and blinded gastroscopy differed, then a subsequent unblinded gastroscopy was performed. Biopsies were taken whenever appropriate. The combined endoscopic assessment (blinded and unblinded

gastroscopy) including biopsy was used as the final gold standard. The primary outcome parameters were the accuracy and the sensitivity, specificity, and predictive values of magnetically guided capsule gastroscopy compared with the final gold standard with regard to major lesions on a per-patient and per-lesion basis. Overall, 23 major lesions were discovered in 21 patients. Capsule accuracy on a per-patient basis was 90.5% (95% CI, 85.4% to 94.3%) with a specificity of 94.1% (95% CI, 89.3% to 97.1%) and a sensitivity of 61.9% (95% CI, 38% to 82%). The PPV and NPV were 56.5% (95% CI, 34.5% to 76.8%) and 95.2% (95% CI, 90.7% to 97.9%), respectively. Similar results for these values were seen on a per-lesion basis. Of the other 168 patients, 94% had minor and mostly multiple lesions; the capsule made a correct diagnosis in 88.1% (95% CI, 82.2% to 92.6%). No complications of capsule or conventional gastroscopy were noted. Patient preference for capsule use for a future gastroscopy, if indicated, was 100%. In this first large study to evaluate magnetically guided capsule gastroscopy in patients with upper abdominal symptoms, the authors concluded that this technique was feasible in practice and clearly preferred by patients; however, further studies are needed to define its role in the clinical setting (e.g., as a filter test to stratify patients to undergo conventional gastroscopy or some other role). Of note, this non-US study reported a low sensitivity with a wide CI and provided an extremely limited discussion of the types of upper abdominal complaints experienced by enrolled patients. No discussion in terms of the severity and duration of the complaints, as well as prior testing and treatment was undertaken, which makes determination of the appropriate place in therapy for magnetic CE in patients with unexplained upper abdominal complaints difficult.

Liao et al (2016) evaluated the accuracy of magnetically controlled CE as compared with conventional gastroscopy in 350 patients with upper abdominal complaints in a prospective, multicenter, blinded comparison study conducted in China.⁵⁷ All patients underwent magnetic CE followed by conventional gastroscopy 2 hours later, without sedation. The primary outcome of the study was an evaluation of gastric focal lesions. Overall, with conventional gastroscopy as the gold standard, magnetic CE detected gastric focal lesions in the entire stomach with 90.4% sensitivity (95% CI, 84.7% to 96.1%), 94.7% specificity (95% CI, 91.9% to 97.5%), and 93.4% accuracy (95% CI, 90.83% to 96.02%). The PPV and NPV were 87.9% (95% CI, 81.7% to 94%) and 95.9% (95% CI, 93.4% to 98.4%), respectively. Similar sensitivity and specificity results were observed with magnetic CE as compared to conventional gastroscopy when detecting focal lesions in the upper or lower stomach specifically. No lesions of significance were missed by magnetic CE. Additionally, 335 (95.7%) patients preferred magnetic CE over conventional gastroscopy and only 5 patients reported an adverse event; the majority of these events were considered to be related to gastric preparation. The authors concluded that magnetic CE detects upper abdominal focal lesions with comparable accuracy to conventional gastroscopy and is a promising alternative for screening for gastric diseases; however, similar to the prior study, this non-US study provided no discussion of the types of upper abdominal complaints experienced by patients or prior tests or treatments undertaken.

The purpose of the limitations tables (Tables 28 and 29) is to display notable limitations 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 28. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Duration of Follow-Up ^e
Denzer et al (2015) ⁵⁶	4. Study population non-U.S. (conducted in France)			1. Sensitivity is low with a wide confidence interval	
Liao et al (2016) ⁵⁷	4. Study population non-U.S. (conducted in China)		2. Conventional gastroscopy performed without sedation		

The study limitations 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 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 29. Study Design and Conduct Limitations

Study	Selection ^a	Blinding ^b	Delivery of Test ^c	Selective Reporting ^d	Data Completeness ^e	Statistical ^f
Denzer et al (2015) ⁵⁶ ,	1. Selection of patients not clearly described	1. Final gold standard of conventional gastroscopy with biopsy was unblinded				
Liao et al (2016) ⁵⁷ ,	1. Selection of patients not clearly described					

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

^a Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).

^b Blinding key: 1. Not blinded to results of reference or other comparator tests.

^c 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.

^d Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^e 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.

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

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals 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 magnetic 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.

Although magnetic CE has a similar diagnostic yield as conventional gastroscopy when evaluating individuals with unexplained upper abdominal complaints, the sequence and chronology of testing and treatment recommended before magnetic CE needs to be defined to determine whether magnetic CE has utility to diagnose the condition.

Section Summary: Unexplained Upper Abdominal Complaints

Studies evaluating the diagnostic characteristics of magnetic CE as compared to conventional gastroscopy in the target population have generally demonstrated similar accuracy, sensitivity, and specificity, with increases in patient preference and an acceptable safety profile with the magnetic CE approach. However, the sequence and chronology of testing and treatment recommended before magnetic CE needs to be defined to determine whether magnetic CE has utility to diagnose the condition. No RCTs assessing the clinical utility of magnetic CE for this indication were identified.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information’ if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Gastroenterology

In 2013, the American College of Gastroenterology (ACG) issued guidelines on the diagnosis and management of celiac disease.⁵⁸ The guidelines recommended that capsule endoscopy (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). These guidelines were updated in 2023, with no mention of CE.⁵⁹

In 2025, the ACG updated its guidelines on the management of Crohn Disease (CD) in adults.⁶⁰ It makes two recommendations specific to video capsule endoscopy:

“Video capsule endoscopy (VCE) is a useful adjunct in the diagnosis of patients with small bowel Crohn’s disease in patients in whom there is a high index of suspicion of disease.”

“Patients with obstructive symptoms should have small bowel imaging and/or patency capsule evaluation before VCE to decrease risk of capsule retention.”

These recommendations are based on multiple studies. Capsule endoscopy was found to be “superior to small bowel barium studies, computed tomography enterography (CTE) and ileocolonoscopy in patients with suspected CD, with incremental yield of diagnosis of 32%, 47%, and 22%, respectively....Capsule endoscopy has a high negative predictive value of 96%.”

In 2015, the ACG issued guidelines on the diagnosis and management of small bowel bleeding.⁶¹ As of October 2025, a guideline update is in progress.⁶² The 2015 guidelines made the following statements related to video CE (Table 30).

Table 30. Recommendations on Diagnosis and Management of Small Bowel Bleeding

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

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

In 2021, the ACG issued guidelines on colorectal cancer screening.⁶³ They “suggest consideration of the following screening tests for individuals unable or unwilling to undergo a colonoscopy or FIT [fecal immunochemical testing]: flexible sigmoidoscopy, multitarget stool DNA test, CT [computed tomography] colonography, or colon capsule [capsule endoscopy]” (conditional recommendation, very low quality of evidence).

American Gastroenterological Association Institute

In 2017, the American Gastroenterological Association Institute issued guidelines on the use of CE.⁶⁴ Table 31 summarizes the most relevant recommendations (not all recommendations are included).

Table 31. AGA 2017 Capsule Endoscopy Recommendations

Statement number	Recommendation	Grade	QOE
Recommendations supporting the use of CE			
1	For suspected CD, with negative ileocolonoscopy and imaging studies (CE of small bowel)	Strong	Very low
2	For CD and clinical features unexplained by ileocolonoscopy or imaging studies	Strong	Very low
3	For CD, when assessment of small-bowel mucosal healing (beyond reach of ileocolonoscopy) is needed	Conditional	Very low
4	For suspected small-bowel recurrence of CD after colectomy, undiagnosed by ileocolonoscopy or imaging studies	Strong	Very low

7	For celiac disease with unexplained symptoms despite treatment and appropriate investigations	Strong	Very low (efficacy)Low (safety)
8	For documented overt GI bleeding (excluding hematoemesis) and negative findings on high-quality EGD and colonoscopy	Strong	Very low
9	For overt, obscure bleeding episode, as soon as possible	Strong	Very low
10	With prior negative CE with repeated obscure bleeding, repeated studies (endoscopy, colonoscopy and/or CE)	Strong	Very low
11	For suspected obscure bleeding and unexplained mild chronic iron-deficiency anemia, in selected cases	Strong	Very low
12	For polyposis syndromes, which require small bowel studies, for ongoing surveillance	Conditional	Very low (efficacy) Low (safety)
Recommendations against the use of CE			
5	For diagnosing CD when chronic abdominal pain or diarrhea are only symptoms, and with no evidence of biomarkers associated with CD	Conditional	Low
6	For diagnosing celiac disease	Strong	Very low (efficacy) Low (safety)
13	For routine substitution of colonoscopy	Strong	Very low
14	For IBD, as substitute for colonoscopy to assess extent and severity of disease	Strong	Very low (efficacy) Low (safety)

AGA: American Gastroenterological Association; CD: Crohn disease; CE: capsule endoscopy; EGD: esophagogastroduodenoscopy; GI: gastrointestinal; IBD: inflammatory bowel disease; QOE: quality of evidence.

American Society of Gastrointestinal Endoscopy

In 2017, the American Society of Gastrointestinal Endoscopy released guidelines for the use of endoscopy in the management of suspected small bowel bleeding.⁶⁵ These guidelines made the following recommendations on capsule endoscopy (VCE) (Table 32).

Table 32. Recommendations on Use of Endoscopy to Manage Suspected Small Bowel Bleeding

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

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

National Comprehensive Cancer Network⁶⁹

NCCN Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric V 1.2025 states the following:

- For first-degree relatives of individuals who meet clinical criteria for PJS without a confirmed *STK11* PV, consider a baseline upper endoscopy, colonoscopy, and VCE at age 8 years. Data are lacking for continued surveillance after the first negative exams. Any symptoms such as bleeding, iron deficiency anemia, or intussusception in the first-degree relative should prompt appropriate workup
- For pediatric surveillance of PJS of the small intestine NCCN recommends the following: Small bowel visualization (video capsule endoscopy(VCE) or CT/MRI enterography) at baseline with follow-up interval based on findings, but at least by age 18 y, then every 2–3 y. Shorter intervals may be indicated based on polyp size, number, and pathology.
- For adult surveillance of PJS of the small intestine NCCN recommends the following: Small bowel visualization (VCE or CT/MR enterography) every 2–3 y. Shorter intervals may be indicated based on polyp size, number, and pathology.

U.S. Multi-Society Task Force

The U.S. Multi-Society Task Force (2017) issued recommendations for colorectal cancer screening with representation from the ACG, the American Gastroenterological Association, and The American Society for Gastrointestinal Endoscopy.⁶⁶ Capsule endoscopy every 5 years received a tier 3 ranking with the following recommendation:

“We suggest that capsule colonoscopy (if available) is an appropriate screening test when patients decline colonoscopy, FIT, FIT-fecal DNA, CT colonography, and flexible sigmoidoscopy (weak recommendation, low-quality evidence).”

In tandem with the U.S. Preventative Services Task Force (USPSTF) 2021 recommendations, the Multi-Society Task Force released a focused update to these guidelines in 2021, however, no changes were made regarding CE.⁶⁷

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

The USPSTF published its most recent recommendations for colorectal cancer screening in 2021.⁶⁸ Colorectal cancer screening was recommended starting at age 50 years and continuing until age 75 years (A recommendation) and in adults aged 45 to 49 years (B recommendation). The USPSTF recommendation for screening for colorectal cancer does not include serum tests, urine tests, or CE for colorectal cancer screening because of the limited available evidence on these tests and because other effective tests are available.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently unpublished trials that might influence this review are listed in Table 33.

Table 33. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT07197424	The Use of Robot Assisted Magnetically Controlled Capsule Endoscopy in Patients With Iron Deficiency Anaemia	100	Mar 2027
NCT07032961	A Cohort Study of Mobile Capsule Gastroscopy for Gastric Pathologies Screening	10,000	Oct 2030
NCT02738359	Efficacy of Colonoscopy, Colon Capsule and Fecal Immunological Test for Colorectal Cancer Screening in First Degree Relatives of Patients With Colorectal Neoplasia: a Prospective Randomized Study	3250	Nov 2024

NCT04307901	Safety of Colorectal Assessment and Tumor Evaluation by Colon Capsule Endoscopy (SOCRATEC)	600	Dec 2030 (recruiting)
NCT05108844	A Randomized Controlled Trial Evaluating the Efficacy of Early Videocapsule Endoscopy Following Negative Gastroscopy in Patients Presenting With Suspected Upper Gastrointestinal Bleeding	70	Oct 2024 (recruiting)
NCT03616041	Video Capsule Endoscopy for Lesion Localization and Diagnosis in Patients With Severe Hematochezia	23	Dec 2024
Unpublished			
NCT03458000 ^a	Capsule Endoscopy for Hemorrhage in the ER	24	Sep 2020 (completed with results)

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

Regulatory Status

Table 34. summarizes various wireless CE devices with clearance by the U.S. Food and Drug Administration. Code used: NEZ.

Table 34. Wireless Capsule Endoscopy Devices Cleared/by the U.S. Food and Drug Administration

Device	Manufacturer	Date Cleared	510(k) No.	Indication
Pillcam SB 3 Capsule Endoscopy System, Pillcam Software 9.0e	Given Imaging Ltd.	8/27/2021	K211684	For visualization of the small bowel mucosa. It may be used in the visualization and monitoring of lesions that may indicate Crohn's disease not detected by upper and lower endoscopy; lesions that may be a source of obscure bleeding not detected by upper and lower endoscopy; lesions that may be potential causes of iron deficiency anemia not detected by upper and lower endoscopy.
NaviCam Stomach Capsule System	AnX Robotica, Inc.	5/22/2020	K203192	For visualization of the stomach of adults (≥22 years) with a body mass index <38. The system can be used in clinics and hospitals, including emergency room settings.
CapsoCam Plus (SV-3)	CapsoVision Inc.	4/19/2019	K183192	For visualization of the small bowel mucosa in adults. It may be used as a tool in the detection of abnormalities of the small bowel.
Olympus Small Intestinal Capsule Endoscope System	Olympus Medical Systems Corp.	3/5/2019	K183053	For visualization of the small intestine mucosa.
MiroCam Capsule Endoscope System	IntroMedic Co. Ltd.	11/8/2018	K180732	May be used as a tool in the detection of abnormalities of the small bowel and this device is indicated for adults and children from 2 years of age.

Olympus Small Intestinal Capsule Endoscope System	Olympus Medical Systems Corp.	3/13/2018	K173459	May be used in the visualization and monitoring of lesions that may indicate Crohn's disease not detected by upper and lower endoscopy. It may be used in the visualization and monitoring of lesions that may be a source of obscure bleeding (either overt or occult) not detected by upper and lower endoscopy. It may be used in the visualization and monitoring of lesions that may be potential causes of iron deficiency anemia (IDA) not detected by upper and lower endoscopy. The Red Color Detection Function is intended to mark frames of the video suspected of containing blood or red areas.
PillCam Patency System	Given Imaging Ltd.	3/8/2018	K180171	Intended to verify adequate patency of the gastrointestinal tract prior to administration of the PillCam video capsule in patients with known or suspected strictures.
MiroCam Capsule Endoscope System	IntroMedic Co. Ltd.	1/30/2018	K170438	For visualization of the small intestine mucosa.
PillCam SBC capsule endoscopy system PillCam Desktop Software 9.0	Given Imaging Ltd.	9/1/2017	K170210	For visualization of the small intestine mucosa.
RAPID Web	Given Imaging Ltd.	5/26/2017	K170839	Intended for visualization of the small bowel mucosa.
AdvanCE capsule endoscope delivery device	United States Endoscopy Group Inc.	3/10/2017	K163495	Intended for visualization of the small bowel mucosa.
OLYMPUS SMALL INTESTINAL CAPSULE ENDOSCOPE SYSTEM	OLYMPUS MEDICAL SYSTEMS CORP.	1/19/2017	K163069	Intended for visualization of the small bowel mucosa.
CapsoCam Plus (SV-3) Capsule Endoscope System	CapsoVision Inc	10/21/2016	K161773	Intended for visualization of the small bowel mucosa.
CapsoCam (SV-1)	CapsoVision Inc.	2/9/2016	K151635	For use in diagnosing disorders of the small bowel, esophagus, and colon.
PillCam COLON 2	Given® Imaging	01/14/2016	K153466	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 in the event a clinically significant colon abnormality was identified on capsule endoscopy.
MiroCam Capsule Endoscope System	INTROMEDIC CO. LTD	3/17/2015	K143663	Intended for visualization of the small bowel mucosa.

GI: gastrointestinal.

Government Regulations

National:

There is no national coverage determination.

Local:

Wisconsin Physicians Service Insurance Corporation

Local Coverage Determination (LCD): Colon Capsule Endoscopy (CCE) (L38837)

Original Effective Date: For services performed on or after 05/29/2025

Covered Indications

For diagnostic and/or surveillance purposes, Colon capsule endoscopy (CCE) is medically necessary when EITHER of the following criteria are met:

1. Primary procedure in patients with major risks for Optical Colonoscopy (OC) or moderate sedation as indicated from an evaluation of the patient by a board certified or board eligible gastroenterologist, a surgeon trained in endoscopy, or a physician with equivalent endoscopic training and EITHER of the following criteria are met:
 - Fecal Occult Blood Test (FOBT) positive (guaiac or immunochemical) **OR**
 - Multitarget Stool DNA (sDNA) Test positive **OR**
 - Other evidence of lower GI bleeding in hemodynamically stable patients
2. Secondary procedure:
 - For the detection or surveillance of colon polyp(s) if the diagnostic OC was incomplete **OR**
 - When an incomplete diagnostic OC was performed for either:
 - Fecal Occult Blood Test (FOBT) positive (guaiac or immunochemical) **OR**
 - Multitarget Stool DNA (sDNA) Test positive **OR**
 - Other evidence of lower GI bleeding in hemodynamically stable patients

Limitations

The following are considered not medically reasonable and necessary:

1. Patients with known or suspected gastrointestinal obstruction, stricture, or fistula.
2. Patients with a cardiac pacemaker or another implanted electro-medical device.
3. Patients with swallowing disorder(s).
4. Patients with a known contraindication or allergy to any medication or preparation agent used before or during the procedure.
5. When performed in conjunction with CT Colonography (CTC).
6. CCE is not a Medicare Benefit for colorectal cancer screening, regardless of family history or other risk factors for the development of colonic disease. Please refer to NCD 210.3 for colorectal cancer screening coverage.

Wisconsin Physicians Service Insurance Corporation

Local Coverage Determination (LCD): Capsule Endoscopy (L34613)

Original effective date 10/01/2015, Retirement date 05/01/2016

Indications

- I. Occult gastrointestinal bleeding. This test is indicated for the diagnosis of occult gastrointestinal bleeding in the anemic patient when:

1. The site of bleeding has not previously been identified by upper gastrointestinal endoscopy, colonoscopy, push endoscopy or other radiologic procedure, and EGD endoscopy and colonoscopy have been performed during the same episode of illness.
 2. The diagnosis of angiodysplasias of the GI tract is suspected, and EGD endoscopy and colonoscopy have been performed during the same episode of illness.
 3. Patients have documented continuing GI blood loss and anemia secondary to bleeding, and EGD endoscopy and colonoscopy have been performed during the same episode of illness.
- II. Other indications:
1. When the diagnosis of Crohn's disease is suspected but not diagnosed.
 2. When the diagnosis of Crohn's disease is known but it is necessary to determine whether there is involvement of the small bowel as well.
 3. When a diagnosis of colitis of an indeterminate type, affecting the colon, is known and a more specific diagnosis is sought by evaluating possible small bowel involvement.
 4. As a primary procedure in the evaluation of suspected, but undiagnosed, small bowel neoplasm, regional enteritis, or malabsorption syndrome.
- III. Capsule Endoscopy is payable when all of the following criteria are met:
1. Patients are receiving services using FDA approved devices.
 2. The service is performed by physicians trained in endoscopy or in an independent diagnostic testing facility under the general supervision of a physician trained in endoscopy procedures.

Limitations

- IV. Capsule Endoscopy is not considered medically necessary, and is not covered, for:
1. The confirmation of lesion pathology, or the management of conditions diagnosed by prior endoscopy (including push enteroscopy), colonoscopy or radiological procedures.
 2. Patients with hematemesis.
 3. The management, as opposed to the diagnosis, of Crohn's Disease, other inflammatory conditions, neoplasms and mal-absorption syndromes of the small intestine.
- V. Capsule endoscopy of the esophagus has been used by some practitioners for patients with suspected gastroesophageal reflux disease, Barrett's Esophagus, or esophageal varices. However, mere visualization will not diagnose Barrett's Esophagus (i.e., a biopsy is needed), and there is no need, nor is it standard, to monitor treatment of GERD, varices, etc. by this method (i.e., patients with symptoms will need upper endoscopy to determine severity of disease and potential complications). Since the findings will not alter the treatment plan, these will be denied as not medically necessary.
- VI. Patency Capsule testing is not covered. It is used to verify adequate patency of the gastrointestinal tract prior to administration of the PillCam video capsule in patients with known or suspected strictures. There are insufficient studies available to support coverage. The ASGE Technology Status Evaluation Report Wireless Capsule Endoscopy lists, "Patients with known or suspected gastrointestinal (GI) obstruction, strictures, or fistulas based on the clinical picture or preprocedure testing" under contraindications for the small bowel capsule.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Ingestible Capsule (e.g., Smart Pill) for Assessment of GI Motility Disorders
Virtual Colonoscopy/CT Colonography

References

1. Joseph DA, King JB, Dowling NF, et al. Vital Signs: Colorectal Cancer Screening Test Use - United States, 2018. *MMWR Morb Mortal Wkly Rep.* Mar 13 2020; 69(10): 253-259. PMID 32163384
2. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. *CA Cancer J Clin.* May 2020; 70(3): 145-164. PMID 32133645
3. Cross A, Szoka N. SAGES NaviCam stomach capsule system. March 10, 2021. <https://www.sages.org/publications/tavac/navicam-stomach-capsule-system/>. Accessed 3/10/26.
4. Koulaouzidis A, Rondonotti E, Giannakou A, et al. Diagnostic yield of small-bowel capsule endoscopy in patients with iron-deficiency anemia: a systematic review. *Gastrointest Endosc.* Nov 2012;76(5):983-992. PMID 23078923
5. Leung WK, Ho SS, Suen BY, et al. Capsule endoscopy or angiography in patients with acute overt obscure gastrointestinal bleeding: a prospective randomized study with long-term follow-up. *Am J Gastroenterol.* Sep 2012;107(9):1370-1376. PMID 22825363
6. Hartmann D, Schmidt H, Bolz G, et al. A prospective two-center study comparing wireless capsule endoscopy with intraoperative enteroscopy in patients with obscure GI bleeding. *Gastrointest Endosc.* Jun 2005;61(7):826- 832. PMID 15933683
7. Pennazio M, Santucci R, Rondonotti E, et al. Outcome of patients with obscure gastrointestinal bleeding after capsule endoscopy: report of 100 consecutive cases. *Gastroenterology.* Mar 2004;126(3):643-653. PMID 14988816
8. Choi M, Lim S, Choi MG, et al. Effectiveness of Capsule Endoscopy Compared with Other Diagnostic Modalities in Patients with Small Bowel Crohn's Disease: A Meta-Analysis. *Gut Liver.* Oct 13 2016. PMID 27728963
9. El-Matary W, Huynh H, Vandermeer B. Diagnostic characteristics of given video capsule endoscopy in diagnosis of celiac disease: A meta-analysis. *J Laparoendosc Adv Surg Tech A.* Dec 2009: 19(6):815-820. PMID 19405806
10. Rokkas T, Niv Y. The role of video capsule endoscopy in the diagnosis of celiac disease: a meta-analysis. *Eur J Gastroenterol Hepatol.* Mar 2012; 24(3):303-8. PMID 22266837
11. Kurien M, Evans KE, Aziz I, et al. Capsule endoscopy in adult celiac disease: a potential role in equivocal cases of celiac disease? *Gastrointest Endosc.* Feb 2013;77(2):227-232. PMID 23200728
12. Culliford A, Daly J, Diamond B, et al. The value of wireless capsule endoscopy in patients with complicated celiac disease. *Gastrointest Endosc.* Jul 2005;62(1):55-61. PMID 15990820
13. Xue M, Chen X, Shi L, et al. Small-bowel capsule endoscopy in patients with unexplained chronic abdominal pain: a systematic review. *Gastrointest Endosc.* Jul 8 2014. PMID 25012561

14. Yang L, Chen Y, Zhang B, et al. Increased diagnostic yield of capsule endoscopy in patients with chronic abdominal pain. *PloS One*. 2014;9(1):e87396. PMID 24498097
15. Kopylov U, Yung DE, Engel T, et al. Diagnostic yield of capsule endoscopy versus magnetic resonance enterography and small bowel contrast ultrasound in the evaluation of small bowel Crohn's disease: Systematic review and meta-analysis. *Dig Liver Dis*. Aug 2017;49(8):854-863. PMID 28512034
16. Bruining DH, Oliva S, Fleisher MR, et al. Panenteric capsule endoscopy versus ileocolonoscopy plus magnetic resonance enterography in Crohn's disease: a multicentre, prospective study. *BMJ Open Gastroenterol*. Jun 2020; 7(1). PMID 32499275
17. Elosua A, Rullan M, Rubio S, et al. Does capsule endoscopy impact clinical management in established Crohn's disease?. *Dig Liver Dis*. Jan 2022; 54(1): 118-124. PMID 34518128
18. Shi HY, Chan FKL, Higashimori A, et al. A prospective study on second-generation colon capsule endoscopy to detect mucosal lesions and disease activity in ulcerative colitis (with video). *Gastrointest Endosc*. Dec 2017;86(6):1139-1146 e1136. PMID 28713062
19. San Juan-Acosta M, Caunedo-Alvarez A, Arguelles-Arias F, et al. Colon capsule endoscopy is a safe and useful tool to assess disease parameters in patients with ulcerative colitis. *Eur J Gastroenterol Hepatol*. Aug 2014;26(8):894-901. PMID 24987825
20. Oliva S, Di Nardo G, Hassan C, et al. Second-generation colon capsule endoscopy vs. colonoscopy in pediatric ulcerative colitis: a pilot study. *Endoscopy*. Jun 2014;46(6):485-492. PMID 24777427
21. Sung J, Ho KY, Chiu HM, et al. The use of Pillcam Colon in assessing mucosal inflammation in ulcerative colitis: a multicenter study. *Endoscopy*. Aug 2012;44(8):754-758. PMID 22696193
22. Gudur P, Sagi SV, Ahn D et al. Capsule endoscopy with PILLCAM ESO for detecting esophageal varices: a meta-analysis. *Minerva Gastroenterol Dietol* 2011; 57(1):1-11.
23. Usman O, Prabakar D, Malik MA, et al. Use of wireless capsule endoscopy for the diagnosis and grading of esophageal varices in patients with portal hypertension: A systematic review and meta-analysis. *Saudi J Gastroenterol*. Nov 01 2025; 31(6): 329-337. PMID 40994035
24. Bhardwaj A, Hollenbeak CS, Pooran N et al. A meta-analysis of the diagnostic accuracy of esophageal capsule endoscopy for Barrett's esophagus in patients with gastroesophageal reflux disease. *Am J Gastroenterol* 2009; 104(6):1533-9.
25. Urquhart P, Grimpén F, Lim GJ, et al. Capsule endoscopy versus magnetic resonance enterography for the detection of small bowel polyps in Peutz-Jeghers syndrome. *Fam Cancer*. Jun 2014;13(2):249-255. PMID 24509884
26. Brown G, Fraser C, Schofield G et al. Video capsule endoscopy in Peutz-Jeghers syndrome: a blinded comparison with barium follow-through for detection of small-bowel polyps. *Endoscopy*. Apr 2006; 38(4):385-90. PMID 16680639
27. Mata A, Llach J, Castells A, et al. A prospective trial comparing wireless capsule endoscopy and barium contrast series for small-bowel surveillance in hereditary GI polyposis syndromes. *Gastrointest Endosc*. May 2005;61(6):721-725. PMID 15855978
28. Haanstra JF, Al-Toma A, Dekker E, et al. Prevalence of small-bowel neoplasia in Lynch syndrome assessed by video capsule endoscopy. *Gut*. Oct 2015;64(10):1578-1583. PMID 25209657

29. Saurin JC, Pilleul F, Soussan EB, et al. Small-bowel capsule endoscopy diagnoses early and advanced neoplasms in asymptomatic patients with Lynch syndrome. *Endoscopy*. Dec 2010;42(12):1057-1062. PMID 20821360
30. McCarty TR, Afinogenova Y, Njei B. Use of Wireless Capsule Endoscopy for the Diagnosis and Grading of Esophageal Varices in Patients With Portal Hypertension: A Systematic Review and Meta-Analysis. *J Clin Gastroenterol*. Feb 2017;51(2):174-182. PMID 27548729
31. Colli A, Gana JC, Turner D, et al. Capsule endoscopy for the diagnosis of oesophageal varices in people with chronic liver disease or portal vein thrombosis. *Cochrane Database Syst Rev*. Oct 01 2014;10(10):CD008760. PMID 25271409
32. Sung JJ, Tang RS, Ching JY, et al. Use of capsule endoscopy in the emergency department as a triage of patients with GI bleeding. *Gastrointest Endosc*. May 6 2016. PMID 27156655
33. Gutkin E, Shalomov A, Hussain SA, et al. Pillcam ESO® is more accurate than clinical scoring systems in risk stratifying emergency room patients with acute upper gastrointestinal bleeding. *Therap Adv Gastroenterol*. May 2013;6(3):193-198. PMID 23634183
34. Chandran S, Testro A, Urquhart P, et al. Risk stratification of upper GI bleeding with an esophageal capsule. *Gastrointest Endosc*. Jun 2013;77(6):891-898. PMID 23453185
35. Gralnek IM, Ching JY, Maza I, et al. Capsule endoscopy in acute upper gastrointestinal hemorrhage: a prospective cohort study. *Endoscopy*. 2013;45(1):12-19. PMID 23254402
36. Spada C, Pasha SF, Gross SA, et al. Accuracy of first- and second-generation colon capsules in endoscopic detection of colorectal polyps: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. Nov 2016;14(11):1533-1543 e1538. PMID 27165469
37. Kjolhede T, Olholm AM, Kaalby L, et al. Diagnostic accuracy of capsule endoscopy compared with colonoscopy for polyp detection: systematic review and meta-analyses. *Endoscopy*. Aug 28 2020. PMID 32858753
38. Saito Y, Saito S, Oka S, et al. Evaluation of the clinical efficacy of colon capsule endoscopy in the detection of lesions of the colon: prospective, multicenter, open study. *Gastrointest Endosc*. Nov 2015;82(5):861-869. PMID 25936450
39. Morgan DR, Malik PR, Romeo DP, et al. Initial US evaluation of second-generation capsule colonoscopy for detecting colon polyps. *BMJ Open Gastroenterol*. 2016;3(1):e000089. PMID 27195129
40. Parodi A, Vanbiervliet G, Hassan C, et al. Colon capsule endoscopy to screen for colorectal neoplasia in those with family histories of colorectal cancer. *Gastrointest Endosc*. May 26 2017. PMID 28554656
41. Cash BD, Fleisher MR, Fern S, et al. Multicentre, prospective, 49 randomized study comparing the diagnostic yield of colon capsule endoscopy versus CT colonography in a screening population (the TOPAZ study). *Gut*. Nov 2021; 70(11): 2115-2122. PMID 33443017
42. Kobaek-Larsen M, Kroijer R, Dyrvig AK, et al. Back-to-back colon capsule endoscopy and optical colonoscopy in colorectal cancer screening individuals. *Colorectal Dis*. Jun 2018; 20(6): 479-485. PMID 29166546
43. Rondonotti E, Borghi C, Mandelli G, et al. Accuracy of capsule colonoscopy and computed tomographic colonography in individuals with positive results from the fecal

- occult blood test. *Clin Gastroenterol Hepatol*. Aug 2014; 12(8): 1303-10. PMID 24398064
44. Eliakim R, Yassin K, Niv Y, et al. Prospective multicenter performance evaluation of the second-generation colon capsule compared with colonoscopy. *Endoscopy*. Dec 2009; 41(12): 1026-31. PMID 19967618
 45. Franco DL, Leighton JA, Gurudu SR. Approach to Incomplete Colonoscopy: New Techniques and Technologies. *Gastroenterol Hepatol (N Y)*. Aug 2017; 13(8): 476-483. PMID 28867979
 46. Hussey M, Holleran G, Stack R, et al. Same-day colon capsule endoscopy is a viable means to assess unexplored colonic segments after incomplete colonoscopy in selected patients. *United European Gastroenterol J*. Dec 2018; 6(10): 1556-1562. PMID 30574326
 47. Baltes P, Bota M, Albert J, et al. PillCamColon2 after incomplete colonoscopy – A prospective multicenter study. *World J Gastroenterol*. Aug 21 2018; 24(31): 3556-3566. PMID 30131662
 48. Negreanu L, Babiuc R, Bengus A, et al. PillCam Colon 2 capsule in patients unable or unwilling to undergo colonoscopy. *World J Gastrointest Endosc*. Nov 16 2013; 5(11): 559-67. PMID 24255748
 49. Pioche M, de Leusse A, Filoche B, et al. Prospective multicenter evaluation of colon capsule examination indicated by colonoscopy failure or anesthesia contraindication. *Endoscopy*. Oct 2012; 44(10): 911-6. PMID 22893133
 50. Nogales O, Garcia-Lledo J, Lujan M, et al. Therapeutic impact of colon capsule endoscopy with PillCam COLON 2 after incomplete standard colonoscopy: a Spanish multicenter study. *Rev Esp Enferm Dig*. May 2017; 109(5): 322-327. PMID 28229607
 51. Spada C, Shah SK, Riccioni ME et al. Video capsule endoscopy in patients with known or suspected small bowel stricture previously tested with the dissolving patency capsule. *J Clin Gastroenterol*. Jul 2007; 41(6):576-82. PMID 17577114
 52. Delvaux M, Ben Soussan E, Laurent V et al. Clinical evaluation of the use of the M2A patency capsule system before a capsule endoscopy procedure, in patients with known or suspected intestinal stenosis. *Endoscopy*. Sep 2005; 37(9):801-7. PMID 16116529
 53. Herrerias JM, Leighton JA, Costamagna G et al. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. *Gastrointest Endosc*. May 2008; 67(6):902-9. PMID18355824
 54. Postgate AJ, Burling D, Gupta A et al. Safety, reliability and limitations of the given patency capsule in patients at risk of capsule retention: a 3-year technical review. *Dig Dis Sci*. Oct 2008; 53(10):2732-8. PMID 18320313
 55. Banerjee R, Bhargav P, Reddy P et al. Safety and efficacy of the M2A patency capsule for diagnosis of critical intestinal patency: results of a prospective clinical trial. *J Gastroenterol Hepatol*. Dec 2007; 22(12):2060-3. PMID 187614957
 56. Denzer UW, Rosch T, Hoytat B, et al. Magnetically guided capsule versus conventional gastroscopy for upper abdominal complaints: a prospective blinded study. *J Clin Gastroenterol*. Feb 2015; 49(2): 101-7. PMID 24618504
 57. Liao Z, Hou X, Lin-Hu EQ, et al. Accuracy of Magnetically Controlled Capsule Endoscopy, Compared With Conventional Gastroscopy, in Detection of Gastric Diseases. *Clin Gastroenterol Hepatol*. Sep 2016; 14(9): 1266-1273.e1. PMID 2721150
 58. Rubio-Tapia A, Hill ID, Kelly CP, et al. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol*. May 2013;108(5):656-676; quiz 677. PMID 23609613

59. Rubio-Tapia A, Hill ID, Semrad C, et al. American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease. Am J Gastroenterol. Jan 01 2023; 118(1): 59-76. PMID 36602836
60. Lichtenstein GR, Hanauer SB, Sandborn WJ, et al. Management of Crohn's disease in adults. Am J Gastroenterol. Feb 2009;104(2):465-483; quiz 464, 484. PMID 19174807
61. Gerson LB, Fidler JL, Cave DR, et al. ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding. Am J Gastroenterol. Sep 2015;110(9):1265-1287; quiz 1288. PMID 26303132
62. American College of Gastroenterology Guidelines. 2025. <https://gi.org/guidelines/>. Accessed 3/10/26
63. Shaukat A, Kahi CJ, Burke CA, et al. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol. Mar 01 2021; 116(3): 458-479. PMID 33657038
64. Enns RA, Hookey L, Armstrong D, et al. Clinical Practice Guidelines for the Use of Video Capsule Endoscopy. Gastroenterology. Feb 2017; 152(3): 497-514. PMID 28063287
65. Gurudu SR, Bruining DH, Acosta RD, et al. The role of endoscopy in the management of suspected small-bowel bleeding. Gastrointest Endosc. Jan 2017;85(1):22-31. PMID 27374798
66. Rex DK, Boland CR, Dominitz JA, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer. Gastroenterology. Jul 2017; 153(1): 307- 323. PMID 28600072
67. Patel SG, May FP, Anderson JC, et al. Updates on Age to Start and Stop Colorectal Cancer Screening: Recommendations From the U.S. Multi-Society Task Force on Colorectal Cancer. Gastroenterology. Jan 2022; 162(1): 285-299. PMID 34794816
68. Davidson KW, Barry MJ, Mangione CM, et al. U.S. Preventive Services Task Force. Colorectal Cancer: Screening. May 18, 2021. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/colorectal-cancer-screening> Accessed 3/10/26
69. National Comprehensive Cancer Network (NCCN). NCCN Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric V 1.2025 June 13, 2025 [genetics_ceg.pdf](#) Accessed 3/31/26

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through March, 2026 the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
8/9/02	7/31/02	8/9/02	Joint policy established
3/18/03	3/18/03	3/4/03	Routine maintenance
3/10/04	3/10/04	4/7/04	Routine maintenance; added Crohn's disease diagnosis and new CPT code
2/28/05	2/28/05	2/25/05	Routine maintenance
7/1/06	5/2/06	3/13/06	Routine maintenance
7/1/07	5/10/07	6/30/07	Routine maintenance
9/1/08	7/25/08	9/1/08	Routine maintenance
3/1/09	12/9/08	12/9/08	Maintenance, added capsule patency system
3/1/12	12/13/11	12/21/11	Routine maintenance
9/1/13	6/18/13	6/26/13	Routine maintenance; updated policy criteria, rationale and references.
9/1/15	6/16/15	7/16/15	Routine maintenance - Deleted NOC code; added new CPT code 0355T. - Added ulcerative colitis, acute GI bleeding, Lynch syndrome, portal hypertensive enteropathy, unexplained chronic abdominal pain, and initial evaluation of individuals with acute upper GI bleeding as exclusions. - Added individuals with established Crohn disease for unexpected change(s) in course of disease or response to treatment as a covered indication.
9/1/16	6/21/16	6/21/16	Routine maintenance
9/1/17	6/20/17	6/20/17	Routine maintenance "Obscure gastrointestinal bleeding" changed to "suspected small bowel bleeding" throughout policy Title changed from "Wireless Capsule Endoscopy as a Diagnostic Technique in Disorders of the Small

			Bowel, Esophagus, and Colon” to “Wireless Capsule Endoscopy to Diagnose Disorders of the Small Bowel, Esophagus, and Colon”
9/1/18	6/19/18	6/19/18	Routine maintenance
11/1/18	8/21/18	8/21/18	Updated MPS to include patency capsule is E/I; added CPT 91299
11/1/19	8/20/19		Routine maintenance
11/1/20	8/18/20		Routine maintenance Ref 46 deleted.
11/1/21	8/17/21		Routine maintenance Ref 15,34,38,39,40,41,42,43,44,45, 46,57,58 added Code 0651T added, with rationale and Ref 59,60,61,62 added
7/1/22	4/19/22		Routine maintenance Code 0355T deleted; 91113 added Ref 2,39,55 added
7/1/23	4/18/23		Routine maintenance (jf) Vendor Managed: NA Ref added 1,2,18,59,62 -Individuals replaced patients in the medical policy statement and inclusions and exclusions.
7/1/24	4/16/24		Routine maintenance (jf) Vendor Managed: NA Ref added: 59,62,64,67 Updated rationale to support the inclusionary addition that was made in 2015.
7/1/25	4/15/25		Routine maintenance (jf) Minor Edits: Title Changes: From: Wireless Capsule Endoscopy to Diagnose Disorders of the Small Bowel, Esophagus, and Colon

			• To: New Policy Name: Wireless Capsule Endoscopy for Gastrointestinal Disorders • The policy evaluates the use of this technology in both screening and diagnostic settings. The title now reflects this. Routine maintenance (jf) Vendor Managed: NA Edits to Description, Exclusions, MPS: Removed safe and effective
7/1/26	4/21/26		Routine maintenance (jf/mk) Vendor Managed: NA • Formatting changes made: ○ Sections rearranged for better flow ○ Added Description and Background separated ○ MPS edited ○ Notes edited in code section ○ Edits to inclusions and exclusions to provide clarity Ref Added: 69

Next Review Date: 2nd Qtr, 2027

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: WIRELESS CAPSULE ENDOSCOPY FOR GASTROINTESTINAL DISORDERS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; policy guidelines apply Patency capsule not covered
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.