Regence

Medical Policy Manual Radiology, Policy No. 38

Wireless Capsule Endoscopy for Gastrointestinal (GI) Disorders

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Next Review: January 2026
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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

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

MEDICAL POLICY CRITERIA

I. Wireless capsule endoscopy of the ***small bowel*** may be considered **medically necessary** for one or more of the following:

   A. Evaluation of suspected small bowel bleeding when both of the following Criteria (1. and 2.) are met:

      1. Prior upper and lower gastrointestinal (GI) endoscopic studies performed during the current episode of illness are inconclusive; and

      2. Clinical documentation of suspected gastro-intestinal bleeding including anemia (e.g., iron-deficiency anemia and/or positive fecal occult blood test, or visible bleeding) is provided.

   B. Evaluation of Crohn's disease when either of the following are met:

1. Re-evaluation in diagnosed Crohn's disease, when there are unexpected change(s) in the course of disease or response to treatment, suggesting the initial diagnosis may be incorrect and reexamination may be indicated.
2. Initial diagnosis in suspected Crohn's disease when both of the following Criteria (a. and b.) are met:
    a. Clinical documentation of abdominal pain or diarrhea, plus 1 or more signs of inflammation (e.g., fever, elevated white blood cell count, elevated erythrocyte sedimentation rate, elevated C reactive protein, bleeding, terminal ileitis, or other signs of inflammation that are non-diagnostic on conventional tests) is provided; and
    b. The diagnosis has not been previously confirmed by conventional diagnostic tests. Conventional tests may include one or more of the following: small bowel follow-through, upper and lower endoscopy, MR enterography or CT enterography.

C. Surveillance of the small bowel in patients with hereditary GI polyposis syndromes, including familial adenomatous polyposis and Peutz-Jeghers syndrome.

D. Evaluation of celiac disease when either of the following are met:
1. Individuals with clinical evidence of celiac disease and positive celiac-specific serology when upper endoscopy with biopsy is not indicated.
2. Re-evaluation of individuals with celiac disease who remain symptomatic despite treatment.

II. Wireless capsule endoscopy is considered **investigational** for evaluation of the small bowel not meeting Criterion I. and for all other indications, including but not limited to:

A. Evaluation of the extent of involvement of known Crohn's disease or ulcerative colitis.

B. Evaluation of the esophagus, including in patients with gastroesophageal reflux or other esophageal pathologies.

C. Evaluation of other GI diseases and conditions not presenting with GI bleeding, including but not limited to the following: irritable bowel syndrome, hereditary *non*polyposis syndromes (including but not limited to Lynch syndrome), small bowel neoplasm, portal hypertensive enteropathy, and unexplained chronic abdominal pain.

D. Evaluation of the colon, including but not limited to detection of colonic polyps or colon cancer.

E. Initial evaluation of patients with acute upper GI bleeding.

F. Evaluation of patients with evidence of lower GI bleeding, including in the context of major risks for colonoscopy or moderate sedation.

G. Evaluation of patients following incomplete colonoscopy.

III. The patency capsule is considered **investigational** for all indications, including to evaluate patency of the GI tract before wireless capsule endoscopy.

IV. Magnetic capsule endoscopy is considered **investigational** for all indications including

but not limited to the evaluation of patients with unexplained upper abdominal complaints.

V. An upper gastrointestinal optical sensor capsule (e.g., PillSense System™) is considered **investigational** for all indications, including but not limited to the evaluation of patients with suspected upper gastrointestinal bleeding.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

LIST OF INFORMATION NEEDED FOR REVIEW

REQUIRED DOCUMENTATION:

The information below **must** be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

1. Medical records related to Criterion I. above:
    - History and physical/chart notes
    - Description of suspected disorder

2. Additional medical records related to Criterion I. above, examples include:
    - Previous imaging or diagnostic testing results, if any
    - Documentation of signs of inflammation that are non-diagnostic on conventional tests, if relevant
    - Conservative treatment provided, if any
    - Genetic syndrome testing, if relevant.

CROSS REFERENCES

1. Ingestible pH and Pressure Capsule Medicine, Medicine, Policy No. 117

BACKGROUND

WIRELESS CAPSULE ENDOSCOPY

Capsule endoscopy (CE) is performed using a disposable imaging capsule which is ingested by the patient. The capsule measures 11 by 30 mm and contains video imaging, self-illumination, and image transmission modules, as well as a battery supply that lasts up to eight hours. The indwelling camera takes images at a rate of up to 35 frames per second as peristalsis carries the capsule through the gastrointestinal tract. The average transit time from ingestion to evacuation is 24 hours. The device uses wireless radio transmission to send the images to a receiving recorder device that is worn around the waist. This receiving device also contains sensors that can roughly gauge where the image was taken over the abdomen. Images are then downloaded onto a workstation for viewing and processing.

Capsule endoscopy has been proposed as a method for identifying Crohn's disease. There is no single criterion standard diagnostic test for Crohn's disease; rather, diagnosis is based on a corroboration of findings.[1] Thus it is difficult to identify a unique reference standard for the diagnosis of CD.

Gastrointestinal tract obstruction is a contraindication for CE. Patients who are at risk for obstruction, have swallowing disorders, pacemakers or other implanted cardiac devices, or are pregnant and should have careful evaluation by a specialist before undergoing a CE procedure. In addition, contraindications to capsule endoscopy are also noted by manufacturers and may include, but are not limited to, known or suspected GI obstruction/ obstacles, fistulae, relevant (small bowel) diverticulosis, motility disorder, cardiac pacemakers or other implanted electromedical devices, and age-specific contraindications.[2 3]

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.[4] 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 two weeks. The device is contraindicated for use in patients with gastrointestinal obstruction, stenosis, fistula, or those with dysphagia. Other contraindications include patients with cardiac pacemakers or other implantable electronic medical devices as well as pregnant women, those <22 years of age, and those with a body mass index ≥38 kg/m^2.

REGULATORY STATUS

Table 1 summarizes some of the wireless CE devices with clearance by the FDA.

Code: NEZ

Table 1. 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.

Device	Manufacturer	Date Cleared	510(k) No.	Indication
Olympus Small Intestinal Capsule Endoscope System	Olympus Medical Systems Corp.	3/5/2019	K183053	For visualization of the small intestine mucosa. Intended for use in adults only.
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 PilCam 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 COLON2	Given® Imaging	1/14/2016	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

Device	Manufacturer	Date Cleared	510(k) No.	Indication
				patients with evidence of GI bleeding of lower GI origin with major risks for colonoscopy or moderate sedation, but who could tolerate 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.
Endocapsule software 10 and light	Olympus Medical Systems Corp.	2/8/2015	K142680	Intended for visualization of the small bowel mucosa.
EnteraSense PillSense System™	EnteraSense LTD	2/24/2023	DEN220065	Intended for the detection of blood in hemodynamically stable adults suspected of having upper gastrointestinal bleeding.

GI: gastrointestinal.

EVIDENCE SUMMARY

STUDY SELECTION CRITERIA

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful.

Clinically Valid

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

Below are selection criteria for studies to assess whether a test is clinically valid.

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

Clinically Useful

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

Direct Evidence

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

SUSPECTED SMALL BOWEL BLEEDING

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

Systematic Reviews

Rossi (2024) published a systematic review (SR) and meta-analysis examining the diagnostic effectiveness of Video Capsule Endoscopy (VCE) in patients with Iron Deficiency Anemia (IDA) without overt bleeding.[5] The SR included twelve studies encompassing 1,703 patients (47% male, aged 19-92 years). The VCE demonstrated a diagnostic yield of 61% (95% CI=44-77; 95 CI=97.2-98.1; I2 =97.7%) for overall small bowel lesions, while the yield specifically for lesions likely causing IDA was 40% (95% CI=27-53; 95% CI=95.3-97; I2 =96.3%). The high inconsistency squared (I2) values indicated substantial heterogeneity among the studies.

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

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

Study	Dates	Trials	Participants	N (Range)	Design	QUADAS Assessment of Included Trials
Koulaouzidis (2012)[6]	2004-2011	24	Patients with iron-deficiency anemia who had SBCE and at least 1 lower and upper GI endoscopy prior to CE	1960 (35 to 652)	Observational	Low-to-moderate quality

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

Table 3. 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 (2012)[6]				
Total N	1960	264		• Angioectasias: 293 (45.9) • Inflammatory lesions: 126 (19.7) • Polyp/mass lesions: 42 (6.6) • Not classified: 177 (27.7)

Study	Overall Diagnostic Yield[a]	Diagnostic Yield of Patients With IDA[b]	I^2, %	Diagnostic Yield, n (%)[c]
Pooled effect (95% CI), %	47 (42 to 52)	66.6 (61.0 to 72.3)	78.8	
p			<0.001	

CI: confidence interval; IDA: iron-deficient anemia.
[a] Per-patient analysis.
[b] From 4 studies (n=264 patients; 13.47% of total).
[c] Patients with positive Small Bowel Capsule Endoscopy findings.

Randomized Controlled Trials

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

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

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Leung (2012)[7]	China	1	2005-2007	Consecutive adults with active overt obscure GI bleeding	30 randomized to CE	30 randomized to mesenteric angiography

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

Table 5. Results of RCT Evaluating 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 (2012)[7]					
CE	53.3 (36.1 to 69.8)	16.7 (7.3 to 33.6)	5 (16.7)	3 (10)	48.5 (20.9)
Angiography	20 (9.5 to 37.3)	33.3 (19.2 to 51.2)	5 (16.7)	3 (10)	
Difference	33.3 (8.9 to 52.8)	16.7 (-5.3 to 36.8)			
p	0.016	0.23	1.0	1.0	

CI: confidence interval; CE: capsule endoscopy; GI: gastrointestinal; RCT: randomized controlled trial; SD: standard deviation.
[a] Percentage identified with a high probability of bleeding.

The purpose of the limitations tables (Tables 6 and 7) 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 the evidence supporting the position statement.

Table 6. 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 (2012)[7]	2. It is possible patients with moderate bleeding would not undergo		2. A criterion standard is lacking for evaluation of		

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
	angiography in a clinical setting 4. Patients with overt but nonmassive bleeding may not be ideal for CE or angiography		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 7. Study Design and Conduct Limitations of RCT Evaluating Capsule Endoscopy for Obscure GI Bleeding

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Leung (2012)[7]					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 8 and 9 summarize the characteristics and results of selected case series.

Table 8. Characteristics of Case Series Evaluating Capsule Endoscopy for Obscure GI Bleeding

Study	Country	Participants	Treatment Delivery	Follow-Up mo (Range)
Hartmann (2005)[8]	Germany	47 patients >18 y with obscure GI bleeding	Patients received CE and criterion standard, intraoperative endoscopy	NR

Study	Country	Participants	Treatment Delivery	Follow-Up mo (Range)
Pennazio (2004)[9]	Italy	100 patients ≥18 y with obscure GI bleeding	51 patients received CE and PE before or after the procedure	Mean: 18 (5 to 25)

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

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

Study	Treatment	Locating Bleeding With CE, %		Diagnostic Yield for Positive Lesions, %	PPV of CE, %
		Sensitivity	Specificity[a]		
Hartmann (2005)[8]	CE and intraoperative endoscopy	95	75	Both procedures: 76.6	95
Pennazio (2004)[9]	CE and PE	89	95	67 (95% CI, 54 to 80)	97

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

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

Section Summary: Suspected Small Bowel Bleeding

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

ESTABLISHED CROHN'S DISEASE

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

Systematic Reviews

Tamilarasan (2022) published a SR with meta-analysis to compare the diagnostic accuracy of panenteric capsule endoscopy (PCE) with endoscopic evaluation, intestinal ultrasound (IU) or magnetic resonance enterography (MRE) in patients with inflammatory bowel disease (IBD).[10] Fourteen studies were included (seven for CD and seven for Ulcerative Colitis [UC])). For CD, PCE had an increased diagnostic yield of 5% and 7% compared with MRE and colonoscopy, respectively. With a pooled odds ratio (OR) of 1.25 (95% CI, 0.85 to 1.86%) for the detection of CD. Panenteric capsule endoscopy had a diagnostic sensitivity for the detection of UC of 93.8% (95% CI, 87.6 to 97.0%) and a specificity of 69.8% (95% CI, 38.2 to 89.6%). The authors concluded that there remains a lack of standardization of PCE scoring systems and a lack of transmural assessment for diagnosing CD. In UC, PCE has an excellent diagnostic

sensitivity and positive predictive value, limitations to its use include the lack of histologic assessment and poor specificity.

Kopylov (2017) published a SR of data evaluating the diagnostic yield (DY) of CE in detection and monitoring of small bowel for CD.[11] Reviewers included prospective studies comparing CE with MRE and/or small bowel contrast ultrasound (SICUS) in patients who had suspected and/or established CD. Studies were generally of good quality with low risk of bias. The DY of CE for detection of active SB CD was similar to that of MRE (10 studies, 400 patients, OR 1.17; 95% CI 0.83 to 1.67) and SICUS (5 studies, 142 patients, OR 0.88; 95% CI 0.51 to 1.53). The outcomes were similar for the subgroups of suspected versus established CD and adult versus pediatric patients. CE was superior to MRE for proximal SB CD (7 studies, 251 patients, OR 2.79; 95% CI 1.2 to 6.48). No significant difference between CE and SICUS was found.

Non-Randomized Studies

Calabrese (2022) completed a retrospective, matched cohort analysis to compare clinical outcomes between CE and standard of care (SOC), ileocolonoscopy/MRE in patients with suspected CD.[12] A total of 100 cases were included in the analysis (50 per arm, matched for demographics and clinical characteristics). Overall there were no significant differences in biologics and surgery in either group. The authors indicate that an analysis by disease location (L1-L4) resulted in less biologics and surgery in the L4 diagnosis only. No difference was found between groups in flare occurrence and duration. The authors conclude that more extensive, prospective, multicentre, randomized studies are needed.

Kawano (2022) published a retrospective study to evaluate the safety and efficacy of CE and analyze patient characteristics, clinical course, characteristics of CE, and safety and efficacy of CE in newly diagnosed CD patients (n=32).[10] Patency Capsules (PC) were performed in 26 (81%) of patients. The total small intestine was observed in 93% of patients and there were two reported adverse events (unable to swallow the capsule and capsule retention). The authors point out that the capsule retention occurred in a patient that did not undergo PC. No abnormality was identified by ileocolonoscopy in 46% (15/32), and transition of small bowel lesions (TSL) was found in 35% (12/34) of the patients. The most common CE findings were erosions (n=23), followed by ulcers (n=21), and cobble stone appearance (n=9). Some limitations include retrospective design, small sample size, safety maybe misrepresented as those with prior diagnosed stenosis were likely not provided CE.

Elosua (2022) evaluated the therapeutic impact of CE in patients with established Crohn's CD in a retrospective, single-center study.[13] Therapeutic impact was defined as change in CD-related treatment recommended based on CE results. A total of 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 single-center group of clinicians limited heterogeneity. These results are limited by the retrospective design of the study.

Bruining (2020) reported results from the multicenter, prospective BLINK trial comparing the diagnostic accuracy of CE to ileocolonoscopy and/or MRE in patients with established CD.[14] The per-protocol analysis included 99 of 158 enrolled subjects with 16 patients tested by all three 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 three gastroenterologists. Overall sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 94% (95% CI 86% to 98%), 74% (95% CI 55% to 87%), 91% (95% CI 82% to 96%), and 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 ileocolonoscopy and/or MRE. Sensitivity of CE was significantly higher compared to MRE for enteric inflammation in the proximal small bowel (97% vs. 71%, p=0.021) and similar in the terminal ileum and colon (p=0.500 to 0.625). 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.

Section Summary: Established Crohn’s Disease

Two SRs compared CE with radiography, MRE or ultrasound for CD. One study found slightly higher diagnostic yield compared to MRE and UI. A second SR A systematic review found a similar diagnostic yield with CE compared with radiography. A diagnostic accuracy study found a comparable sensitivity, higher specificity and PPV, and lower NPV with CD compared to ileocolonoscopy and/or MRE in patients with established CD. Differences may be attributed to high rates of discrepant reads between modalities, and high consensus panel agreement with CE results in cases of discrepancy. Randomized controlled trails are needed to further assess the impact of CE results on therapy management.

SUSPECTED CROHN’S DISEASE

The purpose of CE for patients with suspected CD is to confirm a diagnosis and inform a decision to proceed to appropriate treatment.

Systematic Reviews

Lei (2024) published a systematic review and meta-analysis evaluating the diagnostic accuracy of Colon Capsule Endoscopy (CCE) for inflammatory bowel conditions, particularly Ulcerative Colitis (UC) and Crohn's Disease (CD).[15] The analysis included 23 studies with 1,353 patients, comparing CCE against standard optical endoscopy. The results demonstrated high diagnostic accuracy across both conditions: for UC, CCE showed 92% sensitivity (95% CI, 88-95%), 71% specificity (95% CI, 35-92%), and an AUC of 0.93 (95% CI, 0.89-0.97); for CD, sensitivity was 92% (95% CI, 89-95%), specificity 88% (95% CI, 84-92%), and AUC 0.87 (95% CI, 0.76-0.98). Overall, for inflammatory bowel disease, CCE demonstrated 90% sensitivity (95% CI, 85-93%), 76% specificity (95% CI, 56-90%), and an AUC of 0.92 (95% CI, 0.94-0.97), indicating strong diagnostic performance despite challenges in standardized disease scoring and lack of histological confirmation.

Results from a meta-analysis by Choi (2017), which compared CE with various modalities for diagnosing CD, are summarized in Tables 10 and 11. The reference standards varied for the selected studies, so quantitative data were not synthesized for diagnostic accuracy. In the

pooled analysis, in patients with suspected CD, the sensitivity of CE ranged from 89.6% to 92.0% and the specificity was 100%.

Table 10. Characteristics of Systematic Reviews Assessing the Diagnostic Yield of Capsule Endoscopy versus Other Modalities[a]

Study	Dates	Trials	Participants	N (Range)	Design
Choi (2017)[16]	2002-2013	24	Patients with suspected or established CD	NR	RCT, nonrandomized, and diagnostic accuracy studies

CD: Crohn's disease; CE: capsule endoscopy; NR: not reported; RCT: randomized controlled trial.
[a] Other modalities include small bowel follow-through, enteroclysis, computed tomography enterography, and magnetic resonance enterography.

Table 11. Results of Systematic Reviews Assessing the Diagnostic Yield of Capsule Endoscopy versus Other Modalities

Study	CE vs SBFT[a]	CE vs EC[b]	CE vs CTE[b]	CE vs MRE[b]
Choi (2017)[16]				
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.

Non Randomized Studies

Broderson (2023) a prospective blinded multicenter study, patients (n=99) with suspected CD were examined with CE and IC within two weeks.[17] The ileocolonic disease severity was assessed with the Simple Endoscopic Score for Crohn's Disease (SES-CD). CD was diagnosed in 30 patients with IC and CE. The mean SES-CD was 9.8 (CI 7.9 to 11.8) and 10.6 (CI 8.2 to 13.1), respectively (p=0.69). There was a substantial agreement (ICC 0.83, CI 0.68 to 0.92) and a strong correlation between SES-CD assessed with IC and CE (rs=0.78, p <0.001). A total of 55 bowel segments had ulcerations identified with both modalities (terminal ileum 24, right colon 12, transverse colon eight, left colon eight and rectum three). Mean sub-scores for ulcer size, area of ulcerated surface and area of affected surface did not differ between modalities. The inter-modality agreement (κ) was 0.46, 0.34 and 0.43, respectively (p<0.001). The authors conclude that there is a strong correlation between IC and CE for the severity of ileocolonic CD and the agreement for SES-CD sub-scores is fair to moderate. The authors state that CE could be an alternative to IC for the assessment of endoscopic severity in selected patients with suspected CD.

Broderson (2022) published a prospective, blinded, multicenter study of the diagnostic accuracy, image quality, and patient experienced discomfort with CE, magnetic resonance enterocolonography (MREC) and ileocolonoscopy (IC) in patients with suspected CD.[18] A total of 153 patients were included in the study and IC, MREC, and CE was performed in 152, 151, 133 patients, respectively. Crohn's Disease was diagnosed with IC in 59 (39%) patients (terminal ileum (TI) 22, colon 20, TI and colon 17). The sensitivity and specificity for diagnosing ileocolonic CD with MREC was 67.9% (CI 53.7 to 80.1) and 76.3% (CI 65.2 to 85.3) (TI 76.9% and 85.6%; colon 27% and 93%) compared to 87.5% (CI 73.2 to 95.8) and 87.8% (CI 78.2 to 94.3) with CE (TI 96.6% and 87.5%; colon 75.0% and 93.0%). The sensitivity of CE was

superior to that of MREC (p = 0.02). The patient experienced discomfort was equal with CE and MREC and significantly less than with IC.

Section Summary: Suspected Crohn's Disease

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

CELIAC DISEASE

Systematic Reviews

A meta-analysis by El-Matary (2009) compared the diagnostic performance of CE with a reference standard of duodenal biopsy.[19] The pooled analysis of three studies showed a sensitivity of 83% and a specificity of 98%. No major complications were reported. Another meta-analysis by Rokkas and Niv (2012) also compared the diagnostic performance of CE with biopsy, summarizing six studies (n=166).[20] 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 when endoscopy with biopsy is possible, however, the authors conclude this method may be a reasonable alternative method of diagnosing CD.

Nonrandomized Studies

In a study by Kurien (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.[21] 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 three 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 two cases of enteropathy-associated lymphoma, four type 1 refractory disease cases, one fibroepithelial polyp, and one 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.

Rondonotti (2007) published the results of a multi-center study in 43 consecutive patients with clinical symptoms suggesting celiac disease and positive serology in which CE was used to assess the severity and extent of mucosal changes.[22] CE was comparable to EGD for the diagnosis of celiac disease when there are overt villous changes. Capsule findings were evaluated for the presence of lesions compatible with celiac disease (scalloping of duodenal folds, fissures, flat mucosa, and mosaic appearance). Duodenal histology was normal in 11 and compatible with celiac disease in 32 of 43 patients studied. Using duodenal histology as the gold standard, the performance characteristics of capsule endoscopy for the diagnosis of celiac disease were: sensitivity 87.5 % (95 % confidence interval [CI]: 76.1 to 98.9 %), specificity 90.9 % (95 % CI: 81.0 to 100 %), positive predictive value 96.5 % (95 % CI: 90.1 to 100 %), negative predictive value 71.4 % (95 % CI: 55.8 to 87 %), positive and negative likelihood ratios 9.6 and 0.14, respectively. Eighteen patients had mucosal changes extending

beyond the duodenum, involving the entire small bowel in three. These patients tended to have more severe symptoms, but the difference was not statistically significant. Interobserver agreement for the diagnosis of celiac disease by capsule endoscopy ranged between 79.2 and 94.4%; kappa values ranged between 0.56 and 0.87. The authors concluded that capsule endoscopy shows good sensitivity and excellent specificity for the detection of villous atrophy in patients with suspected celiac disease.

Capsule endoscopy in nonresponsive celiac disease

A study published by Barret (2012) evaluated the ability of CE to detect disease severity or complications compared to upper endoscopy or enteroscopy in refractory celiac disease.[23] In this study, nine patients with symptomatic celiac disease, 11 patients with refractory celiac disease type I (RCDI), 18 patients with refractory celiac disease type II (RCDII), and 45 patients without celiac disease underwent both CE and upper endoscopy or enteroscopy. A total of 47 CEs (10, 11, and 26 CEs in the symptomatic CD, RCDI, and RCDII groups, respectively) from the 38 celiac patients and 47 CEs from the 45 nonceliac patients were reviewed. Among celiac patients, CE was of acceptable quality in 96% of cases and was complete in 62% of cases. Concordance of CE with histology for villous atrophy was higher than for optic endoscopy (κ coefficient=0.45 vs. 0.24, $p<0.001$). In addition, extensive mucosal damage on CE was associated with low serum albumin ($p=0.003$) and the RCDII form ($p=0.02$). Three cases of overt lymphoma were detected by CE.

Atlas (2011) published the results of a comparative study of 42 patients with nonresponsive celiac disease matched by age and sex to 84 celiac disease-free controls, as well as retrospective evaluation in 30 patients with uncomplicated celiac disease.[24] Among nonresponsive cases, the overall sensitivity and specificity of CE for the detection of any degree of villous atrophy as graded by histology were 56% and 85%, respectively. Mucosal abnormalities were observed by CE in patients with both nonresponsive uncomplicated celiac disease and erosions/ulcerations of the gut were observed in 19% of nonresponsive celiac disease patients, 18% of controls, and 31% of patients with uncomplicated celiac disease ($p=0.35$). Importantly, two severe complications (ulcerative jejunitis and adenocarcinoma) were detected by CE in nonresponsive celiac disease patients.

Culliford (2005) published a case series evaluating 47 patients with complicated celiac disease.[25] Findings were consistent with celiac disease in 87%: atrophy (68%), fissuring (62%), and mosaic pattern (19%), extending to the ileum in 34%. Unexpected additional findings were observed in 60% of patients, most of which were ulcerations (45%), and also included cancer, polyps, submucosal mass, and ulcerated nodular mucosa.

Section Summary: 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. However, in cases where the diagnosis of celiac disease is equivocal, or when diagnosis with endoscopy with biopsy is not possible, there is evidence that CE can reveal morphologic changes in the small bowel consistent with celiac disease and studies of patients with unresponsive celiac disease undergoing CE have shown some yield of actionable diagnoses that have the potential to improve patient outcomes.

UNEXPLAINED CHRONIC ABDOMINAL PAIN

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

Systematic Reviews

Xue (2015) reported on a systematic review of 21 studies (n=1520 patients) evaluating CE for unexplained chronic abdominal pain.[26] The pooled diagnostic yield was 20.9% (95% confidence interval [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 the use of different tests before CE.

Nonrandomized Studies

Wang (2022) published a retrospective study on patients (n=80) with chronic and recurrent abdominal pain who underwent CE for diagnostics. They reported abnormal findings in 54 patients (67.5%) including small intestinal erosion and congestion, small intestinal ulcers, small intestinal parasites, small intestinal vascular malformations, small intestinal polyps, small intestinal diverticulum, and small intestinal lymphangiectasia.[27] The authors reported that there were no significant side effects for up to one month after capsule ingestion and that the capsule was evacuated by all patients.

In a study not included in the systematic review, Yang (2014) reported on a case series evaluating 243 patients with CE for unexplained chronic abdominal pain.**[28]** 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 (eg, small bowel tumor, ascariasis, anaphylactoid purpura).

Section Summary: Unexplained Chronic Abdominal Pain

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

ULCERATIVE COLITIS

The purpose of wireless CE for patients who have ulcerative colitis is to inform management decisions based on disease status. No peer-reviewed systematic reviews or randomized controlled trials of wireless CE in ulcerative colitis have been published.

Nonrandomized studies

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

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

Study	Study Type	Country	Dates	Participants	Treatment	Follow-Up
Shi (2017)[29]	Single-center prospective observational	China	2014-2016	Patients 18-80 y with UC requiring colonoscopy	150 patients underwent CE-2 and colonoscopy	NR

Study	Study Type	Country	Dates	Participants	Treatment	Follow-Up
San Juan-Acosta (2014)[30]	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 (2014)[31]	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 (2012)[32]	Prospective cohort	China and Singapore	2000-2008	Patients with suspected or known UC	100 patients underwent CE and same-day colonoscopy	NR

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

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

Study	Active Colonic Inflammation, %		PPV, %	NPV, %	Correlation Between Colon CE and Colonoscopy	
	Sensitivity[a]	Specificity			Disease Severity	Extent of Inflammation
Shi (2017)[29]						
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					<0.001	<0.001
San Juan-Acosta (2014)[30]						
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 (2014)[31]						
N	30	30	30			
% (95% CI)	96 (79 to 99)	100 (61 to 100)	100 (85 to 100)	85 (49 to 97)		
Sung (2012)[32]						
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 (2014), although the correspondence between the two methods was reasonably good, it is uncertain whether management changes based on one or the other test would result in similar or different patient outcomes.[30]

Oliva (2014) evaluated 30 patients with known ulcerative colitis with both CE and colonoscopy to assess disease activity.[31] The reference standard for disease activity was a Matts score greater than 6 as judged by colonoscopy. Although the two methods had a high concordance at this cutoff level of disease in this study, patient outcomes linked to these assessments of disease activity cannot be determined.

Section Summary: Ulcerative Colitis

Several diagnostic accuracy studies have compared CE with colonoscopy to assess disease activity in patients with ulcerative colitis. Two of the four studies were limited in their sample size (i.e., <50 patients) and thus data on diagnostic accuracy are limited. No RCTs assessing the clinical utility of wireless CE for ulcerative colitis were identified. Additional evidence is needed to determine the impact of CE on net health outcomes in patients with ulcerative colitis.

ESOPHAGEAL DISORDERS

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

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 (2011) evaluated nine studies comparing CE with traditional endoscopy for detecting esophageal varices and calculated a sensitivity of 83% and specificity of 85%.[33] A meta-analysis by Bhardwaj (2009) assessed nine studies comparing CE with traditional endoscopy for detecting Barrett esophagus and reported a sensitivity of 77% and specificity of 86%.[34] Because of the lower sensitivity and specificity, CE cannot substitute for traditional endoscopy nor can it be used to triage patients to endoscopy.

Section Summary: Esophageal Disorders

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

HEREDITARY GASTROINTESTINAL POLYPOSIS SYNDROMES

The purpose of wireless CE for patients who have hereditary GI polyposis syndromes is to inform management decisions based on disease status. Patients with familial adenomatous polyposis (FAP) and Peutz-Jeghers syndrome (PJS) are genetically at high-risk of small bowel polyps and tumors.

Fukushi (2023) utilized SBCE to investigate the genotype-phonotype correlation of small-intestinal polyps in patients with FAP.[35] Patients (n=41) who underwent SBCE,

Esophagogastroduodenoscopy (EGD), and adenomatous polyposis coli (APC) gene analysis were included in the study. More small-intestinal polyps were found in Spigelman stage III and IV groups than in the stage 0 group ($p<0.05$). The APC variant was negative for 6 patients (15%), and the sites associated with more than 5 small-intestinal polyps were codons 278, 1062, 1114, 1281, 1307, 1314, and 1504. The authors conclude that SBCE surveillance is potentially recommended for patients with pathogenic variants in the APC gene at codons 278 and 1062 to 1504 or with Spigelman stage III or higher.

Urquhart (2014) compared CE with MRE in 20 patients with PJS.[36] 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% PPV of finding a polyp on balloon enteroscopy with MRE versus 60% for CE. A study by Brown (2006) in 19 patients showed a greater number of polyps identified with CE than with barium follow-through examinations.[37] Mata (2005) studied the role of CE in 24 patients with hereditary GI polyposis syndromes, including familial adenomatous polyposis (n=20) or PJS (n=4).[38] Compared with barium studies using small bowel enteroclysis, CE identified four 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 (2015) evaluated 200 patients with Lynch syndrome who underwent CE.[39] Small bowel neoplasia was detected in the duodenum in two patients (one adenocarcinoma, one adenoma). These lesions would have been in the reach of a gastroduodenoscope. In a smaller study by Saurin (2010), 35 asymptomatic patients with Lynch syndrome underwent colon CE.[40] Small bowel neoplasms were diagnosed in three (8.6%) patients (one adenocarcinoma, two adenomas with low-grade dysplasia).

Section Summary: Hereditary Gastrointestinal Polyposis Syndromes

There is enough evidence that CE can identify additional lesions compared with other diagnostic methods in persons with hereditary polyposis syndrome including familial adenomatous polyposis and Peutz-Jeghers syndrome. Although studies have shown at least a low prevalence of small bowel neoplasms in Lynch syndrome, these data are insufficient to determine whether evaluation with CE would improve patient outcomes. Additional data on the prevalence and natural history of small bowel polyps in Lynch syndrome patients are necessary. At this time, surveillance of the small bowel is not generally recommended as a routine intervention for patients with Lynch syndrome.

PORTAL HYPERTENSIVE ENTEROPATHY

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

Systematic Reviews

Several systematic reviews relevant to wireless CE for portal hypertensive enteropathy, including a Cochrane review, have been published. Tables 14 and 15 summarize the characteristics and results of select systematic reviews.

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

Study	Dates	Trials	Participants	N (Range)	Design
McCarty (2017)[41]	2005-2015	17	Patients with portal hypertension	1328 (8 to 330)	NR
Colli (2014)[42]	2005-2014	16	Adults with cirrhosis	936 (NR)	Cohort

NR: not reported.

Table 15. 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 (2017)[41]						
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 (2014)[42]						
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.

Section Summary: Portal Hypertensive Enteropathy

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

ACUTE UPPER GASTROINTESTINAL TRACT BLEEDING

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

Randomized Controlled Trials

Sung (2016) reported on a prospective RCT to evaluate the use of CE in the emergency department for patients with suspected upper GI bleeding.[43] Capsule endoscopy was used to determine whether patients would be admitted to the hospital or sent home, versus an alternative strategy of admitting all patients. Eligible patients presented with signs and/or symptoms of acute upper GI bleeding but were without hemodynamic shock or conditions likely to preclude the use of the capsule endoscope. Seventy-one patients were randomized to CE in the emergency department (n=37), followed by monitoring for upper GI bleeding, or standard care (n=34), which included mandatory hospital admission. Seven CE patients with active bleeding or endoscopic findings were admitted, with the remainder discharged home. There were no deaths or morbid outcomes in either group, indicating that CE could result in equivalent patient outcomes with many patients safely avoiding emergency hospitalization.

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

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

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Sung (2016)[43]	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 (2013)[44]	U.S.	3	NR	Patients ≥18 y with history suggestive of acute UGIB ≤48 h prior to ED presentation	12 randomized to VCE prior to endoscopy	12 randomized to endoscopy

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

Table 17. Results of RCTs Assessing 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 (2016)[43]					
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 • 3 patients: 1 • 25 patients: ≥2	
SOC	• Peptic ulcer: 14 • 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 (2013)[44]					

Study	Active Bleeding or Endoscopic Findings, n	Hospitalization, n	Mortality, n	GBS Score	Agreement Between CE and EGD
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; SOC: standard of care; VCE: video capsule endoscopy.

The purpose of the limitations tables (see Tables 18 and 19) 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 the evidence supporting the position statement.

Table 18. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Sung (2016)[43]					
Gutkin (2013)[44]					

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 19. Study Design and Conduct Limitations

Study	Selection[a]	Blinding[b]	Delivery of Test[c]	Selective Reporting[d]	Data Completeness[e]	Statistical[f]
Sung (2016)[43]						3. As a feasibility study, confidence intervals and p values were not reported
Gutkin (2013)[44]					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.

Two 2013 studies with small cohorts of patients (range, 49 to 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.[45 46] These studies reported that CE provides useful information, such as identifying gross bleeding and inflammatory lesions in a substantial proportion of patients and in stratifying patients into high- or low-risk categories. However, the yield of CE in localizing the bleeding source was lower than for esophagogastroduodenoscopy, which is the standard initial evaluation for acute upper GI bleeding.

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

COLON CANCER SCREENING

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

Systematic Reviews

Several studies have assessed the accuracy of CE for detecting colonic lesions. Spada (2016) published a systematic review with meta-analysis of the diagnostic accuracy of CE for detecting colorectal polyps with stratified results for first- and second-generation capsules.[47] Across the 14 eligible studies, the indications for endoscopy included colorectal cancer screening (n=1261 [47%]), postpolypectomy surveillance or family history of colorectal cancer (n=636 [24%]), symptoms suggestive of cancer and/or fecal occult blood test positivity (n=619 [23%]), positive imaging tests (n=136 [5%]), or other indication (24 [1%]). 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%).

Kjolhede (2020) published a systematic review with meta-analysis of the diagnostic accuracy of CE compared to colonoscopy with stratified results for polyps of any size, polyps ≥ 6 mm, and polyps ≥ 10 mm.[48] 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 one 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 20 and 21, respectively.

Table 20. Characteristics of Systematic Reviews Assessing Capsule Endoscopy for Colon Cancer Screening

Study	Dates	Trials	N (Range)	Design	Outcome
Spada (2016)[47]	2006-2015	14	2681 (40 to 884)	Diagnostic accuracy studies	Per-patient sensitivity of CCE for different categories of polyp size and for cancer
Kjolhede (2020)[48]	2009-2020	12	2199 (20 to 884)	Diagnostic accuracy studies	Per-patient sensitivity of CCE for various polyp size thresholds

CCE: colon capsule endoscopy.

Table 21. Results of Systematic Reviews Assessing Capsule Endoscopy for Colon Cancer Screening

Random-Effects Model	Trials	N	Outcomes	Effect Size	95% CI	I^2, %
Spada (2016)[47]						
For ≥10 mm polyps	10	NR	Diagnostic accuracy for ≥10 mm polyps	Sens=80.0% Spec=96.2% PLR=18.6 NLR=0.22 DOR=90.4	66% to 90.3%; 94.0% to 97.6% 12.0 to 28.2 0.13 to 0.34 44 to 163	53.4 31.3
For ≥6 mm polyps	7	NR	Diagnostic accuracy for ≥6 mm polyps using 1st-generation CCE	Sens=58% Spec=85.7% PLR=3.7 NLR=0.51 DOR=7.4	44% to 70% 80.2% to 90.0%	65
For ≥6 mm polyps	6	NR	Diagnostic accuracy for ≥6 mm polyps using 2nd-generation CCE	Sens=86% Spec=88.1% PLR=7.9 NLR=0.16 DOR=50.5	82% to 89% 74.2% to 95.0% 3.7 to 16.1 0.12 to 0.21 20.3 to 107.0	0
For ≥10 mm polyps	3	NR	Diagnostic accuracy for ≥6 mm polyps using 1st-generation CCE	Sens=54% Spec=97.4% PLR=NR NLR=NR DOR=NR	29% to 77% 96.0% to 98.3%	76.2 0
For ≥10 mm polyps	6	NR	Diagnostic accuracy for ≥6 mm polyps using 2nd-generation CCE	Sens=88% Spec=95.3% PLR=NR NLR=NR DOR=NR	81% to 91% 91.5% to 97.5%	0 67
For ≥10 mm polyps	10	NR	Diagnostic accuracy for ≥10 mm polyps	Sens=80.0% Spec=96.2% PLR=18.6 NLR=0.22 DOR=90.4	66% to 90.3%; 94.0% to 97.6% 12.0 to 28.2 0.13 to 0.34 44 to 163	53.4 31.3
Kjolhede (2020)[48]						

Random-Effects Model	Trials	N	Outcomes	Effect Size	95% CI	I^2, %
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.

Nonrandomized Studies

Other studies have evaluated the diagnostic characteristics of CE, using subsequently performed colonoscopy as the reference standard.[49-52] Of note, the Cash (2021) study randomized patients to colon CE or CT colonography followed by optical colonoscopy.[52] In the Saito (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 (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%).[51] In the Cash (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.[52] 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.

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

The purpose of wireless CE for patients with evidence of GI bleeding of lower GI origin and major risks for colonoscopy or moderate sedation is to visualize the colon for the detection of polyps or other sources of lower GI bleeding and inform a decision to proceed to further treatment and testing.

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 (eg, hematochezia, positive fecal occult blood test [FOBT]). Study characteristics and results are described in Table 22 and 23.

Table 22. 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 (2017)[53]	FOBT-positive individuals participating in a CRC screening program in Denmark (N=253; median age, 64 y)	OC adjusted by any findings from all follow-up procedures; repeat colonoscopy was offered for suspected missed polyps	Polyps >9 mm within ±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 (2014)[54]	FOBT-positive individuals participating in a CRC screening program in Italy (N=54; age range, 50-69)	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 (2009[55]	Individuals with known or suspected colonic disease in Israel; 21% of patients had	OC	Polyps ≥6 mm and ≥10 mm within +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

Study	Study Population	Reference Standard	Threshold for Positive Index Test	Timing of Reference and Index Tests	Blinding of Assessors	Comments
	hematochezia or positive FOBT (N=104; mean age, 49.8)					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 23. 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 (2017)[53]						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 (2014)[54]						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 (2009)[55]						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 (2017) reported on FOBT-positive individuals participating in a colorectal cancer screening program in Denmark.[53] The reference standard consisted of 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. The CE completion rate was significantly lower than optical colonoscopy (p<.001), with only 50% of patients (n=126) having complete optical colonoscopy and CE investigations.

Rondonotti (2014) reported on FOBT-positive individuals participating in a colorectal cancer screening program in Italy.[54] Unblinded colonoscopy, integrating optical colonoscopy, computed tomography colonography, and CE results, was used as the reference standard. Investigations were completed in all patients with a positive likelihood ratio and negative likelihood ratio of 3.75 and 0.06 for CE, respectively.

Eliakim (2009) conducted a prospective, multicenter study evaluating CE compared to colonoscopy in individuals with known or suspected colonic disease.[55] Twenty-one percent of patients had hematochezia or positive FOBT. The majority of patients were referred for optical colonoscopy due to a 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 24 and 25.

Table 24. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Kobaek-Larsen (2017)[53]	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 patients.	1,3. Impact of findings on health outcomes not assessed. Predictive values not reported.	
Rondonotti (2014)[54]	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 (2009)[55]	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.	

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 25. Study Design and Conduct Limitations

Study	Selection[a]	Blinding[b]	Delivery of Test[c]	Selective Reporting[d]	Data Completeness[e]	Statistical[f]
Kobaek-Larsen (2017)[53]	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 (2014)[54]	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 (2009)[55]	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.

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 optical colonoscopy or moderate sedation. The studies are 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 one 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 CIs. While one study reported a higher sensitivity and specificity compared to optical colonoscopy versus the defined reference standard, a consistent reference standard was not applied to all patients and carried a low combined rate of complete optical colonoscopy 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

The purpose of wireless CE for patients with an incomplete colonoscopy after adequate preparation where a complete evaluation of the colon was not technically possible is to visualize the colon for the detection of polyps and inform a decision to proceed to further treatment and testing.

The comparator of interest is repeat optical colonoscopy. Repeat colonoscopy following a prior incomplete procedure may be modified with adjusted endoscopic techniques, pediatric instruments, abdominal pressure and position changes, water exchange and water immersion techniques, carbon dioxide insufflation, magnetic endoscope imaging, alternate sedation methods, anesthesia assistance, and management with more experienced physicians.[56]

Nonrandomized Studies

Havshoi (2022) published a prospective study comparing the quality of Colon Capsule Endoscopy (CCE), defined by completion rate (CR) and polyp detection rate (PDR), with that of CT colonography (CTC) and AA colonoscopy (AAC), respectively.[57] A total of 65 patients were included in the analysis (n=36 as an alternative to CTC and n=27 as an alternative to AAC). The PDR was 75% in CCE compared to 20% in CT colonography ($p < 0.001$) and 78% in CCE compared to 35% in AA colonoscopy ($p = 0.013$). The CCE completion rate was low in both groups: 44% compared to 96% in CTC ($p < 0.001$) and 33% compared to 100% in AAC ($p < 0.001$). The authors conclude The PDR of CCE was high, indicating an acceptable sensitivity in complete investigations, and that the CR of CCE on this indication is unacceptably low.

Additional prospective case series describing the diagnostic yield of CE following incomplete colonoscopy for various indications are summarized in Table 26. Study relevance, design, and conduct limitations are described in Table 27 and 28.

Table 26. 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 (2018)[58]	Patients aged ≥18 y who had an incomplete OC for reasons other than poor bowel preparation or suspected obstruction of the colonic lumen (N=50)	NR	> 6 mm or ≥ 3 polyps	Administered 90 min after IC	CE (any polyps): 19/50 (38) CE (significant polyps): 7/50 (14) CE + IC (any diagnosis): 37/50 (74)	CE: 38/50 (76) CE + IC: 42/50 (84)	CCE Findings (n): normal (13), polyps (19; 7/19 significant), inflammation (1), diverticular disease (1), angiodysplasia (1), cancer (1). 7 patients with significant polyps were referred for polypectomy, which detected 14 adenomas and hyperplastic polyps.
Baltes (2018)[59]	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%), hematochezia (15%), irregular stool (12%), abdominal pain (12%), colitis (5%), other reasons (12%)	≥ 6 mm 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 (2017)[60]	Patients aged ≥18 y who had an incomplete OC when cecal intubation was not achieved despite adequate bowel	NR	>6 mm or > 3 polyps	Within 72 hours in 8 cases of suspected CRC. During the	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

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
	preparation (N=96)			following week for all other patients.			modified the therapeutic approach.
Negreanu (2013)[61]	Patients who are at 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 >6 mm (5), ≥3 polyps (10), multiple colonic angiomas (2), newly discovered Crohn's 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 (2012)[62]	Patients with an indication for OC per the recommendations of the French National Authority	Abnormal transit (14), abdominal pain (22), anemia or overt bleeding (30), weight	>5 mm or ≥ 3 polyps	NR	CE (significant polyps, screening): 12/39 (30.8) [95% CI, 22.1 to 39.5]	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)

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
	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) contraindications to OC with anesthesia due to cardiovascular or respiratory disease (n=30) (N=107)	loss (2), CRC screening (39)			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]		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])

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

Table 27. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Hussey (2018)[58]	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 (2018)[59]	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 (2017)[60]	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 (2013)[61]	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 (2012)[62]	1,4. It is not clear whether detection of polyps was the primary goal of CE for symptomatic patients. Only		2. Not compared to a reference standard.	1,3. Impact of findings on health outcomes not assessed. Clinical validity outcomes	1. No follow-up with reference standard.

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
	a subset of study patients reported IC.			cannot be assessed.	

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 28. Study Design and Conduct Limitations

Study	Selection[a]	Blinding[b]	Delivery of Test[c]	Selective Reporting[d]	Data Completeness[e]	Statistical[f]
Hussey (2018)[58]	1. Selection not described.	1. No comparison to reference standard.		1. Not registered.		2. Comparison to other tests not reported.
Baltes (2018)[59]	1. Selection not described.	1. No comparison to reference standard.		1. Not registered.		2. Comparison to other tests not reported.
Nogales (2017)[60]		1. No comparison to reference standard.		1. Not registered.		2. Comparison to other tests not reported.
Negreanu (2013)[61]	1. Selection not described.	1. No comparison to reference standard.		1. Not registered.		2. Comparison to other tests not reported.
Pioche (2012)[62]	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.

Section Summary: Incomplete Colonoscopy

No randomized controlled 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 one study. Successful CE completion rates were low (range, 33% to 83.2%) with three out of five studies reporting full visualization of the colon for combined CE and 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.

PATENCY CAPSULE

The purpose of the patency capsule is to inform the decision to proceed to CE by confirming adequate patency of the gastrointestinal tract in patients with known or suspected strictures.

Systematic Review

Wang (2021) published a systematic review with meta-analysis of the pooled rates, predictors, and temporal-trend of video capsule endoscopy (VCE) adverse events.[63] The review included data from 402 studies, including 108,079 VCE procedures. Most studies were observational (360 [89.55%]; including 156 prospective and 204 retrospective studies), forty-two (10.45%) studies were RCTs. Egger's test did not indicate the existence of obvious publication bias for retention rate (p=0.6063), incomplete examination rate of esophagus (p=0.7632), small bowel (p=0.1315), and colon (p=0.1393), however, the rate of stomach incomplete examination (p=0.0017), swallow disorder (p<0.0001), aspiration (p<0.0001), technical failure (p<0.0001), and procedural adverse events (p<0.0001) showed significant asymmetry. The authors found that a patency capsule reduced retention rate by 5.04% (95% CI − 8.75% to − 1.33%, p=0.0077). While these data suggest patency capsule before VCE in patients with a high-risk of retention may be useful to avoid retention, the authors note not all patients undergoing VCE should be offered a patency capsule since several complications have been reported, including small bowel obstruction and perforation.

Nonrandomized studies

Ukashi (2022) published a post-hoc analysis of two prospective cohort studies of adult patients with quiescent small-bowel CD that underwent PC between 2013 and 2020.[64] A total of 190 patients were included (47-failed PC, 143-passed PC, median follow-up 34.12 months) The primary composite-outcome was the need for intestinal surgery or endoscopic-dilation during follow-up with or without failed PC. Patients with a failed-PC had higher rates of the primary composite-outcome (21.3% vs. 1.4%, Hazard ratio [HR] 20.3, 95% confidence interval [CI] 4.4 to 93.7, p<0.001) and also secondary outcomes including intestinal-surgery (14.9% vs. 0.70%, p<0.001), endoscopic-dilation (14.9% vs. 0.70%, p<0.001), admissions (23.3% vs. 5.7%,

p<0.001) and clinical-flares (43.9% vs. 27.7%,p=0.005) during follow-up compared with controls. The authors conclude that clinically stable CD patients with failed-PC have worse long-term clinical outcomes than those without, independently of CD phenotype.

A prospective, multicenter study of a patency capsule to preclude subsequent small bowel capsule endoscopy (SBCE) retention in 1096 patients with suspected or established small bowel stenosis was published by Nakamura (2021).[65] Patency was confirmed in 976 (89.1%) of the patients and capsule excretion occurred in 579 patients. Of the remaining 517 patients, patency was confirmed using imaging in 401 (77.5%). SBCE retention occurred in five (0.51%) of 963 patients who underwent SBCE. Non-confirmation of patency was associated with established Crohn's disease, stenosis, abdominal fullness, serum albumin levels <4.0 g/dL, and previous small bowel obstruction (adjusted odds ratios: 4.21, 2.60, 2.47, 2.12, and 2.00; 95% confidence intervals: 2.62 to 6.78, 1.62 to 4.17, 1.43 to 4.27, 1.32 to 3.40, and 1.15 to 3.47, respectively).

Spada (2007) reported findings for 27 patients, 24 with CD.[66] In this study, 25 (92.6%) patients retrieved the patency capsule in their stools. Six patients complained of abdominal pain, four of whom excreted a nonintact capsule, and hospitalization was required in one patient due to the occlusive syndrome.

Delvaux (2005) reported findings in 22 patients with suspected intestinal stricture, 15 of whom had CD.[67] 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 three patients, the delay in the progression of the patency capsule led to the cancellation of CE. In three patients, the patency capsule induced a symptomatic intestinal occlusion, which resolved spontaneously in one and required emergency surgery in two. The authors commented that the current technical development of the patency capsule limits its use in clinical practice, because it did not detect stenoses undiagnosed by CT or small bowel follow-through, and the start of dissolution at 40 hours after ingestion is too slow to prevent episodes of intestinal occlusion. They also commented that a careful interview eliciting the patient's history and symptoms remains the most useful indicator for suspicion of an intestinal stenosis.

Several studies have shown that patients who had an uncomplicated passage of the patency capsule subsequently underwent uncomplicated CE.[68-70] These patients often had significant findings on CE.[68 69] However, it is difficult to determine whether CE findings in these patients improved their outcomes beyond any alternative testing regimen available. In one of these studies, three of 106 patients had severe adverse events, including one patient who required surgery.[68]

Section Summary: Patency Capsule

The use of the patency capsule has some associated risk. Published studies are small and do not provide comparative data on the incremental value of this capsule over standard clinical evaluation. In some series, the administration of the patency capsule has produced adverse events including symptoms requiring hospitalization and surgery.

MAGNETIC CAPSULE ENDOSCOPY FOR UNEXPLAINED UPPER ABDOMINAL COMPLAINTS

The purpose of magnetic CE for patients who have unexplained upper abdominal complaints is

to confirm a diagnosis and inform a decision to proceed to appropriate treatment.

Diagnostic Accuracy Studies

Denzer (2015) prospectively evaluated a magnetically guided gastric capsule as compared to conventional gastroscopy in 189 patients with upper abdominal complaints (eg, upper abdominal pain and/or anemia) from two centers.[71] In this study, capsule gastroscopy was performed initially followed by conventional gastroscopy, with a maximum delay of one day but a minimum delay of four 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 (eg, 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 (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.[72] All patients underwent magnetic CE followed by conventional gastroscopy two 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 five 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 29 and 30) 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 29. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Denzer (2015)[71]	4. Study population non-U.S. (conducted in France)			1. Sensitivity is low with a wide confidence interval	
Liao (2016)[72]	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 30. Study Design and Conduct Limitations

Study	Selection[a]	Blinding[b]	Delivery of Test[c]	Selective Reporting[d]	Data Completeness[e]	Statistical[f]
Denzer (2015)[71]	1. Selection of patients not clearly described	1. Final gold standard of conventional gastroscopy with biopsy was unblinded				
Liao (2016)[72]	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.

Section Summary: Magnetic Capsule Endoscopy for 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.

OPTICAL SENSOR CAPSULE FOR PATIENTS WITH SUSPECTED UPPER GASTROINTESTINAL BLEEDING

The purpose of an optical sensor capsule is to detect upper gastrointestinal bleeding. The PillSense™ capsule is a single-use digestible capsule that uses wirelessly transmitted light absorption data to provide a yes/no blood detection readout. It is designed to be a simpler, more cost-effective alternative to image-based capsule endoscopy.

Diagnostic Accuracy Studies

Akiki (2024) published a prospective, open-label, single-arm manufacturer-sponsored study of the PillSense System™ for diagnosing upper GI bleeding.[73] The study included 126 patients with suspected upper GI bleeding. The capsule's performance was compared with EGD findings performed within four hours of ingestion. Among 124 evaluable patients, the PillSense System™ detected blood with 92.9% sensitivity and 90.6% specificity compared with EGD, exceeding the performance goals of 75% and 60% respectively. The positive predictive value was 74.3%, and the negative predictive value was 97.8%. Capsule passage was confirmed in 87.3% of patients with a mean transit time of 3.6 days. No adverse events related to the device were reported. This study is limited by high loss to follow-up, leaving capsule passage unconfirmed in 12.7% of participants and a small sample size in the “with blood” group (n=28 patients). In addition, the study excluded patients with certain GI disorders (e.g., strictures, dysmotility), limiting generalizability of this technology.

PRACTICE GUIDELINE SUMMARY

AMERICAN COLLEGE OF GASTROENTEROLOGY

The American College of Gastroenterology (ACG) published colorectal cancer screening clinical guidelines in 2021.[74] They provide the following conditional recommendation (very low quality of evidence):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].

In 2023, ACG issued updated guidelines on the diagnosis and management of celiac disease.[75] The guideline does not mention the use of capsule endoscopy (CE) at any stage of the diagnosis or treatment in patients with celiac disease. These guidelines were updated from those of 2013, which stated 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). Capsule

endoscopy should be considered for the evaluation of small bowel mucosa in patients with complicated celiac disease (strong recommendation, moderate level of evidence)."[76]

In 2018, the ACG updated its guideline on the management of Crohn's disease in adults.[77] The guideline provides recommendations specific to video capsule endoscopy, which states, "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." The guideline also states, "some studies have questioned the specificity of capsule endoscopy findings for CD, and to date there is no consensus as to exactly which capsule endoscopy findings constitute a diagnosis of CD."[77]

In 2015, the ACG issued a guideline on the diagnosis and management of small bowel bleeding (including using "small bowel bleeding" to replace "obscure GI [gastrointestinal] bleeding," which should be reserved for patients in whom a source of bleeding cannot be identified anywhere in the GI tract).[78] The guideline made the following statements related to video CE (Table 31).

Table 31. 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.

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.[79] These guidelines made the following recommendations on capsule endoscopy (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.

AMERICAN GASTROENTEROLOGICAL ASSOCIATION (AGA) INSTITUTE

In 2025, the AGA released a clinical practice update and expert review for nonampullary duodenal lesions: Expert Review. [80] They recommend that routine small bowel investigation (i.e., capsule endoscopy) is not advised in patients with sporadic and nonsporadic duodenal adenomas. Periodic small bowel inspection with capsule endoscopy may be of benefit in patients with Peutz-Jeghers syndrome (Practice advice 5).

In 2017, the American Gastroenterological Association Institute issued guidelines on the use of CE.[81] Table 33 summarizes the most relevant recommendations (not all recommendations are included).

Table 33. AGA 2017 Capsule Endoscopy Recommendations

Stmt No.	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 hematemesis) 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 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 Gastroenterology Association; CD: Crohn's disease; CE: capsule endoscopy; EGD: esophagogastroduodenoscopy; GI: gastrointestinal; IBD: inflammatory bowel disease; QOE: quality of evidence; Stmt: statement.

The AGA institute issued updated practice guidelines (2022) on the management of refreactory celiac disease.[82] The guidelines recommend to perform small bowel imaging with CE and computed tomography or magnetic resonance enterography to exclude enteropathy-associated T-cell lymphoma and ulcerative jejunoileitis at initial diagnosis of type 2 refractory celiac disease.

U.S. MULTI-SOCIETY TASK FORCE

The U.S. Multi-Society Task Force (2021) issued recommendations for colorectal cancer screening with representation from the American College of Gastroenterology, the American Gastroenterological Association, and The American Society for Gastrointestinal Endoscopy.[83 84] Capsule endoscopy every five 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)."

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF) published its most recent recommendations for colorectal cancer screening in 2021.[85] 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.

NATIONAL COMPREHENSIVE CANCER NETWORK (NCCN)

The NCCN Genetic/Familial High-Risk Assessment: Colorectal Guidelines (v.4.2024) state the following regarding capsule endoscopy:[86]

- Familial Adenomatous Polyposis: High level evidence to support routine small bowel screening distal to the duodenum is lacking. However, may consider small bowel visualization (e.g. capsule endoscopy), especially if advanced duodenal polyposis.
- Peutz- Jeghers Syndrome: Small bowel visualization (video capsule endoscopy or CT/MRI enterography) every 2-3 years. Shorter intervals may be indicated based on polyp size, number, and pathology.
- Endoscopic duodenal surveillance based on modified Spigelman score and stage:
    - Small bowel evaluation with capsule endoscopy or CT/MRI enterography may be considered prior to surgical management of duodenal findings to identify large lesions that might modify the surgical approach.
    - Utility of routine small bowel surveillance (such as with capsule endoscopy or enterography) has not been proven, but may be considered in patients at high risk (eg, history of advanced duodenal polyps, history of duodenal/ampullary cancer).

The NCCN Guidelines for Small Bowel Adenocarcinoma (v.3.2025) state the following regarding capsule endoscopy:[87]

- Consider when radiographic imaging and other forms of endoscopy fail to reveal a suspected primary lesion. This is not the preferred primary method for diagnostic workup due to inability to obtain tissue for diagnosis. Contraindicated where small bowel obstruction or strictures exist.
- While capsule endoscopy allows for a more detailed examination of the entire small bowel mucosa, possibly resulting in the diagnosis of SBA when other imaging methods

have failed to reveal a primary lesion, it is not the preferred method for initial workup due to its inability to biopsy tissue for diagnosis. In the case of a small bowel obstruction or stricture, the capsule may not be excreted naturally, requiring surgical removal. Therefore, capsule endoscopy is contraindicated for these conditions.

- Routine capsule endoscopy is not indicated for surveillance.

SUMMARY

WIRELESS CAPSULE ENDOSCOPY

Suspected small bowel bleeding

For individuals with recurrent, obscure gastro-intestinal bleeding who have suspected small bowel bleeding, there is enough evidence to show that wireless capsule endoscopy (CE) can locate the source of bleeding at least as well as other diagnostic methods and direct treatment to the source of bleeding when prior upper and lower gastrointestinal (GI) endoscopic studies are inconclusive. Clinical guidelines based on research recommend CE for selected individuals who have suspected small bowel bleeding. Therefore, wireless capsule endoscopy (CE) may be considered medically necessary for individuals with recurrent, obscure gastro-intestinal bleeding who have suspected small bowel bleeding when prior upper and lower gastrointestinal (GI) endoscopic studies are inconclusive. In all other situations, there is not enough research to show that CE improves health outcomes for people with suspected small bowel bleeding and is therefore considered investigational.

Crohn’s disease (CD)

For individuals who have suspected small bowel Crohn’s disease (CD) who receive wireless capsule endoscopy (CE), there is enough evidence to show that diagnostic yields are as good as or better than other diagnostic options, and these data are likely to improve health outcomes by identifying some cases of CD and directing specific treatment. Clinical guidelines based on research recommend CE for individuals who have suspected small bowel CD in these cases. Therefore, wireless capsule endoscopy (CE) may be considered medically necessary for the initial diagnosis of suspected Crohn's disease when clinical signs of Crohn’s disease are present and there is not evidence of disease on conventional diagnostic tests.

For individuals who have an established diagnosis of Crohn’s disease (CD) and there are unexpected change(s) in the course of disease or response to treatment who receive wireless capsule endoscopy (CE), there is evidence that the diagnostic yields are as good as or better than other diagnostic options. Clinical guidelines based on research recommend CE for individuals who have suspected small bowel CD in certain scenarios. Therefore, CE may be considered medically necessary in individuals who have an established diagnosis of CD and there are unexpected change(s) in the course of disease or response to treatment.

In all other situations, there is not enough research to show that CE improves health outcomes for people with suspected or established Crohn’s disease and is therefore considered investigational.

Hereditary GI polyposis syndromes

There is enough evidence that wireless capsule endoscopy (CE) can identify additional lesions compared with other diagnostic methods in individuals with hereditary GI polyposis syndromes including familial adenomatous polyposis and Peutz-Jeghers syndrome. Clinical guidelines based on research recommend CE in patients with hereditary GI polyposis syndromes. Therefore, wireless CE may be considered medically necessary in individuals with hereditary GI polyposis syndromes including familial adenomatous polyposis and Peutz-Jeghers syndrome.

Celiac disease

Small bowel biopsy, celiac serologies, and human leukocyte antigen typing remain the standard tests for confirming celiac disease. However, in cases where the diagnosis of celiac disease is equivocal, there is enough evidence that wireless capsule endoscopy (CE) can reveal morphologic changes in the small bowel consistent with celiac disease and studies of patients with unresponsive celiac disease undergoing CE have shown some yield of actionable diagnoses that have the potential to improve patient outcomes. Clinical guidelines based on research recommend CE for patients with celiac disease in certain scenarios. Therefore, CE may be considered medically necessary in individuals with clinical evidence of celiac disease and positive celiac-specific serology who are unable to undergo upper endoscopy with biopsy and for re-evaluation of individuals with celiac disease who remain symptomatic despite treatment. In all other situations, there is not enough research to show that CE improves health outcomes for people with celiac disease and is therefore considered investigational.

Esophageal disorders

There is not enough research to show that evaluation of the esophagus with wireless capsule endoscopy (CE) improves health outcomes for individuals with gastroesophageal reflux or other esophageal pathologies. Clinical guidelines based on research do not recommend evaluation of the esophagus with CE in patients with gastroesophageal reflux or other esophageal pathologies. Therefore, wireless capsule endoscopy is considered investigational for these patients.

GI diseases and conditions when policy criteria are not met

There is not enough research to show that wireless capsule endoscopy (CE) improves health outcomes for the evaluation of GI diseases and conditions when policy criteria are not met, including but not limited to: irritable bowel syndrome, hereditary *non*polyposis syndromes (including but not limited to Lynch syndrome), small bowel neoplasm, portal hypertensive enteropathy, lower GI tract bleeding, incomplete colonoscopy, and unexplained chronic abdominal pain. Clinical guidelines based on research generally do not recommend CE for patients with these conditions. Therefore, CE is considered investigational for the evaluation of GI diseases and conditions when policy criteria are not met.

Colon Cancer Screening

There is not enough research to show that wireless capsule endoscopy (CE) improves health outcomes when used to screen for colon cancer and there is evidence that the diagnostic performance of CE is worse than standard colonoscopy. Clinical guidelines based on research either recommend against the use of CE for colon cancer screening or provide a

weak recommendation based on low-quality evidence. Therefore, CE is considered investigational for colon cancer screening.

Acute Upper Gastrointestinal Bleeding

There is not enough research to show that wireless capsule endoscopy (CE) improves health outcomes for individuals who have acute upper GI tract bleeding. Clinical guidelines based on research do not recommend CE for acute upper GI tract bleeding. Therefore, CE is considered investigational for acute upper GI tract bleeding.

Patency Capsule for Patients with Bowel Stricture

There is not enough research to show that the use of patency capsules prior to wireless capsule endoscopy improves net health outcomes for patients. While the available studies have reported that endoscopy following a successful patency capsule test results in high rates of success with low rates of adverse events, the patency capsule is also associated with adverse events including small bowel obstruction and perforation. 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. Therefore, the use of patency capsules is considered investigational.

Magnetic Capsule Endoscopy for Patients with Suspected Gastrointestinal Disorders

There is not enough research to show that magnetic capsule endoscopy improves health outcomes for any indication. No clinical guidelines based on research recommend magnetic capsule endoscopy for any indication. Therefore, magnetic capsule endoscopy is considered investigational for all indications.

Optical Sensor Capsule for Patients with Suspected Upper Gastrointestinal Bleeding

There is not enough research to show that an optical sensor capsule improves health outcomes for any indication. No clinical guidelines based on research recommend an optical sensor capsule for any indication. Therefore, an upper gastrointestinal optical sensor capsule is considered investigational for all indications.

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CODES

Codes	Number	Description
CPT	0651T	Magnetically controlled capsule endoscopy, esophagus through stomach, including intraprocedural positioning of capsule, with interpretation and report
	0977T	Upper gastrointestinal blood detection, sensor capsule, with interpretation and report
	91110	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy) esophagus through ileum, with interpretation and report
	91111	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), esophagus, with interpretation and report
	91113	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), colon, with interpretation and report
	91299	Unlisted diagnostic gastroenterology procedure
HCPCS	None	

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