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Number XX

Wireless Motililty Capsule Versus Other Diagnostic Technologies for Evaluating Gastroparesis and Constipation: A Comparative Effectiveness Review

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the State Children's Health Insurance Program (SCHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting Comparative Effectiveness Reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see http://effectivehealthcare.ahrq.gov/reference/purpose.cfm

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

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Structured Abstract

Objectives: To systematically review the evidence comparing wireless motility capsule (WMC) to other diagnostic tests used for the evaluation of gastroparesis and slow-transit constipation in terms of diagnostic accuracy, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization.

Data sources: Medline® and EMBASE® from inception through January 2012. Additionally, we scanned reference lists of relevant articles and queried experts.

Review methods: We included studies in any language that compared WMC with other diagnostic tests among patients with suspected gastroparesis or slow-transit constipation. Two reviewers independently assessed articles for eligibility, serially abstracted data from relevant articles, independently evaluated study quality, and graded the strength of the evidence (SOE). We summarized results qualitatively rather than quantitatively because of the heterogeneity of studies.

Results: We included 11studies (17 publications). Seven studies evaluated diagnosis of gastric emptying delay; we found low SOE that WMC alone was comparable to scintigraphy for diagnostic accuracy, motility assessment, treatment decisions, and resource utilization. Sensitivity of WMC compared with gastric scintigraphy ranged from 59 to 86 percent and specificity ranged from 64 to 81 percent. We found two studies evaluating WMC as an add-on to other testing. The SOE was low for diagnostic accuracy and motility assessment of WMC in combination with other modalities. The addition of WMC increased diagnostic yield. Nine studies analyzed colon transit disorders and provided moderate SOE for diagnostic accuracy, motility assessment, and harms. WMC was comparable to radiopaque markers (ROM), with concordance ranging between 64% and 87%. Few harms were reported. The evidence was insufficient to draw conclusions about effects of WMC on treatment decisions and resource utilization. No studies directly assessed use of WMC in combination with other tests to detect colon transit delay.

Conclusions: WMC is similar to current modalities in use for detection of slow-transit constipation and gastric emptying delay, and therefore is another viable diagnostic modality. Little data is available to determine the optimal timing of WMC in diagnostic algorithms.

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Executive Summary

Introduction

Gastroparesis

Definition and Prevalence

Gastroparesis is a condition in which patients experience symptoms of delayed gastric emptying in the absence of an actual physical blockage.[1] The most common symptoms are nausea, vomiting, early satiety, bloating, abdominal pain, and postprandial fullness.[2] Detection of gastric emptying delay is the essence of diagnosing gastroparesis. For clinical research, gastroparesis has been defined as delayed gastric emptying as detected by clinical testing and the presence of symptoms of nausea and/or vomiting, postprandial fullness, early satiety, bloating, or epigastric pain for more than 3 months. Using this definition, the cumulative incidence of gastroparesis is 4.8 percent in people with type 1 diabetes, 1.0 percent in people with type 2 diabetes, and 0.1 percent in people without diabetes but who may have idiopathic gastroparesis or other etiologies.[2] The prevalence of gastroparesis was estimated by a community-based study in 2007 to be 9.6 per 100,000 for men and 37.8 per 100,000 for women.[2]

Etiology and Clinical Course

The etiologies of gastroparesis are most often idiopathic, diabetic, or postsurgical but can also be autoimmune, paraneoplastic, or neurologic. Assessment usually takes place in the outpatient setting, but some patients become severely ill with intractable vomiting and dehydration and must be admitted to the hospital. Hospitalizations for gastroparesis increased by 158 percent between 1995 and 2004.[3] In individuals with diabetes and gastroparesis, digestion of food is unpredictable, and wild swings in blood glucose can require medical care and increase morbidity.

Evaluation of Possible Gastroparesis

Standard assessment for patients with typical symptoms (nausea, vomiting, bloating, abdominal pain, early satiety) of gastroparesis begins with exclusion of mechanical causes of disease. A typical assessment starts in the office of a physician, where a careful medical history is taken and a physical examination is performed.[4] If mechanical disease it not suspected, then exclusion of medication-induced symptoms must be performed. Delay of gastric emptying is commonly caused by the use of certain medications, such as narcotics or glucagon-like peptide agonists. Methods of testing include gastric emptying scintigraphy, antroduodenal manometry, and now wireless motility capsule technology.

Gastric Scintigraphy

Gastric scintigraphy is the ingestion of a meal commonly standardized to toast, jam, juice, and radiolabeled eggs, which are visible on passage through the gastrointestinal tract during subsequent timed imaging, ideally 4 hours.[5] Interfering medications such as narcotics, motility agents, and glucagon-like peptide agonists are withheld for 5 to 7 days before scintigraphic testing. Full 4-hour testing is more commonly available at regional referral centers or tertiary care centers with established practices of motility specialists.[5] Generally, delayed gastric

emptying is confirmed if less than 90 percent of the gastric content has emptied at 4 hours, meaning that more than 10 percent of the content was retained.

Antroduodenal Manometry

Antroduodenal manometry can provide information about gastric physiology. With a manometry catheter inserted through the pyloric channel, via endoscopic guidance and sedation of the patient, pressure measurements are captured. Antroduodenal manometry may help differentiate myopathic and neuropathic etiologies of symptoms. Myopathy is present if amplitude muscle pressures of less than 30 mmHg are documented, and neuropathy is present if discoordinated bursts of muscle activity are detected.

Wireless Motility Capsule

The wireless motility capsule has been approved by the U.S. Food and Drug Administration (FDA) for identifying motility disorders. This device is a portable, ingestible capsule that, when swallowed, records and transmits data to a receiver as it travels through the gut. The capsule can measure pH, pressure, and temperature to track location, gastric contents, and expellation time from different regions of the bowel. It has been recommended by the American Neurogastroentrology and Motility Society (ANMS) and designated a technology to be watched by the American College of Gastroenterology (ACG). The capsule is a one-time use device that is activated and then swallowed by the patient who has symptoms suggestive of gastric emptying delay. The patient takes the pill after eating a standardized meal and wears a small monitor that allows telemetry recordings to be made. A cutoff point for gastric emptying time has been established to be 300 minutes.[6] Disadvantages of the capsule include failure of the capsule to capture data (requiring repeat testing), delay or total failure of the capsule to pass (requiring serial x-rays to document passage or endoscopic or surgical removal, respectively), and inability to use the capsule for anyone with a possible stricture, altered anatomy, or severe pyloric stenosis.[7] Patients must be able to tolerate stopping proton pump inhibitors and histamine 2 blockers before testing.[7] Advantages include that it is wireless and painless, without radiation.[8, 9]

Use of Gastric Emptying Testing To Guide Treatment

Documentation of gastric emptying delay guides physicians in their recommendations for nutrition, medication, and surgical therapies. Testing can also inform physicians about the length and severity of delay; thus, changes in diet can be made to accommodate better gastric emptying. Recommended changes in diet may include a low-fat diet, a low-residue diet (low fiber, easy to digest), a liquid diet, or increasing consumption to multiple small meals per day. Prokinetic treatment, like erythromycin, is often used to treat patients who have documented gastroparesis. Patients decide about using prokinetics such as oral, intravenous, and sublingual preparations of metoclopramide, based on the confirmation of gastroparesis with testing. This is important to patients because there is an FDA black box warning about the side effects of metoclopramide when used beyond 3 months. Some research protocols involve the use of domperidone (Motilium®), which is not FDA-approved but is available in many countries outside the U.S. and can be used in clinical care and research in the U.S. through an Investigational New Drug Application. Patients with severe symptoms and severe emptying delay despite dietary changes may need feeding tubes such as jejunostomy or gastrojejunostomy tubes that bypass the stomach entirely. As patients undergo consideration for compassionate use of gastric stimulation therapy,

one of the eligibility criteria is the presence of gastric emptying delay on testing. Thus, accurate diagnosis of gastroparesis is integral to decisions about management.

Outcomes

Major outcomes of interest are assessment of motility and diagnosis of gastric emptying delay. Other outcomes include the ability of testing to influence treatment decisions by changes in medications or nutrition or to affect patient-centered outcomes such as symptom improvement, need for surgery, quality of life, and patient satisfaction. It is important to consider potential harms of testing such as capsule retention, radiation exposure, and mortality. Clinicians and policymakers may also be interested in the effects on resource utilization such as the need for additional tests, physician services, or hospitalizations.

Constipation

Definition and Prevalence

Constipation is common, occurring in 15 to 20 percent of the U.S. population.[7, 10, 11] The definition of constipation has been established with slight variation by multiple professional societies, but usually constipation is defined as fewer than two bowel movements per week or a decrease in a person's normal frequency of stools that is accompanied by straining, difficulty passing stool, or passage of hard solid stools.[7] Patients with symptoms of constipation must be assessed by their medical history and a physical examination to exclude malignant or organic causes of constipation. Clinicians should ask about warning signs such as new onset of symptoms, obstructive symptoms, rectal bleeding, unintentional weight loss, or family history of early colon cancer. A rectal examination can help to delineate rectal function and tone and exclude a low rectal cancer. Investigation with colonoscopy is indicated if fecal occult blood or iron deficiency anemia are detected. Patients with symptoms of constipation and warning signs should be investigated with colonoscopy, as should all patients over 50 years of age who have never received a screening colonoscopy;[12] however, the yield of colonoscopy in patients with constipation with warning signs is low. Once organic causes of constipation are excluded, a diagnosis of functional constipation can be made. For individuals who are less than 50 years of age without "red flag" symptoms, no testing is required to make a diagnosis of constipation if they meet the Rome III criteria. The Rome III criteria define functional constipation as follows:[13]

- Must include *two or more* of the following:
  a. Straining during at least 25 percent of defecations
  b. Lumpy or hard stools in at least 25 percent of defecations
  c. Sensation of incomplete evacuation for at least 25 percent of defecations
  d. Sensation of anorectal obstruction/blockage for at least 25 percent of defecations
  e. Manual maneuvers to facilitate at least 25 percent of defecations (e.g., digital evacuation, support of the pelvic floor)
  f. Fewer than three defecations per week
- Loose stools are rarely present without the use of laxatives
- Insufficient criteria for irritable bowel syndrome

Two or more of the above criteria must be fulfilled for the last 3 months, with symptom onset being at least 6 months prior to diagnosis.

Clinically, patients with slow-transit constipation, also known as colonic inertia, often have the most severe symptoms of those patients with constipation, with prolonged periods of time

between bowel movements. Often, standard medical therapies have failed these patients. Slow-transit constipation is defined as retention of greater than six radiopaque markers after 5 days from ingestion.[7, 14] Reported incidence of slow-transit constipation is 1 in 3000. Other studies list an incidence of 0.17 percent.[15] The true incidence is likely unknown.

Etiology and Clinical Course

There are several types of chronic constipation including slow-transit, normal-transit and dyssynergic defecation. Alternatively, there is constipation-predominant irritable bowel syndrome.[7] Lifestyle changes and medical management should be used for all patients with symptoms of constipation. Lifestyle changes include drinking appropriate quantities of liquid, removing all possible offending medications, and eating a sufficient amount of vegetables, fruit, and fiber as recommended by the U.S. Department of Agriculture. Medical management includes avoiding constipating medications and initiating bulking agents (fiber supplements), stool softeners (Colace®, mineral oil), osmotic and stimulant laxatives (lactulose, milk of magnesia, magnesium citrate, senna, Dulcolax®), or prokinetics (such as prucalopride, which is not yet FDA-approved, but available in Europe and elsewhere) as indicated. Thus, the initial evaluation of constipation symptoms does not often involve colonic transit testing.

Evaluation of Possible Slow-Transit Constipation

For certain individuals with suspected slow-transit constipation, colon transit testing can provide insight into the etiology of the constipation. Testing can be used to explain the patient who fails basic therapy and thus assist in identifying or excluding patients as surgical candidates.[7] It is most strongly indicated for anyone considering colon resection or surgery. Transit disorders include slow colonic transit or colonic inertia, a hypomotile disorder of the colon where transit in the proximal colon is slow without evidence of retropulsion of the markers from the left colon and without evidence of anorectal dysfunction. Defecatory dysfunction (or functional outlet dysfunction) is the presence of discoordinated motion of the anorectum muscles causing ineffective or weak expulsion of stool. Idiopathic megacolon (primary or secondary), a pathological enlargement of the colon, can also be present and may occur in conjunction with longstanding neurological diseases or Hirschsprung's disease, a failure of the development of the nerve cells within the colon wall.[16] The main diagnostic methods used to test for colonic motility are radiopaque marker examination, colonic scintigraphy, colonic and anorectal manometry, and wireless motility capsule testing.[17, 18] The reference standard has been radiopaque markers.

Radiopaque Markers

Slow-transit constipation is defined by the reference standard of radiopaque marker testing (commonly known as Sitz Markers).[17, 18] In its simplest form, such testing is performed by having the patient ingest the radiopaque markers on day 0 and then taking x-ray images at intervals to document the excretion of those markers by 5 days after ingestion. Retention of markers after the initial observation period allows identification of patients with slow transit and focuses on the area of the colon that has the greatest delays.[7, 14] One disadvantage to radiopaque marker testing is x-ray exposure. However, the test has been validated and in use since the late 1960s.[14]

Colonic Scintigraphy

Colon scintigraphy is rarely available outside of highly specialized motility research centers. It involves ingestion of a radiolabeled meal or radiolabeled tracer to follow the sequence of transit from the upper to lower gastrointestinal tract. A disadvantage of colonic scintigraphy is that testing requires several days and requires radiation exposure. Studies have assessed the validity relative to radiopaque markers.[19, 20] The ANMS guidelines endorse colon scintigraphy as a potential test for evaluating colon transit.

Wireless Motility Capsule

Wireless motility capsule testing can assess colonic transit. Cecal entry is defined as a sustained drop in pH of greater than 1 unit that occurs more than 30 minutes after gastric emptying. Colonic transit time is the time between cecal entry and rectal exit. Transit time within the colon can be calculated from the cecal entry time until the capsule exits the body, which is marked by a large temperature reduction.[7] One disadvantage is that 5 percent of patients undergoing capsule testing may not collect cecal entry time data, thus limiting the diagnostic potential of the study.[14] Other disadvantages are that radiographic imaging must be used to confirm elimination of the capsule when it fails to pass spontaneously and that the device can fail at a rate up to 3 percent in some studies. In addition, prolonged colon transit time with this technology does not necessarily distinguish slow transit from defecatory dysfunction.

Use of Colon Transit Testing to Guide Treatment

Most patients with chronic constipation have improvement of symptoms with medical therapy and/or lifestyle changes. For some patients, all measures fail and their motility disorders may be identified with colon transit testing. When anorectal or outlet dysfunction is identified, biofeedback therapy can be used for treatment. Evidence of Hirschsprung's disease is an indication for surgical segmental resection. Megacolon requires medical therapy tailored to reducing gas formation, and reduction of fiber intake may paradoxically relieve symptoms. If these conservative measures fail, then megacolon may warrant segmental or total colectomy. If testing confirms the presence of slow-transit constipation (colonic inertia) without use of laxatives, then the next step in evaluation is transit testing with use of laxatives. Only after demonstrating colonic inertia in both of these settings should surgery be considered as a potential therapy. Clear demonstration of severe total or segmental slow-transit constipation is an indication for colectomy; however, most clinicians reserve colectomy for patients with the most terminal or untreatable conditions.

Outcomes

A major outcome of interest to clinicians is the ability to characterize transit time and to diagnose slow-transit constipation. Other outcomes include the ability of testing to influence treatment decisions such as change in medications or change in nutrition or to affect patient-centered outcomes such as symptom improvement, need for surgery, quality of life, and patient satisfaction. It is important to consider potential harms such as capsule retention, radiation exposure, and mortality. Clinicians and policymakers may also be interested in the effects on resource utilization such as the need for additional tests, physician services, and hospitalizations.

Scope of Review and Key Questions

Our objective was to summarize the evidence on how useful current testing modalities for gastric and colonic motility are for diagnosing disease. We sought to determine whether wireless motility capsule testing is useful in conjunction with or instead of other testing modalities for diagnosing and managing motility disorders. We also sought to define the populations that would benefit most from motility testing, including wireless motility capsule testing. Our Key Questions are listed below.

KQ1. In the evaluation of gastric dysmotility, how does the wireless motility capsule alone compare with gastric scintigraphy, antroduodenal manometry, and endoscopy in terms of diagnostic accuracy of gastric emptying delay, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

KQ2. When gastric scintigraphy, antroduodenal manometry, or endoscopy is used in the evaluation of gastric dysmotility, what is the incremental value of also using the wireless motility capsule in terms of diagnostic accuracy of gastric emptying delay, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

KQ3. In the evaluation of colonic dysmotility, how does the wireless motility capsule alone compare with radiopaque markers and scintigraphy in terms of diagnostic accuracy of slow-transit constipation, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

KQ4. When a radiopaque marker or scintigraphy is used in the evaluation of colonic dysmotility, what is the incremental value of also using the wireless motility capsule in terms of diagnostic accuracy of slow-transit constipation, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

Methods

Literature Search Strategy

We searched the following databases for primary studies for the periods in parentheses: MEDLINE® (1966 to January 2012) and Embase® (1974 to January 2012). We developed a search strategy for MEDLINE, accessed via PubMed, based on an analysis of the medical subject headings (MeSH) terms and text words of key articles identified a priori. Additionally, we reviewed the reference lists of included articles and any relevant review articles. We asked the manufacturer of the wireless motility capsule about any published or unpublished randomized controlled trials or observational studies that evaluated the wireless motility capsule, but the manufacturer did not respond.

Study Selection

Each title, abstract, and full article was evaluated by two independent reviewers. We included studies that compared the wireless motility capsule with other diagnostic tests among patients with suspected gastroparesis or slow-transit constipation in terms of diagnostic accuracy, motility

transit time assessment, treatment decisions, patient-centered outcomes, resource utilization, or harms. Other diagnostic tests were gastric scintigraphy, antroduodenal manometry, and endoscopy for the evaluation of gastroparesis, and scintigraphy and radiopaque markers for slow-transit constipation. There were no language restrictions. We resolved differences between investigators regarding eligibility through consensus adjudication.

Data Abstraction

We created and pilot tested standardized spreadsheets for data extraction. The study investigators performed double data abstraction on each article. The second reviewer confirmed the first reviewer's abstracted data for completeness and accuracy. We formed reviewer pairs that included personnel with both clinical and methodological expertise.

For all articles, the reviewers extracted information on study characteristics (e.g., study design, country, location of recruitment, start year of recruitment, multi-center vs. single center, length of followup, and length of time in between diagnostic tests), study participants (e.g., condition, age, gender, race, weight, prior diagnostic tests, blood sugar, smoking status, diabetes status, defecatory dysfunction status, and the use of prokinetics, narcotics, antidepressants, proton pump inhibitors, and laxatives), eligibility criteria, characteristics of the wireless motility capsule testing (e.g., if the pill was swallowed or placed, if a standardized meal was used, if and when patients were given Ensure® shakes), characteristics of the other diagnostic tests, outcome measures, definitions, and the results of each outcome, including measures of variability. For each of the diagnostic tests, we collected information on the criteria used to make a diagnosis of gastroparesis or slow-transit constipation, and whether patients were instructed to not use tobacco, prokinetics, narcotics, antidepressants, proton pump inhibitors, or laxatives at the time of the test.

Quality Assessment

Two reviewers independently assessed article quality. We selected and modified the questions from the QUADAS-2 quality assessment tool.[22] We supplemented this tool with quality-assessment questions (e.g., to assess spectrum bias) based on recommendations in the *Methods Guide for Medical Test Review*.[23] The two reviewers resolved differences in quality assessment.

Applicability

We assessed the applicability of studies in terms of the degree to which the study population (age, etiology, comorbidities, prior surgery or gastric pacer), diagnostic tests (use of narcotics during testing, use of bowel motility-altering agents, such as laxatives or prokinetic agents), outcomes, and settings (referral center) were typical for the treatment of individuals with suspected gastroparesis or slow-transit constipation.

Data Analysis and Synthesis

We had planned to conduct meta-analyses if sufficient data were available (at least three studies) and studies were sufficiently homogenous with respect to key variables (population characteristics, study duration, and diagnostic tests). We qualitatively summarized studies not amenable to pooling.

When the reference standard was a clinical diagnosis, we chose a 10 percent difference between tests in sensitivity or specificity as a clinically meaningful difference because key studies were powered to detect a 10 percent difference.[24] When the reference standard was another diagnostic test, the wireless motility capsule needed a test concordance of at least 80 percent to be considered similar.

Rating the Body of Evidence

At the completion of our review, we graded the strength of the available evidence addressing the Key Questions by adapting an evidence grading scheme recommended in the *Methods Guide for Medical Test Review*[23] and in the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[25, 26] Both of these evidence grading schemes are based on recommendations of the GRADE Working Group.[27] We applied evidence grades to the bodies of evidence about each diagnostic test comparison for each outcome. We assessed the strength of the available evidence by assessing the risk of bias, consistency, directness, and precision.

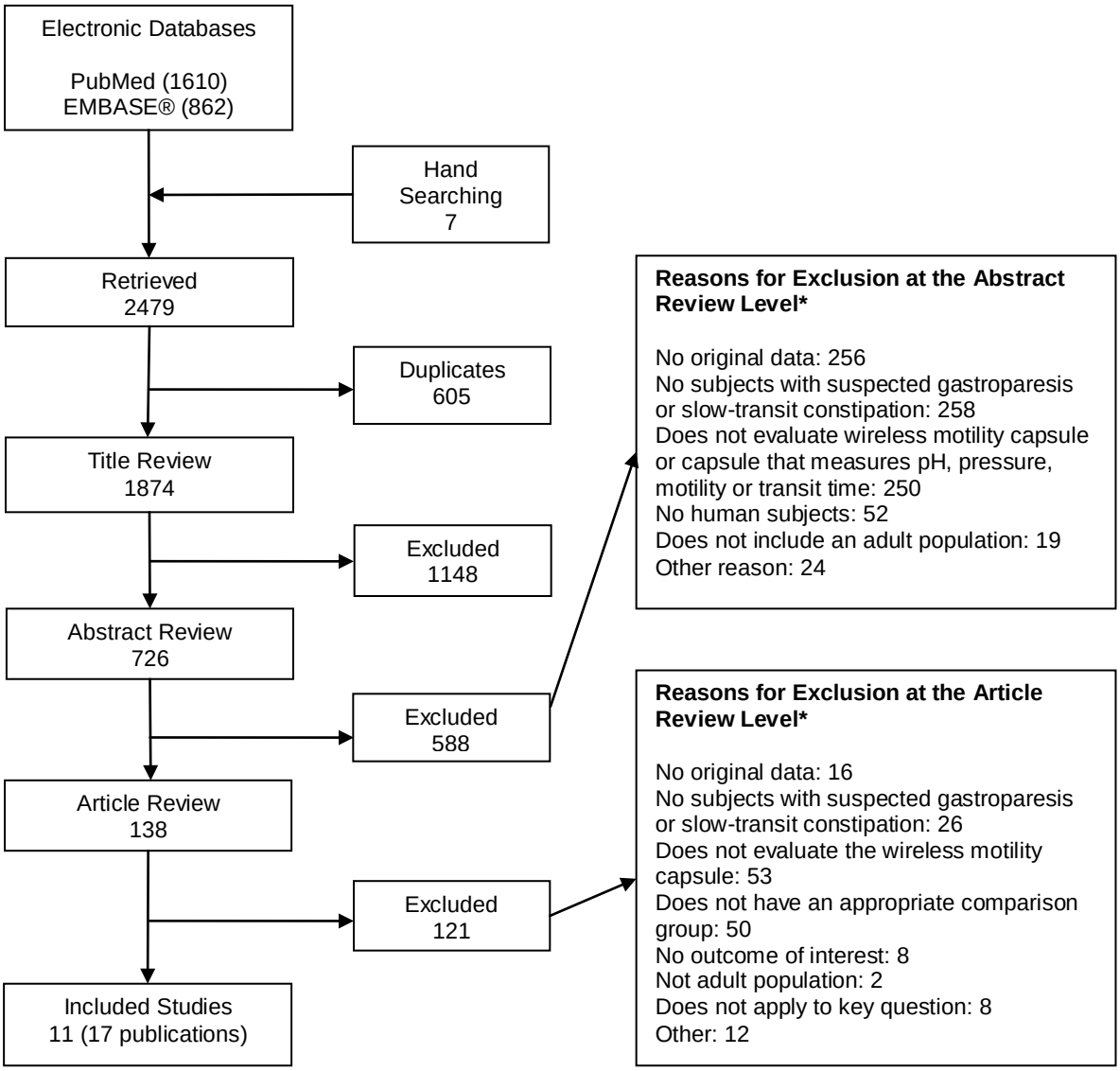
We classified evidence pertaining to the KQs into four basic categories: 1) "high" strength of evidence (indicating high confidence that the evidence reflects the true effect and that further research is very unlikely to change our confidence in the estimate of the effect); 2) "moderate" strength of evidence (indicating moderate confidence that the evidence reflects the true effect and that further research may change our confidence in the estimate of the effect and may change the estimate); 3) "low" strength of evidence (indicating low confidence that the evidence reflects the true effect and that further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate); and 4) "insufficient" strength of evidence (evidence is unavailable or does not permit a conclusion).[27]

Results

Search Results

Figure A summarizes the results of our literature search. Our search retrieved 1874 unique records. After reviewing the titles and abstracts, we considered 138 articles as potentially relevant and we reviewed the full text of the article for eligibility. We included a total of 11[7, 24, 28-36] studies (in 17 publications) in this review. Seven studies (10 publications) evaluated the wireless motility capsule test among patients with gastroparesis[28-34] and eight studies (13 publications) evaluated the wireless motility capsule test among patients with slow-transit constipation.[7, 24, 28, 29, 31, 33, 35, 36]

Figure A. Summary of literature search (number of articles)



* Total may exceed number in corresponding box, as articles could be excluded for more than one reason at this level.

Study Design Characteristics

Six of the 11 studies were prospective,[6, 7, 24, 30, 32, 36] four studies were retrospective,[28, 29, 31, 33] and one did not specify a study design.[35] All prospective studies applied the tests concurrently. Six studies were reported in meeting abstracts,[30-33, 35, 36] with the remainder reported in peer-reviewed publications.

All studies that reported the study location occurred in the U.S.[6, 7, 24, 28-30, 32, 33] One study took place in multiple countries including the U.S.[24] All studies that reported the location of recruitment occurred in tertiary centers.[7, 28-33]

Length of followup for the prospective studies and those with unspecified designs included the day of the testing only,[30, 32, 33, 35-37] 3 days,[6] 14 days,[24] and 21 days.[7]

Prospective studies included patients with known gastroparesis[6, 30, 32] or constipation.[7, 24] Four retrospective studies included patients with suspected gastroparesis or constipation[28, 29, 31, 33] and one included patients with known constipation exclusively.[35] Five of the prospective studies also included patients without gastroparesis or constipation,[6, 7, 30, 32, 36] whereas one study included only patients with known constipation.[24] Two studies that included patients with constipation used the Rome III criteria as inclusion criteria.[7, 24] Two studies reported age restrictions. One allowed patients 18 to 80 years of age[24] and the other included patients older than 65 years of age.[36]

Study Population Characteristics

No gender restrictions were made in the inclusion criteria, although most of participants with gastroparesis or constipation were female. The mean age was 40 or greater in all studies that reported an average.[7, 24, 28, 29, 35, 36] Three studies reported on race or ethnicity.[6, 24, 29] Greater than 80 percent of the participants were white in these studies. No study reported a measure of weight, blood sugar, or smoking status at baseline. Two studies reported on the percent of patients with diabetes.[28, 34] Fifteen and 37 percent had diabetes. Two studies reported on defecatory dysfunction.[28, 35] Twenty of 32 subjects had defecatory dysfunction in one study[35] and another study included 64 percent of patients with dysfunction.[28] Use of medications, including prokinetics, narcotics, antidepressants, proton pump inhibitors, and laxatives, prior to and during the studies were rarely reported. Diagnostic testing prior to the study included scintigraphy[6, 28, 29, 32] and radiopaque markers.[28, 29]

Characteristics of Diagnostic Tests

We summarized the characteristics of the tests used in the studies, taking into consideration how evaluation of gastrointestinal motility is dependent on multiple factors, including not only the type of test but also the specific protocol employed. The specific protocols employed for these studies often were not standardized. Our criteria for study assessment had suggested that best practice studies would report on smoking, use of prokinetics, use of selective serotonin reuptake inhibitiors, use of antacids, and the specific timing of ingestion of test meals. However, only a few of the studies with larger populations specified a pre-determined meal and meal schedule for patients undergoing wireless motility capsule testing. Several of the studies also specified that prokinetics were not used within the immediate timeframe of the wireless motility capsule testing. Gastric scintigraphy was most frequently performed using the Tougas protocol. Radiopaque marker studies were either coordinated by the community referral practice as per their local standards or the study made reference to a variation of the Metcalf protocol, where ingestion of radiopaque markers occurs followed by interval x-ray and assessment of the marker location and number. Few articles gave more specific test characteristics for radiopaque marker testing. Most abstracts did not report on any of these characteristics.

Study Quality

We reported study quality separately for the full-length publications and the abstracts because the abstracts had limited information about study methods. Overall, study quality was fair among the 10 full length publications assessed.[6, 7, 24, 28, 29, 34, 42-45] Half used a uniform

reference standard.[6, 7, 24, 42, 43] Only three publications reported that the wireless motility capsule results were interpreted independently from the reference standard.[7, 24, 29] After contacting the authors, we were able to confirm that the results were interpreted independently in three publications where blinding was not reported.[6, 34, 42]

Key Question 1. Evaluation of gastric dysmotility: wireless motility capsule alone versus other diagnostic tests

Key Question 2. Evaluation of gastric dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

The results for KQ1 and KQ2 are summarized in Table A.

Table A. Summary of the strength of evidence and main findings of studies comparing the wireless motility capsule alone (KQ1) or in combination (KQ2) with other diagnostic tests for the evaluation of gastroparesis

Key question (KQ)	Comparison	Outcome	Strength of evidence*	# of studies	Main findings
KQ1	WMC vs. scintigraphy	Diagnostic accuracy	Low	7	Diagnostic accuracy of WMC is similar to scintigraphy. The sensitivity of WMC compared with clinical gastroparesis ranged from 65 to 68% and the specificity ranged from 82 to 87%. Sensitivity of the wireless motility capsule compared with gastric scintigraphy ranged from 59 to 86 percent and specificity ranged from 64 to 81 percent.
KQ1	WMC vs. other modalities (anteroduodenal manometry, endoscopy)	All outcomes	Insufficient	0	No studies addressed these comparisons.
KQ1	WMC vs. scintigraphy	Motility assessment: Transit	Low	2	Transit data obtained via WMC is similar to scintigraphy.
KQ1	WMC vs. scintigraphy	Motility assessment: Pressure patterns	Low	3	WMC can measure pressure patterns and measurement of pressure patterns adds to diagnostic accuracy. [Scintigraphy does not measure pressure patterns.]
KQ1	WMC vs. scintigraphy	Treatment decisions	Low	3	WMC testing alters management in patients with suspected gastroparesis (50-69% change in management for medicine, diet, or surgery).
KQ1	WMC vs. scintigraphy	Resource utilization	Low	1	WMC testing may reduce the need for other studies, but this conclusion is based on one study with a high risk of bias. Need for anorectal manometry may not be reduced by WMC.
KQ1	WMC vs. scintigraphy†	Harms	Low	2	Harms associated with WMC are minimal and no major safety issues were reported.
KQ1	WMC vs. scintigraphy	Patient-centered outcomes	Insufficient	0	No studies reported on patient-centered outcomes for this comparison.

Table A. Summary of the strength of evidence and main findings of studies comparing the wireless motility capsule alone (KQ1) or in combination (KQ2) with other diagnostic tests for the evaluation of gastroparesis (continued)

Key question (KQ)	Comparison	Outcome	Strength of evidence*	# of studies	Main findings
KQ2	WMC in combination with other tests vs. scintigraphy alone	Diagnostic accuracy	Low	2	Adding WMC to conventional motility testing improves diagnostic accuracy in patients with suspected gastroparesis (sensitivity scintigraphy 42-51%; WMC 60-66%).
KQ2	WMC in combination with other tests vs. scintigraphy	Motility assessment	Low	5	Adding WMC to conventional motility testing improves assessment of motility parameters in patient with suspected gastroparesis. [Scintigraphy does not measure pressure patterns.]
KQ2	WMC in combination with other tests vs. scintigraphy	Treatment decisions, utilization, patient-centered outcomes, harms	Insufficient	0	No studies addressed these outcomes for these comparisons.

KQ = key question; WMC = wireless motility capsule
* The strength of the evidence was defined as follows: High = High confidence that the evidence reflects the true effect. Further research is unlikely to change our confidence in the estimate of the effect. Moderate = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate. Low = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate. Insufficient = Evidence is unavailable or does not permit a conclusion.
† Findings were based on observational studies that did not include a direct comparison of wireless motility capsule with gastric scintigraphy.

Key Question 3. Evaluation of colonic dysmotility: wireless motility capsule alone versus other diagnostic tests

Key Question 4. Evaluation of colonic dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

The results from KQ3 and KQ4 are summarized in Table B.

Table B. Summary of the strength of evidence and main findings of studies comparing the wireless motility capsule alone (KQ3) or in combination (KQ4) with other diagnostic tests for the evaluation of slow-transit constipation

Key question (KQ)	Comparison	Outcome	Strength of evidence*	# of studies	Main findings
KQ3	WMC vs. radiopaque markers	Diagnostic accuracy	Low	6	Diagnostic accuracy of WMC is similar to radiopaque markers. Concordance between ROM and WMC was approximately 80 percent in two larger studies. Sensitivity and specificity, respectively, were estimated to be 46 and 95% for WMC compared with clinical constipation, and 37 and 95% for radiopaque markers.
KQ3	WMC vs. radiopaque markers	Motility assessment: Transit	Low	3	WMC was comparable with radiopaque markers in judgment of colonic transit time and identification of slow-transit constipation.

Table B. Summary of the strength of evidence and main findings of studies comparing the wireless motility capsule alone (KQ1) or in combination (KQ2) with other diagnostic tests for the evaluation of slow-transit constipation (continued)

KQ3	WMC vs. radiopaque markers†	Treatment decisions	Low	2	Very small numbers made comparison difficult for treatment decisions. Studies reported 7.1% change in nutrition, 21% referral to surgery, 4% change in nutritional and behavioral therapies with WMC.
KQ3	WMC vs. radiopaque markers	Resource utilization	Low	3	WMC testing can affect resource utilization.
KQ3	WMC vs. radiopaque markers†	Harms	Low	4	Harms and adverse events were infrequently reported for WMC or radiopaque markers. WMC is comparable to radiopaque markers with regard to harms. Radiopaque marker involves exposure to at least one x-ray. Day 21 x-ray was required in a small proportion of patients who received WMC by protocol if the capsule had not spontaneously passed. Technical failures were reported in prototype devices 3 to 10% in some series.[7]
KQ3	WMC vs. radiopaque markers	Patient-centered outcomes	Insufficient	0	No studies addressed this outcome.
KQ3	WMC vs. colonic scintigraphy	Diagnostic accuracy	Insufficient	0	No studies assessed the role of WMC versus these other modalities in the population of interest for this outcome.
KQ4	WMC in combination with other diagnostic tests versus diagnostic tests alone	Diagnostic accuracy	Insufficient	0	No studies addressed this question.

KQ = key question; WMC = wireless motility capsule

* The strength of the evidence was defined as follows: High = High confidence that the evidence reflects the true effect. Further research is unlikely to change our confidence in the estimate of the effect. Moderate = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate. Low = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate. Insufficient = Evidence is unavailable or does not permit a conclusion.

† Findings were based on observational studies that did not include a direct comparison of wireless motility capsule with radiopaque markers.

Discussion

Potential Niche for Wireless Motility Capsule

The wireless motility capsule has the potential to be an improvement over previous testing modalities for patients with possible gastroparesis or slow-transit constipation because it is small and can be transported to patients wherever they live. Also, the capsule does not involve any radioactive material or x-ray exposure, and can record information about pressure, transit, and location simultaneously. Other testing modalities for gastric emptying and colonic motility assessment do not share these characteristics. Scintigraphy is often used for assessment of gastric transit abnormalities and in certain academic centers also extended to evaluate whole gut

motility; however, this involves radiation exposure, significant patient time requirements, and significant cost. Antroduodenal manometry allows assessment of gastric pressure parameters but has limited availability and is more invasive than other testing modalities. Radiopaque markers are portable and small, but require radiation exposure, access to fluoroscopy, and radiology interpretation. In addition, all other studies used in evaluation of either gastric or colonic motility evaluate either transit or pressure, but not both – yet both are involved in disease pathogenesis. The wireless motility capsule has the potential to evaluate both transit and pressure simultaneously, which in theory could allow more optimal assessment of motility than evaluation of either parameter independently. Likewise, by recording both parameters, the wireless motility capsule has the potential to replace a combination of studies and provide more accurate diagnosis with less resource utilization and enhanced patient convenience.

In light of this potential niche, the wireless motility capsule is becoming much more readily available in both academic and community centers. However, questions remain about the position of the wireless motility capsule in the diagnostic algorithm for suspected motility disorders such as gastroparesis and slow-transit constipation. Is the wireless motility capsule equivalent to conventional testing? Is it superior? Is it more likely to establish a concrete diagnosis or guide medical therapy than conventional motility testing? Should it be used as a stand-alone test or is it better used as an adjunct test after conventional testing has been completed in cases where the diagnosis remains in question? These are questions that have not been clearly addressed in previous clinical practice guidelines.

The potential limitations of the wireless motility capsule must also be considered. The modality is of limited utility in patients with severe gastroparesis as this is listed by the manufacturer as a contraindication to capsule placement due to fear of capsule retention. In addition, by definition, the wireless motility capsule evaluates motility at only a single point, as opposed to antroduodenal manometry which has multiple recording points, or scintigraphy which looks at transit of an entire meal. One assumes that the single point of measurement is representative of motility parameters as a whole; however, this is an assumption only and not clearly established in the literature. In the assessment of constipation, one cannot separate patients with slow-transit constipation from defecatory dysfunction based on only colonic transit time so further motility testing and clinical judgment is needed to evaluate defecation. Finally, parameters of motility for a non-digestible solid are different than those for either liquids or a meal – implying that patients can have abnormalities with one modality that would not be seen with another. In short, while the potential of wireless motility capsule testing is exciting, many questions remain as to whether it is equivalent or superior – and as to the appropriate place in the diagnostic algorithm where it should be used.

Key Findings and Implications

Few studies met our criteria for evaluation. The paucity of full length articles with independent data limited our ability to answer the key questions definitively.

Key Question 1. Evaluation of gastric dysmotility: wireless motility capsule alone versus other diagnostic tests

Wireless Motility Capsule Versus Scintigraphy

We found low strength of evidence from seven studies[6, 28-30, 32-34] to support that wireless motility capsule has comparable diagnostic accuracy with gastric scintigraphy. The sensitivity

was moderately greater in some studies, but there was slightly lower specificity reported. The test agreement and diagnostic gain were moderate. Diagnostic agreement between wireless motility capsule and gastric scintigraphy ranged from 58 to 86 percent positive test agreement and from 64 to 81 percent for negative test agreement.

We found low strength of evidence from five studies[6, 29, 30, 32, 34] that transit data obtained via wireless motility capsule testing correlates well with scintigraphic gastric emptying. The reporting of the results in these studies was heterogeneous. One study reported a correlation coefficient of 0.73 between gastric emptying time measured by the wireless motility capsule and 4-hr gastric emptying measured by gastric scintigraphy.[6] Other studies reported sensitivity, specificity, and device agreement between wireless motility capsule transit data and gastric scintigraphy.[29, 32, 34] All three studies examining transit time showed similar sensitivity and specificity for wireless motility capsule and scintigraphy, and some studies reported increased diagnostic gain of sensitivity with wireless motility capsule.

Low strength of evidence from two studies supports the utility of wireless motility capsule versus scintigraphy in measuring pressure profiles.[32, 34] Pressure patterns are reported by wireless motility capsule, but scintigraphy can not detect pressure patterns. It does appear, however, that abnormalities are more likely to be seen with wireless motility capsule than scintigraphy – especially if one adds assessment of pressure patterns to the equation. However, based on the literature there remains questions as to whether this increased diagnostic detection rate has clinical implications.

Overall, we had graded the strength of evidence for many outcomes addressing KQ1 to be low because we considered the evidence to have medium risk of bias, consistent reporting, direct nature of the data, and imprecise findings. The main limitation weighting the risk of bias was that enrollment of patients was not prespecified or done in a random fashion; in fact many studies did not report how patients were selected for testing and study. Another limitation was the lack of advance prespecification of criteria and values of positivity of the tests being used. The final major limitation was that few studies mentioned whether a person without conflict of interest was selected to manage the data collected. Most studies had limited followup duration, which hampers our ability to draw conclusions about some of the outcomes that are really important to patients. A major strength of the full length articles was that there was reporting of independent review of the results to perform analysis.

We could not conduct a meta-analysis because of the heterogeneity of the data and patient populations in the studies. Our ability to compare studies was limited by lack of consistency in how the reference standards were defined. The reference standard was often reported as a community based gastric scintigraphy testing performed within 2 years of enrollment into a study. Local standards for scintigraphy vary greatly, and this introduced heterogeneity into the patient populations under investigation. Many studies had different definitions for key outcomes such as diagnostic agreement, sensitivity, and specifity, as well as different diagnoses based on similar test results. This latter discrepancy can be explained by changes over time in how investigators considered the cut off values for detection of gastroparesis with wireless motility capsule. It is uncertain if the full spectrum of patients is captured in the available examinations of motility testing as academic referral centers were the primary recruitment site for studies. Overall, seven studies with 560 patients addressed the question of diagnostic accuracy.[28-34] For a rare illness, the large number of patients included for evaluation reflects the great length that researchers have taken to assess the quality of this modality. Several studies suggested there was some diagnostic gain with wireless motility capsule as compared with scintigraphy, assuming all

additional cases identified were correct and not false positives.[6, 28, 29, 32, 34] Employing simultaneous scintigraphy and wireless motility capsule at the time of assessment, the investigators attempted to minimize the impact of having a heterogenous population; sensitivity and specificity for both scintigraphy and wireless motility capsule compared with symptoms in these studies is expectedly low given the issues above and the fact that the denominator may not have truly reflected entirely gastroparetic patients. Device agreement is a more useful parameter to measure in these papers than sensitivity and specificity.[23] However, agreement is likely to be imperfect because these two modalities look at different mechanisms of transit.

Regarding treatment decisions, we did find that, in three studies, wireless motility capsule testing altered management in patients with suspected gastroparesis (50 to 69 percent change in management for medicine, diet, or surgery). However, the strength of evidence was low (i.e., likely to be changed by future evidence).

The evidence was insufficient to draw conclusions regarding the differences or similarities between gastric scintigraphy and wireless motility capsule with regards to patient-centered outcomes or resource utilization. Very little research examined resource utilization, and no studies specifically examined this outcome with any rigor.

The findings reported in the literature are consistent with what would be expected based on the pathophysiology of gastroparesis and the comparative methods of wireless motility capsule and gastric scintigraphy. Comparing scintigraphy with wireless motility capsule is fundamentally a challenging endeavor. Both modalities evaluate different parameters. Scintigraphy looks at transit of a test meal and does not assess pressure. When the stomach processes a meal, fundic accommodation is followed by antral contractions that break up the food into small particles that are then propelled from the antrum to the duodenum. In comparison, the wireless motility capsule is not digested and is believed to exit the stomach when the gastric motility patterns change from a fed to fasting state and migratory motility complexes resume. As such, these two technologies are evaluating different parameters and a direct comparison may be challenging if one looks at transit alone.

Wireless Motility Capsule Versus Anteroduodenal Manometry or Endoscopy

No head-to-head comparison of antroduodenal manometry (which can record pressure patterns) and wireless motility capsule was found in patients with suspected gastroparesis in our review. This makes a more definitive assessment of the ability of wireless motility capsule to detect abnormalities in pressure patterns in our defined populations more difficult at this time. Similarly, we did not find any studies that compared wireless motility capsule testing with endoscopy among patients with suspect gastroparesis.

Key Question 2. Evaluation of gastric dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

Wireless Motility Capsule Plus Gastric Scintigraphy Versus Gastric Scintigraphy Alone

Two studies[29, 34] assessed the incremental value of using the wireless motility capsule with gastric scintigraphy. We found low strength of evidence to suggest that wireless motility capsule is associated with modest improvement in diagnostic accuracy over use of scintigraphy alone for patients with suspected gastroparesis. Low strength of evidence was also present to support the

incremental benefit of wireless motility capsule in evaluation of transit times and pressure patterns. The two studies that did attempt to address this question had a method of data collection that may not have allowed for full understanding of diagnostic discrepancy. Discrepancy is when one test shows disease and the other test does not show disease. The authors assumed that in a population of patients with gastroparesis diagnostic gain (when wireless motility capsule was positive but scintigraphy was not) was always present when there was discrepancy with results.[29] This assumption is difficult to confirm without having an independent gold standard for establishing the diagnosis.

While few studies addressed this question specifically, the ones that did were among the better studies in terms of quality, and demonstrated independent review of the wireless motility capsule and scintigraphy. Risk of bias was assessed as medium and these studies were felt to be consistent and direct. Precision was felt to be low but this is difficult to gauge for this question. The overall strength of evidence was low for this key question. It is very hard to prove an incremental benefit of the test when used in addition to other testing modalities becauseit is hard to determine how clinical decision making was performed. It may be unclear which test the clinician used to form an opinion of the case, and it may be unclear how much the incremental information contributed to the decision making process. The retrospective nature of studies also limited the strength of evidence.

The incremental benefit for wireless motility capsule in diagnostic evaluation of suspected gastroparesis is consistent with the nature of the disorder and the tests, since the wireless motility capsule offers pressure data and motility data which are not discernible by scintigraphy alone, as well as lower gastrointestinal motility data which can be implicated as a cause of symptoms in patients with combinations of motility disorders. Measurable benefit may be gleaned from the additional reported information in combination with scintigraphy especially with regard to identification of a more diffuse motility disorder. The evidence was limited and there was no information to guide any conclusions regarding treatment decisions, utilization, patient-centered outcomes, or harms when evaluating the incremental value of also using the wireless motility capsule.

Incremental Value of Wireless Motility Capsule Compared with Antroduodenal Manometry Alone or Endoscopy Alone

We did not find any studies that evaluated the incremental value of adding the wireless motility capsule test to testing with either antroduodenal manometry or endoscopy in patients with suspected gastroparesis.

Key Question 3. Evaluation of colonic dysmotility: wireless motility capsule alone versus other diagnostic tests

Wireless Motility Capsule Versus Radiopaque Markers

The strength of evidence was low from four studies (six publications) containing 522 patients comparing wireless motility capsule with radiopaque markers in assessment of diagnostic accuracy of identification of slow-transit constipation.[7, 24, 28, 29, 42, 45] The diagnostic accuracy of the wireless motility capsule was similar to scintigraphy (concordance was about 80 percent in two of the larger studies). Sensitivity and specificity were estimated to be 46 and 95 percent for wireless motility capsule compared with clinical constipation, and 37 and 95 percent for radiopaque markers.[7] Of these reported studies, only three were true independent studies and the

remainder were abstracts or ad-hoc analysis of already included studies, which impaired the strength of evidence due to a smaller pool of patients under analysis. The wireless motility capsule was comparable with radiopaque markers in assessment of diagnostic accuracy, and matched the sensitivity in different target populations in a reliable way.

The strength of evidence was low to suggest that the colonic transit time estimated by wireless motility capsule correlates well with the colonic transit times recorded by radiopaque markers. The correlation coefficients between these two measures ranged from 0.69 to 0.71.

The strength of evidence was low regarding the effect of wireless motility capsule testing on treatment decisions based on radiopaque marker testing. We are unable to draw conclusions because only two retrospective chart reviews offered information about change in management for the wireless motility capsule compared with use of radiopaque markers.[28, 29] These two studies differed in the patient populations and the reporting of the outcomes. One of the studies reported few events, providing imprecise results. The data was further limited because not all patients underwent both diagnostic tests of interest. We found low strength of evidence that wireless motility capsule can affect resource utilization.

The strength of evidence was low in the three studies reporting on any harms relevant to wireless motility capsule or radiopaque markers.[7, 24, 35] Harms and adverse events were infrequently reported for the wireless motility capsule or radiopaque markers. The wireless motility capsule is comparable to radiopaque markers with regard to low frequency of harms, as no serious adverse events and no mortality was reported. Radiopaque marker testing involves exposure to at least one x-ray by definition. Day 21 x-ray was required in a small proportion of patients who received wireless motility capsule by protocol if the capsule had not spontaneously passed, but may not be required in practice if a capsule passage is witnessed. Technical failures were reported in prototype devices with reported rates between 3 and 10 percent depending on the study.[7] Other harms or adverse events reported included dysphagia, abdominal discomfort, bloating, or nausea, which happened infrequently. These all resolved spontaneously when reported.[24]

The strength of evidence was insufficient to make any conclusions about patient-centered outcomes like symptom improvement, quality of life, patient satisfaction (0 studies). No included studies addressed these outcomes of interest. These are difficult outcomes to assess without using dedicated symptom scores or mining large sources of data on hospital and physician visits. Longer duration studies will also be needed to address questions about change in quality of life or symptoms, which requires assessment along multiple time points.

Many factors contributed to the overall grading of evidence for outcomes assessed as having low strength of evidence in reference to Key Question 3. The evidence was considered to have moderate risk of bias because many of the studies were retrospective, lacked random patient selection, did not report if there was blinding of assessment, and did not apply the same reference standard to all the patients. Furthermore, many studies recruited patients from academic referral centers; it is uncertain if the full spectrum of patients were captured in the available examinations of motility testing. Most studies had limited followup duration, which hampered our ability to draw conclusions about some of the outcomes that are important to patients such as patient satisfaction or change in symptom scores. We had only imprecise estimates of the effects on treatment decisions and harms. Our conclusions were limited by how the reference standards were defined. The reference standard was often reported as a community based radiopaque marker study of varying protocol. The multiple protocols had different assessment methods, which could have influenced the results. We could not conduct a meta-analysis because of the

heterogeneity of reported data and patient populations in the studies. Although the strength of evidence was low, it is impressive how well these devices correlated given limitations of the studies.

Much like the comparison between scintigraphy and wireless motility capsule, radiopaque markers and wireless motility capsule are assessing different components of transit. Some of the points of assessment coincide and provide comparable data, but the additional pressure and transit data offered by the wireless motility capsule make it a different and possibly complementary modality. Overall, the studies showed diagnostic agreement between wireless motility capsule and radiopaque markers for assessment and diagnosis of slow-transit constipation.

Wireless Motility Capsule Versus Colonic Scintigraphy

We found no evidence to evaluate the wireless motility capsule in comparison with colonic scintigraphy in patients with suspected slow-transit constipation. The reported studies on scintigraphy in the literature were excluded from our analysis because they compared testing in healthy subjects separately from those with constipation or slow-transit constipation and thus were not eligible for inclusion.

Key Question 4. Evaluation of colonic dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

No studies directly addressed any outcomes of interest related to Key Question 4. The little data that was available from small trials about these outcomes were heterogeneous and did not specify the specific patient populations of interest and thus, it was impossible to generalize based on this data. Assessing the incremental value of a new technology could be assessed by diagnostic gain. However, when trying to judge whether a new test can be a replacement or adjunct to an old test, it is difficult to get a clear picture of which test was most helpful in making a diagnosis without a blinded comparison or without follow up that can assess the validity of the diagnosis and or treatment effects over time.

Applicability

The applicability of the literature is limited based on the use of the test in referral centers and no prospective testing of the wireless motility capsule as a diagnostic tool in patients with suspected disease. All studies occurred at referral centers. All prospective studies involved patients with known disease. When a comparison group without constipation or gastroparesis was used, “healthy” controls were included, instead of patients who may have similar presenting symptoms who do not have constipation or gastroparesis. These controls tended to be college-aged men compared with middle-aged females with suspected disease. Additionally, it is unclear how previous treatments or comorbidity, including diabetes, affect test performance or how the test results ultimately affect management.

Limitations and Strengths of Our Review Process

Our review had two major limitations.

(a) No standards exist in the field of motility assessment for determining the minimum improvement of diagnostic accuracy that will identify one test as superior to another test. There are also no standards to establish the equivalence of motility tests. We arbitrarily

chose a 10 percent difference in sensitivity or specificity as a clinically meaningful difference between tests.[24] We felt this threshold was a conservative minimum improvement over a reference standard with moderate diagnostic accuracy (between 50 percent and 80 percent). If the reference standard had a larger diagnostic accuracy (90 percent or greater), a 10 percent absolute difference is too large to expect.

(b) We excluded studies that included non-diseased participants exclusively as our review focused on studies that compared the diagnostic accuracy of the tests for patients with gastroparesis or slow transit constipation. We recognize that many of the most commonly cited studies in the field included non-diseased participants.[8, 9, 46-50, 52-59] Thus, we excluded a number of studies that evaluated characteristics of the wireless motility capsule.

The major strength of our review process was the comprehensiveness. We included abstracts, contacted industry for unpublished studies, and contacted study authors for missing data.

Limitations of the Identified Literature

Our aim was to compare the diagnostic accuracy of the wireless motility capsule to other testing modalities to diagnose and manage gastroparesis and slow transit constipation. The identified literature limited our ability to answer our key questions for several reasons.

(a) No study directly addressed the incremental value of using the wireless motility capsule in addition to using a radiopaque marker or scintigraphy in the evaluation of colonic dysmotility (KQ4). Only limited data addressed the incremental value of using the wireless motility capsule in addition to using gastric scintigraphy, antroduodenal manometry, or endoscopy in the evaluation of gastric dysmotility (KQ2).

(b) All study sites were referral centers that tend to have patients with more severe disease. The study results have limited generalizability to general gastroenterology or primary care clinics where a greater spectrum of disease severity is observed. The sensitivity and specificity of the wireless motility capsule may be different in referral center settings than in other settings, and the positive and negative predictive values will be different when the prevalence of disease is different.

(c) Many studies included non-diseased patients in the comparison of the diagnostic accuracy of the wireless motility capsule with other tests, using a clinical diagnosis of disease as the reference standard rather than the results of the other diagnostic tests.

(d) The non-diseased participants had very different demographic characteristics than the gastroparesis and slow transit constipation patients. For example, the majority of the non-diseased participants were college-aged males whereas the gastroparesis and slow transit constipation patients were middle-aged women. Using clinical diagnosis as the reference standard, it is difficult to determine if the wireless motility capsule and other tests are distinguishing disease from non-disease or measuring differences in motility by demographic differences such as age and sex.

(e) Variability in the administration of the motility tests and outcome assessments may explain some of the heterogeneity in the study results. Many studies used similar protocols to perform the wireless motility capsule testing and other tests, but with slight modifications, such as in the contents of the meal. Frequently, the timing of the motility assessment differed for the wireless motility capsule and the alternative test within and between studies, which may explain differences in the test results and the diagnostic accuracy differences between studies.

(f) The abstracts we included did not report enough data to fully understand the study population, answer our key questions, and assess the quality of the studies.
(g) We were unable to compare the results of studies with and without industry or investigator conflicts of interest because most studies were sponsored by the company that manufactures the wireless motility capsule. The other studies did not report on conflicts of interest. No study stated that it was performed independent of industry sponsorship with authors who had no previous or current financial relationships with the manufacturer of the wireless motility capsule.
(h) We attempted to assess publication bias by contacting the manufacturer of the wireless motility capsule and requesting any unpublished data, but received no response. Therefore, publication bias may affect our findings, and this is a limitation as well.

Future Research Needs

Future research should ideally emphasize a cure to these diseases that is nontoxic, cheap, easily available, and safe without major surgery or implanted devices. As far as diagnostic testing, the goal is always to find accurate, effective, inexpensive tools to diagnose or exclude cases and qualify their severity in a reproducible way, especially when treatment is expensive, unavailable, or accompanied by great risks. Studies that compare the diagnostic modalities should have blinded interpretation of the results and make every attempt to classify patients by identical criteria and standardized protocols that can be repeated and verified at other centers. We recommend that research focus more on prospectively studied patients in larger numbers with an appropriate spectrum of symptoms and adequate follow up to determine whether the diagnosis was accurate over time. Due to the difficulty enrolling patients, carefully crafted retrospective analyses should also be considered.

Research also is needed to evaluate how the wireless motility capsule should be used in combination with or instead of other testing modalities for evaluation of slow-transit constipation. The studies we reviewed used alternative measures to assess anorectal function, such as anorectal manometry, as wireless motility capsule does not capture data about this region reliably. Thus, wireless motility capsule will likely be used in combination with this test.

Eventually, outcomes studies are needed to see if testing helps to improve quality of life or symptom control. It is unclear at present whether a more sensitive diagnostic test might just provide lead-time bias for diagnosis but not actually change the outcomes or management steps overall for the patient. As other targeted therapies are identified, the value of testing will need to be reassessed. We are aware that a new therapy is in Stage II trials for patients with diabetes and gastric emptying delay, which may increase the need for research into this area if it becomes available for use.[60] Currently, most patients with nausea- and vomiting-predominant symptoms of gastroparesis receive similar first-line treatment with antiemetics or prokinetics. As treatment options for gastroparesis expand (some at great expense), then more accurate detection of disease prior to initiation of therapy may play a more prominent role in disease management. Resource utilization with and without using the wireless motility capsule is not currently reported in the literature, and more studies evaluating these measures will be needed.

Little data is available to support determination of the optimal timing of wireless motility capsule testing in the diagnostic and therapeutic approach to patients with symptoms of possible gastroparesis or slow transit constipation. Further work needs to be done to classify the types of patients within subgroups of gastroparesis or slow-transit constipation to identify severe cases that may need more urgent evaluation. Finally, little is known about whether testing should be

used to assess the effectiveness of treatment or if subsequent testing would offer any benefit in long-term management of patients. Currently, symptoms and symptom resolution guide therapeutic decisions, but these require careful interpretation.

Conclusions

Based on the current literature, the wireless motility capsule appears to be accurate in detection of gastroparesis and slow-transit constipation and may provide increased diagnostic gain as compared with standard motility testing. While the strength of evidence is low, the data were relatively consistent and suggested that this modality is no less sensitive than conventional testing. The evidence is insufficient to determine whether use of the wireless motility capsule will improve outcomes of care.

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Introduction

Delayed gastric emptying and slow-transit constipation are disorders of gastrointestinal (GI) physiology that may cause persistent troubling symptoms. When patients present with their symptoms, clinicians frequently try empiric therapy first because the disorders are not easy to measure. When empiric therapy is unsuccessful or symptoms are severe enough to prompt immediate investigation, clinicians usually will recommend diagnostic evaluation of GI physiology with one or more of the available tests. Unfortunately, all of the traditional tests of GI physiology have limitations. To give patients and their clinicians another option, a new test has been developed and approved for use in the U.S. – the wireless motility capsule.[1]

Gastroparesis

Definition and Prevalence

Gastroparesis is a condition in which patients experience symptoms of delayed gastric emptying in the absence of an actual physical blockage.[2] The most common symptoms are nausea, vomiting, early satiety, bloating, abdominal pain, and postprandial fullness.[3] Detection of gastric emptying delay is the essence of diagnosing gastroparesis. Since the common symptoms for gastroparesis overlap with symptoms of functional GI disorders such as dyspepsia, cyclical vomiting, and irritable bowel syndrome, a more stringent definition of gastroparesis has been established. For clinical research, gastroparesis has been defined as delayed gastric emptying as detected by clinical testing and the presence of symptoms of nausea and/or vomiting, postprandial fullness, early satiety, bloating, or epigastric pain for more than 3 months.[4] Using this definition, the cumulative incidence of gastroparesis is 4.8 percent in people with type 1 diabetes, 1.0 percent in people with type 2 diabetes, and 0.1 percent in people without diabetes but who may have idiopathic gastroparesis or other rare etiologies.[3] A multicenter study revealed that 88 percent of patients with idiopathic gastroparesis were female, and the average age at the time of diagnosis was 41 years.[5, 6] The prevalence of gastroparesis was estimated by a community-based study in 2007 to be 9.6 per 100,000 for men and 37.8 per 100,000 for women.[3]

Etiology and Clinical Course

The etiologies of gastroparesis are most often idiopathic, diabetic, or postsurgical, but can be autoimmune, paraneoplastic, or neurologic. Idiopathic gastroparesis is the most common etiology, estimated by some small studies to range between 36 and 64 percent of patients with the condition. Diabetes mellitus is the primary cause of gastroparesis in 29 to 31 percent of patients. Assessment usually takes place in the outpatient setting, but some patients become severely ill with intractable vomiting and dehydration and must be admitted to the hospital. Hospitalizations for gastroparesis increased by 158 percent between 1995 and 2004.[7] In individuals with diabetes and gastroparesis, digestion of food is unpredictable, and wild swings in blood glucose can require medical care and increase morbidity. This unpredictability highlights the need for accurate diagnosis of gastroparesis so that available treatments can be applied.

Evaluation of Possible Gastroparesis

Standard assessment for patients with typical symptoms (nausea, vomiting, bloating, abdominal pain, early satiety) of gastroparesis begins with exclusion of mechanical causes of disease. A typical assessment starts in the office of a physician, where a careful medical history is taken and a physical examination is performed.[8] If mechanical disease it not suspected, then exclusion of medication-induced symptoms must be performed. Delay of gastric emptying is commonly caused by the use of medications such as narcotics or glucagon-like peptide agonists. If there is any clinical suggestion of mechanical obstruction as the etiology, then imaging with x-rays or computed tomography can confirm obstruction and exclude gastric emptying delay as a primary etiology. If there is any possible offending medication use, the medication can be stopped and the patient can be observed for improvement of symptoms. Methods of testing include gastric emptying scintigraphy, antroduodenal manometry, and now wireless motility capsule technology. Electrogastrography is an older form of testing that is rarely offered, even in most academic centers.[2]

Gastric Scintigraphy

According to the American College of Gastroenterology (ACG) and the American Gastroenterological Association (AGA), gastric emptying scintigraphy of a radiolabeled solid meal is the most recognized method, or reference standard, by which delayed gastric emptying can be determined.[8] Gastric scintigraphy is the ingestion of a meal commonly standardized to toast, jam, juice, and radiolabeled eggs, which are visible on passage through the GI tract during subsequent timed imaging. Most radiology centers require that all possible interfering medications such as narcotics, motility agents, and glucagon-like peptide agonists be withheld for 5 to 7 days before scintigraphic testing. According to the consensus statement issued by the American Neurogastroenterology and Motility Society (ANMS) and Society of Nuclear Medicine in 2011,[9] gastric scintigraphy should be performed over a period of 4 hours after consumption of a standardized meal to be reproducible and to detect more abnormalities among symptomatic patients. Motility specialists find that community-based radiology practices often provide shorter versions of the scintigraphic examination with durations between 60 and 120 minutes. Full 4-hour testing is more commonly available at regional referral centers or tertiary care centers with established practices of motility specialists.[9] Standards of abnormal emptying have been established for 1, 2, 3, and 4 hours. Generally, delayed gastric emptying is confirmed if more than 90 percent of the gastric content has not emptied at 4 hours, meaning that more than 10 percent of the content was retained. Scintigraphy has not been shown to be useful as a diagnostic tool to judge response to treatment. Scintigraphy has other disadvantages such as low-dose radiation exposure, lack of sensitivity in detecting delayed emptying, lack of a standardized protocol in widespread use, duration of up to 4 hours, a half-day lost from work for the patient, and a high cost of interpretation.

Antroduodenal Manometry

Antroduodenal manometry is a technically cumbersome technology, only offered in a few specialized centers, that can provide information about gastric physiology. In this testing procedure, a manometry catheter is inserted through the pyloric channel, often with endoscopic guidance and sedation of the patient. Then pressure measurements are captured, which provide information about the small bowel and gastric pressure patterns during resting, mealtime, and after medication usage. Antroduodenal manometry may help differentiate myopathic and

neuropathic etiologies of symptoms. Myopathy is present if amplitude muscle pressures of less than 30 mmHg are documented, and neuropathy is present if discoordinated bursts of muscle activity are detected.

Wireless Motility Capsule

A new modality, the wireless motility capsule, is available and has been approved by the U.S. Food and Drug Administration (FDA) for identifying motility disorders.[1] This new modality is a portable, ingestible capsule that, when swallowed, records and transmits data to a receiver as it travels through the gut. The capsule can measure pH, pressure, and temperature to track location, gastric contents, and expellation time from the different regions of the bowel. Wireless motility capsule testing has been studied in small trials to assess gastric emptying. It has been recommended by the ANMS and designated a technology to be watched by the ACG. The capsule is a one-time use device that is activated and then swallowed by the patient who has symptoms suggestive of gastric emptying delay. The device provides frequent measures of pH, temperature, and pressure to determine its approximate location along the gut at any given time. The patient takes the pill after eating a standardized meal and wears a small monitor that allows telemetry recordings to be made. Gastric emptying time is assessed from ingestion of the capsule, a point at which there is a low pH reading, to an abrupt rise in pH after it moves into the small bowel.[10] A cutoff point for gastric emptying time has been established to be 300 minutes in a tandem scintigraphic study of the capsule alone in comparison with a radiolabeled meal.[11] Disadvantages of the capsule include failure of the capsule to capture data (requiring repeat testing), delay or total failure of the capsule to pass (requiring serial x-rays to document passage or endoscopic or surgical removal, respectively), and inability to use the capsule for anyone with a possible stricture, altered anatomy, or severe pyloric stenosis.[12] Most patients do not mind wearing the data receiver during testing, but this may limit some patients in their daily life. Also, patients must be able to tolerate stopping all proton pump inhibitors and histamine 2 blockers before testing.[12] Advantages of testing with the wireless motility capsule include that it is wireless and painless, can be used in an office setting without sedation or radiation, and provides information for the whole gut in addition to the area of interest for gastric emptying.[13, 14] Most physicians would assess patients for evidence or history of stricture before using the capsule; this assessment might include additional imaging studies that would not have been performed otherwise.

Use of Gastric Emptying Testing To Guide Treatment

Documentation of gastric emptying delay guides physicians in their recommendations for nutrition, medication, and surgical therapies. Testing can also inform physicians about the length and severity of delay. Thus, changes in diet can be made to accommodate better gastric emptying. Recommended changes in diet may include a low-fat diet, a low-residue (low fiber, easy to digest) diet, a liquid diet, or increasing consumption to multiple small meals taken 4 to 6 times per day. Prokinetic treatment, like erythromycin, is often used to treat patients who have documented gastroparesis. Patients can make better decisions about using prokinetics such as oral, intravenous, and sublingual preparations of metoclopramide, based on the confirmation of gastroparesis with testing. This is important to patients because there is an FDA black box warning about the side effects of metoclopramide when used beyond 3 months. Some research protocols involve the use of domperidone (Motilium®), which is not FDA-approved but is available in many countries outside the U.S. and can be used in clinical care and research in the

U.S. through an Investigational New Drug Application encouraged by the FDA. Without documentation of gastroparesis, most physicians would be reluctant to use domperidone. Patients with severe symptoms and severe emptying delay despite dietary changes may need feeding tubes such as jejunostomy or gastrojejunostomy tubes that bypass the stomach entirely. Patients with total failure of gastric emptying may not tolerate feeding tubes and may require intravenous nutrition. As patients undergo consideration for compassionate use of gastric stimulation therapy, one of the key eligibility criteria is the presence of gastric emptying delay on testing. Thus, accurate diagnosis of gastroparesis is integral to decisions about management.

Outcomes

The main outcomes of interest are assessment of motility and diagnosis of gastric emptying delay. Other outcomes include the ability of testing to influence treatment decisions by changes in medications or nutrition or to affect patient-centered outcomes such as symptom improvement, need for surgery, quality of life, and patient satisfaction. It is important to consider potential harms of testing such as capsule retention, radiation exposure, and mortality. Clinicians and policymakers may also be interested in the effects on resource utilization such as the need for additional tests, physician services, or hospitalizations.

Controversy

The controversy surrounding the accuracy of the cutoff point for scintigraphy in differentiating patients with true gastroparesis from those with more functional symptoms was acknowledged at the 2011 ANMS meeting. A suggestion was made to use stricter criteria for diagnosing gastroparesis: only patients who were off all possible offending medications and who had retained at least 25 percent of gastric content at 4 hours would be diagnosed with the condition. Greater retention of gastric content is related to greater severity of disease, which may have implications for how patients with abnormal gastric emptying on capsule testing get stratified for treatment. Previous consensus recommendations from 2008 established baseline standards for scintigraphy and discussed grading severity of the gastric emptying delay as relevant to clinical research, but did not establish how that grading would affect decisions about patients.[15] We will address this issue by looking for data on how treatment decisions differ between testing methods. Another controversy was the lack of information regarding whether or not scintigraphy or wireless motility capsule testing could offer any guidance in assessing response to treatment or whether they would remain purely diagnostic tools. We will address this issue by looking for data on treatment response in terms of patient-reported outcomes. It is also unclear at this time which populations would benefit most from the wireless motility capsule or which order of testing is best to diagnose patients. Currently, wireless motility capsule testing is being used in a complementary fashion as an addition to reference standard tests like scintigraphy. Whether it can replace or should supersede other testing methods is controversial.

Constipation

Definition and Prevalence

Constipation is a common symptom, reportedly occurring in 10 to 20 percent of the U.S. population.[16, 17] The definition of constipation has been established with slight variation by multiple professional societies, but usually constipation is defined as fewer than two bowel

movements per week or a decrease in a person's normal frequency of stools that is accompanied by straining, difficulty passing stool, or passage of hard solid stools.[12] Patients with symptoms of constipation must be assessed by their medical history and a physical examination to exclude malignant or organic causes of constipation. A careful history should be able to elicit warning signs such as new onset of symptoms, obstructive symptoms, rectal bleeding, unintentional weight loss, or family history of early colon cancer. A rectal examination can further delineate rectal function and tone, and it can help to exclude a low rectal cancer. Investigation with colonoscopy is indicated if fecal occult blood or iron deficiency anemia are detected. Patients with symptoms of constipation and warning signs should be investigated with colonoscopy, as should all patients over 50 years of age who have never received a screening colonoscopy;[18] however, the yield of colonoscopy is low in patients with constipation and warning signs. Once organic causes of constipation are excluded, a diagnosis of functional constipation can be made. For individuals who are less than 50 years of age without "red flag" symptoms, no testing is required to make a diagnosis of constipation if they meet the Rome III criteria. The Rome III criteria define functional constipation as follows:

- Must include *two or more* of the following:
  a. Straining during at least 25 percent of defecations
  b. Lumpy or hard stools in at least 25 percent of defecations
  c. Sensation of incomplete evacuation for at least 25 percent of defecations
  d. Sensation of anorectal obstruction/blockage for at least 25 percent of defecations
  e. Manual maneuvers to facilitate at least 25 percent of defecations (e.g., digital evacuation, support of the pelvic floor)
  f. Fewer than three defecations per week
- Loose stools rarely present without the use of laxatives
- Insufficient criteria for irritable bowel syndrome

Two or more of the above criteria must be fulfilled for the last 3 months, with symptom onset being at least 6 months prior to diagnosis.[19]

Basic Management

Lifestyle changes and medical management should be used for all patients with symptoms of constipation. Lifestyle changes include drinking appropriate quantities of liquid, removing all possible offending medications, and eating a sufficient amount of vegetables, fruit, and fiber as recommended by the U.S. Department of Agriculture. Medical management includes avoiding constipating medications, and initiating bulking agents (fiber supplements), stool softeners (Colace®, mineral oil), osmotic and stimulant laxatives (lactulose, milk of magnesia, magnesium citrate, senna, Dulcolax®), or prokinetics (such as prucalopride, which is not yet FDA-approved, but available in Europe and elsewhere) as indicated. Thus, the initial evaluation of constipation does not often involve colonic transit testing.

Evaluation of Possible Slow-Transit Constipation

For certain individuals with suspected slow-transit constipation — defined as persistent symptoms of constipation despite medical management and lifestyle changes — colon transit testing can provide insight into the etiology of the constipation. Testing can be used to explain the patient who fails first-line therapy and thus assist in identifying or excluding patients as surgical candidates.[12] It is most strongly indicated for anyone considering colon resection or

surgery. Transit disorders include slow colonic transit or colonic inertia, a hypomotile disorder of the colon where transit in the proximal colon is slow without evidence of retropulsion of the markers from the left colon and without evidence of anorectal dysfunction. Defecatory dysfunction (or functional outlet dysfunction) is the presence of discoordinated motion of the anorectum muscles causing ineffective or weak expulsion of stool. Idiopathic megacolon (primary or secondary), a pathological enlargement of the colon, can also be present and may occur in conjunction with longstanding neurological diseases or Hirschsprung's disease, a failure of the development of the nerve cells within the colon wall.[20] The main diagnostic methods used to test for colonic motility are radiopaque marker examination, colonic scintigraphy, colonic and anorectal manometry, and wireless motility capsule testing.[21, 22] The reference standard has been radiopaque markers; however, scintigraphy has also been selected as a comparable measure of colonic transit. Other investigatory tools that can provide complementary information are imaging tests such as defacography with barium or magnetic resonance imaging, barium enema, endorectal ultrasound, and magnetic resonance imaging of the pelvis.

Radiopaque Markers

Slow-transit constipation is defined by the reference standard of radiopaque marker testing (commonly known as Sitz Markers).[21, 22] Varied protocols for radiopaque marker testing are employed by different institutions and there is no one standard recommended protocol endorsed by the major GI societies at present. In its simplest form, such testing is performed by having the patient ingest the radiopaque markers on day 0 and then taking x-ray images at intervals to document the excretion of those markers by 5 days after ingestion. Retention of markers after the initial observation period allows identification of patients with slow transit and focuses on the area of the colon that has the greatest delays.[10, 12] One disadvantage to radiopaque marker testing is x-ray exposure in individuals with constipation. However, the test has been validated and in use since the late 1960s.[10]

Colonic Scintigraphy

Colon scintigraphy can also be performed but is rarely available outside of highly specialized motility research centers. It involves ingestion of a radiolabeled meal or radiolabeled tracer to follow the sequence of transit from the upper to lower GI tract. This method has been validated and has been used to study treatment response in several drug trials. Two protocols exist. The protocol from Temple University is based on a seven-region analysis in which a numeric value represents overall colon transit and emptying of the ascending colon, summarized in terms of the half-life of the radiolabeled substance. The protocol from the Mayo Clinic combines the results of a five-region analysis. A disadvantage of colonic scintigraphy is that testing requires several days and requires radiation exposure. Studies have assessed the validity relative to radiopaque markers.[23, 24] The ANMS guidelines endorse colon scintigraphy as a potential test for evaluating colon transit.

Total Colonic Manometry

Colonic manometry has been described more recently but is not widely available and is only performed in specialized centers. For this test, the manometry catheter is placed with endoscopic and fluoroscopic guidance after a full bowel preparation. The catheter is left in place in some cases for up to 24 hours, and recordings are obtained after sedation wears off from the procedure used to place the catheter. One disadvantage of this method is its limited availability, which is

due to the specialized technical expertise that is required to perform and interpret this labor-intensive procedure.

Wireless Motility Capsule

Wireless motility capsule testing involves ingesting a capsule and wearing a receiver to collect data. Cecal entry is defined as a sustained drop in pH of greater than 1 unit that occurs more than 30 minutes after gastric emptying. Colonic transit time is the time between cecal entry and rectal exit. Transit time within the colon can be calculated from the cecal transit time until the capsule exits the body, which is marked by a large temperature reduction.[12] One disadvantage is that 5 percent of patients undergoing capsule testing may not collect cecal entry-time data, thus limiting the diagnostic potential of the study.[10] Other disadvantages are that radiographic imaging must be used to confirm elimination of the capsule when it fails to pass spontaneously and that the device can fail to work at a rate of up to 3 percent in some studies. In addition, prolonged colon transit time with this technology does not necessarily distinguish slow transit from defecatory dysfunction. One advantage of capsule testing is the simultaneous collection of data for the whole gut with one test. Other advantages include the lack of radiation exposure when the capsule is passed spontaneously and is observed in the stool after safe passage, and the fact that it can be performed in the outpatient setting, thereby providing accurate information about real-life conditions. Capsule testing cannot be performed in any patient expected to have stricture or stenosis. Other testing might be required to ensure that no narrowing is present. Another advantage of capsule testing is that it provides a more complete picture of colonic transit (like whole-bowel scintigraphy might if it were more widely available); whereas, radiopaque marker testing only offers static imaging. It is uncertain whether all the extra data will be useful to change outcomes in any way.

Use of Colon Transit Testing to Guide Treatment

Most patients with chronic constipation have improvement of symptoms with medical therapy and/or lifestyle changes. For some patients, all measures fail and their motility disorders may be identified with colon transit testing. When anorectal or outlet dysfunction is identified, biofeedback therapy can be used for treatment. Evidence of Hirschsprung's disease is an indication for surgical segmental resection. Megacolon requires medical therapy tailored to reducing gas formation, and reduction of fiber intake may paradoxically relieve symptoms. If these conservative measures fail, then megacolon may warrant segmental or total colectomy. If testing confirms the presence of slow-transit constipation (colonic inertia) without use of laxatives, then the next step in evaluation is transit testing with use of laxatives. Only after demonstrating colonic inertia in both of these settings should surgery be considered as a potential therapy.[25] Clear demonstration of severe total or segmental slow-transit constipation is an indication for colectomy; however, most clinicians reserve colectomy for patients with the most untreatable conditions. Sometimes an individual may have features of both outlet dysfunction and inertia; in these cases, outlet dysfunction must be addressed before making decisions about slow transit. If outlet dysfunction does not improve with biofeedback therapy, then surgical options may be limited to ileostomy rather than primary anastomosis. Therefore, accurate diagnosis is essential to proper management of slow-transit motility disorders.

Outcomes

A major outcome of interest to clinicians is the ability to diagnose slow-transit constipation. Clinical outcomes include the ability of testing to influence treatment decisions such as change in medications or change in nutrition or to affect patient-centered outcomes such as symptom improvement, need for surgery, quality of life, and patient satisfaction. It is important to consider potential harms such as capsule retention, radiation exposure, and mortality. Clinicians and policymakers may also be interested in the effects on resource utilization such as the need for additional tests, physician services, and hospitalizations.

Controversy

Controversy regarding the role of capsule testing in the diagnostic evaluation of constipation was addressed at the 2011 ANMS conference. Some experts thought that it would likely be a complementary test rather than an independent test for patients with this disease.

Scope and Key Questions

Our objective is to summarize the evidence on how useful current testing modalities for colonic and gastric motility are for diagnosing disease. Additionally, we seek to determine whether wireless motility capsule testing is useful in conjunction with or instead of other testing modalities for diagnosing and managing delayed gastric emptying or slow-transit constipation. Our goal is to define the populations that would benefit most from motility testing, including wireless motility capsule testing.

Key Questions

Our finalized Key Questions (KQs) are below, and graphically depicted in Figure 1:

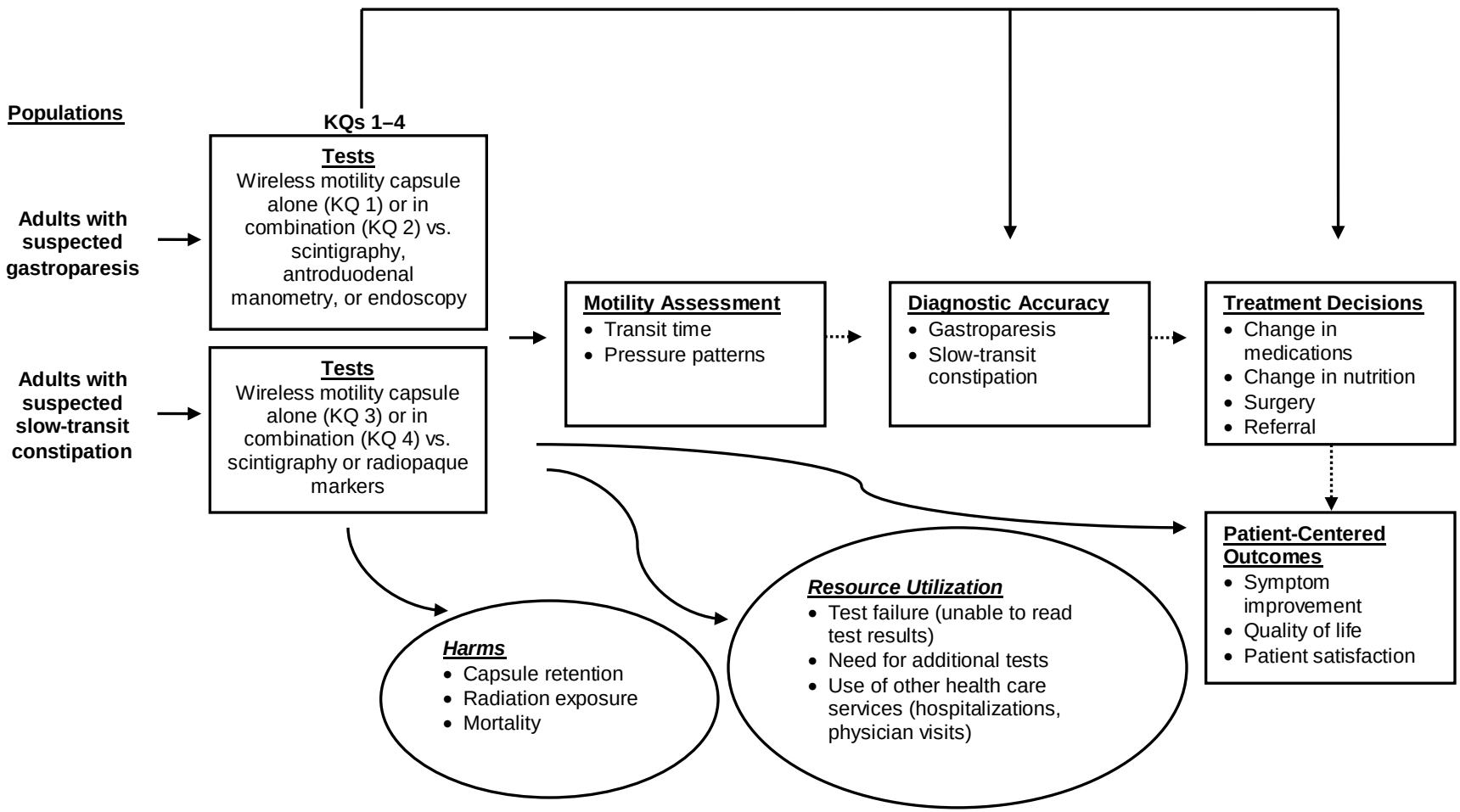
KQ1. In the evaluation of gastric dysmotility, how does the wireless motility capsule alone compare with gastric scintigraphy, antroduodenal manometry, and endoscopy in terms of diagnostic accuracy of gastric emptying delay, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

KQ2. When gastric scintigraphy, antroduodenal manometry, or endoscopy is used in the evaluation of gastric dysmotility, what is the incremental value of also using the wireless motility capsule in terms of diagnostic accuracy of gastric emptying delay, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

KQ3. In the evaluation of colonic dysmotility, how does the wireless motility capsule alone compare with radiopaque markers and scintigraphy in terms of diagnostic accuracy of slow-transit constipation, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

KQ4**.** When a radiopaque marker or scintigraphy is used in the evaluation of colonic dysmotility, what is the incremental value of also using the wireless motility capsule in terms of diagnostic accuracy of slow-transit constipation, motility assessment, treatment decisions, patient-centered outcomes, harms, and resource utilization?

Figure 1. Analytic framework of the comparative effectiveness of diagnostic technologies for evaluating gastroparesis and constipation



KQ = Key Question

Methods

This topic was nominated via the Agency for Healthcare Research and Quality's (AHRQ) Web site. Our Evidence-based Practice Center (EPC) established a team and a work plan to develop the evidence report. The project involved formulating and refining the questions, developing a protocol with input from selected technical experts, performing a comprehensive literature search, summarizing the state of the literature, constructing evidence tables, synthesizing the evidence, and submitting the report for peer review.

Topic Refinement

We recruited a panel of Key Informants to provide input on the selection and refinement of the questions to be examined. The Key Informants included three gastroenterologists who specialize in motility disorders, a representative from a patient advocacy group, and a representative from a payer organization. We posted our draft Key Questions (KQs) on AHRQ's Web site in December 2011 for public comment.

With input from the Key Informants, representatives of AHRQ, and public comments, we developed the KQs that are presented in the Scope and Key Questions section of the Introduction. The KQs focus on the diagnostic accuracy of the wireless motility capsule alone or in combination with other diagnostic tests in the evaluation of gastroparesis and slow-transit constipation.

Technical Expert Panel

We recruited a panel of technical experts to review a draft of the protocol for preparing this evidence report. The Technical Expert Panel included five gastroenterologists with expertise in motility disorders, a patient representative, and an expert in diagnostic accuracy. The Technical Expert Panel reviewed our protocol, and provided feedback on the proposed methods for addressing the KQs. With the feedback from the Technical Expert Panel and AHRQ representatives, we finalized the protocol and posted it on AHRQ's Web site.

Search Strategy

We searched the following databases for original studies for the periods in parentheses: MEDLINE® (1966 to January 2012) and Embase® (1974 to January 2012). We developed a search strategy for MEDLINE, accessed via PubMed, based on an analysis of the medical subject headings (MeSH) terms and text words of key articles identified a priori (Appendix A). Additionally, we reviewed the reference lists of included articles and any relevant review articles.

We downloaded the results of the searches and imported them into ProCite® version 5 (ISI ResearchSoft, Carlsbad, CA). We scanned for exact article duplicates, author/title duplicates, and title duplicates using the duplication check feature in ProCite®. We uploaded the articles from ProCite to DistillerSR (Evidence Partners, Ottawa, Ontario, Canada), a Web-based software package developed for systematic review data management. We used this database to track the search results at the levels of title review, abstract review, and article inclusion/exclusion.

To identify additional studies, the EPC's Scientific Resource Center submitted a request to the manufacturer of the motility capsule, the SmartPill® Corporation, for any published or

unpublished randomized controlled trials or observational studies that evaluated the wireless motility capsule. The SmartPill® Corporation did not send any materials.

Study Selection

Each title from the literature search was scanned by two independent reviewers. Both reviewers had to indicate that the title was obviously ineligible for it to be eliminated at this level. If they disagreed, they promoted the article to the next level of review (Appendix B, Title Review Form). We designed the title review to capture as many studies as possible that reported on the diagnostic accuracy of the wireless motility capsule.

Two investigators reviewed abstracts independently, and excluded an article if both investigators agreed it met one or more of the exclusion criteria (see inclusion and exclusion criteria listed in Table 1 and the Abstract Review Form in Appendix B). The team resolved differences between investigators regarding abstract eligibility through consensus adjudication.

Two reviewers performed another independent parallel full-text review of articles promoted on the basis of abstract review to determine if we should include these articles for data abstraction (Appendix B, Article Review Form). We resolved differences regarding article inclusion through consensus adjudication.

Data Abstraction

We used a systematic approach to extract all data to minimize the risk of bias in this process. We created and pilot tested standardized spreadsheets for data extraction. By creating standardized spreadsheets for data extraction, we sought to maximize consistency in identifying all pertinent data available for synthesis.

The study investigators performed double data abstraction on each article. The second reviewer confirmed the first reviewer's abstracted data for completeness and accuracy. We formed reviewer pairs that included personnel with both clinical and methodological expertise. We did not hide from the reviewers the identity of the authors of the articles, their respective institutions, or the journals in which their articles were published.

For all articles, the reviewers extracted information on general study characteristics (e.g., study design, country, location of recruitment, start year of recruitment, multi-center vs. single center, length of followup, and length of time in between diagnostic tests), study participants (e.g., condition, age, gender, race, weight, prior diagnostic tests, blood sugar, smoking status, diabetes status, defacatory dysfunction status, and the use of prokinetics, narcotics, antidepressants, proton pump inhibitors, and laxatives), eligibility criteria, characteristics of the wireless motility capsule testing (e.g., if the pill was swallowed or placed, if a standardized meal was used, if and when patients were given Ensure® shakes), comparisons, outcome measures, definitions, and the results of each outcome, including measures of variability. For endoscopy, we would capture the number of hours without anything by mouth before the procedure and the method of sedation. For gastric scintigraphy, we would collect data on duration of testing (e.g., 4 hours) and if liquid or solid components were used. For antroduodenal manometry, we would collect data on which catheter was used and how the catheter was placed. For radiopaque markers, we would collect data on the type of radiopaque markers used, the timing of dosing of markers and the surveillance x-rays, and if counts were recorded in each segment of the colon, or if a total count was used, or both. For colon scintigraphy, we would collect data on the type of protocol used, and the duration of testing. For each of the diagnostic tests, we would collect information on the criteria used to make a diagnosis of gastroparesis and slow-transit

constipation, and whether patients were instructed to not use tobacco, prokinetics, narcotics, antidepressants, proton pump inhibitors, or laxatives at the time of the test.

The individual completing the review entered all information from the article review process into a Microsoft Excel (Microsoft, Redmond, WA) spreadsheet. Reviewers entered comments into the system whenever applicable.

Table 1. Inclusion and exclusion criteria

Population and condition of interest	• We included studies that evaluated patients with suspected gastroparesis and/or slow-transit constipation. • We included only adult human subjects.
Diagnostic test of interest	• We included all studies that evaluated the wireless motility capsule alone or in combination with other tests.
Comparisons of interest	• For KQs 1 and 2, we included studies that compared the wireless motility capsule with other conventional diagnostic tests for suspected gastroparesis, including scintigraphy, antroduodenal manometry, and endoscopy. • For KQs 3 and 4, we included studies that compared the wireless motility capsule with other conventional diagnostic tests for suspected slow-transit constipation, including scintigraphy and radiopaque markers.
Outcomes	• We included studies that reported on at least one of the following outcomes: o Diagnostic accuracy ▪ Gastroparesis: The reference standard is a 4-hour gastric emptying study. ▪ Slow-transit constipation: There is no consensus on a standard, so we examined this outcome relative to each existing standard (radiopaque markers and colonic scintigraphy). o Motility assessment ▪ Transit time ▪ Pressure patterns o Treatment decisions ▪ Change in medications ▪ Change in nutrition ▪ Need for surgery ▪ Need for a referral o Patient-centered outcomes ▪ Symptom improvement ▪ Quality of life ▪ Patient satisfaction o Resource utilization ▪ Test failure (unable to read test results) ▪ Need for additional tests because of continued uncertainty about diagnosis ▪ Utilization of other health care services such as hospitalizations and physician visits o Harms, such as capsule retention, radiation exposure, and mortality
Type of study	• We excluded articles with no original data (e.g., editorials, commentaries, reviews). • We included all types of studies with a comparison group that evaluated the wireless motility capsule.
Timing and setting	• We included all clinical settings in developed countries. • We included all durations of followup, but our desired length of followup for symptom improvement, quality of life, and need for additional tests was at least 3 months.

KQ = key question

Quality Assessment

Two reviewers independently assessed article quality. We selected and modified the questions from the QUADAS-2 quality assessment tool.[26] We supplemented this tool with additional quality-assessment questions (e.g., to assess spectrum bias) based on recommendations in the *Methods Guide for Medical Test Review*.[27] Our quality assessment included items on: (1) whether healthy subjects were excluded from the diagnostic accuracy comparison; (2) whether severely affected patients were excluded; (3) whether a random sample

of patients was enrolled; (4) whether all patients received the same reference standard; (5) whether all patients were included in the analysis; (6) whether the results of the test were interpreted independently; (7) whether the time period between tests was reasonable short (within 3 months) to ensure the condition did not change; (8) whether the cut-off values for test positivity were established before the study started; (9) whether a stated aim of the study was to compare diagnostic accuracy between wireless motility capsule testing and other diagnostic tests; (10) whether the study reported on conflicts of interst; (11) whether the study was funded by a commercial source related to motility testing; and (12) whether any of the authors were employed by or received funding or fees from a commercial source related to motility testing.

When multiple publications reported on the same study and the assessments of study quality differed, we did not change the unclear responses to a yes or no based on reporting in a different publication. We assessed study quality for each individual publication because the analyses often differed even though it was conducted among the same patient population.

The two reviewers resolved differences in quality assessment.

Applicability

We assessed the applicability of studies in terms of the degree to which the study population (age, etiology, comorbidities, prior surgery or gastric pacer), diagnostic tests (use of narcotics during testing, use of bowel motility-altering agents, such as laxatives or prokinetic agents), outcomes, and settings (e.g., referral center) are typical for the treatment of individuals with suspected gastroparesis or slow-transit constipation.

Data Analysis and Synthesis

We had planned to conduct meta-analyses when there was sufficient data (at least three studies) and studies were sufficiently homogenous with respect to key variables (population characteristics, study duration, and diagnostic tests). We qualitatively summarized studies not amenable to pooling. For measures of diagnostic accuracy, we summarized the results in terms of sensitivity, specificity, and test concordance. For any given study, the results can be described in terms of the number of positive and negative tests detected by the index test and reference standard (see Figure 2). We report the diagnostic test accuracy results separately for studies that included known patients and non-diseased controls and for studies that included patients suspected of having the condition.

Figure 2. Calculation for sensitivity, specificity, and test concordance

	Reference standard – positive result	Reference standard – negative result
Index test – positive test result	a	b
Index test – negative test result	c	d

Sensitivity = a / (a+c)

Specificity = d / (b + d)

Test concordance = (a + d) / (a + b + c + d)

When the reference standard was a clinical diagnosis, we chose a 10 percent difference between tests in sensitivity or specificity as a clinically meaningful difference because key studies were powered to detect a 10 percent difference.[28] When the reference standard was another diagnostic test, the wireless motility capsule needed a test concordance of at least 80 percent to be considered similar.

Data Entry and Quality Control

A second reviewer checked the data that had been entered into the Excel spreadsheets. Second reviewers were generally more experienced members of the research team. Any problems with a reviewer's data abstraction were discussed at a meeting with the reviewers. In addition, 10 percent of the included studies were audited by a third team member. A few discrepancies were found. For that reason, the lead investigators re-checked the outcome data as they prepared the text of the results on each KQ.

Rating the Body of Evidence

At the completion of our review, we graded the strength of the best available evidence addressing KQs 1-4 by adapting an evidence grading scheme recommended in the *Methods Guide for Medical Test Review*[27] and in the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[29, 30] Both of these evidence grading schemes are based on the recommendations of GRADE Working Group.[31] We applied evidence grades to the bodies of evidence about each diagnostic test comparison for each outcome. We assessed the strength of the best available evidence by assessing the risk of bias, consistency, directness, and precision.

To evaluate the risk of bias, we considered: (1) if the study was published as an abstact only or as a peer-reviewed manuscript; (2) whether the results of the wireless motility capsule were interpreted independently from the results of other diagnostic tests; and (3) if there were other major quality issues. We contacted the authors regarding blinding of diagnostic test results if it was unclear in the manuscript. We did not evaluate abstracts on blinding. We considered spectrum bias (i.e., the extent to which disease severity affects the test results) as part of the assessment of risk of bias. We rated the body of evidence as "low risk of bias" if the diagnostic test results were interpreted independently and there were no other major quality issues (see above list of items included in the quality assessment). We rated the body of evidence as "medium risk of bias" if the diagnostic test results were interpreted independently and there was one major quality issue from our quality assessment, or the results of the diagnostic test results were not interpreted independently and there were no other major quality issues. We rated the body of evidence as "high risk of bias" if the diagnostic test results were interpreted independently and there was more than one major quality issues, or the results of the diagnostic test results were not interpreted independently and there were at least one major quality issue.

We rated the body of evidence as "consistent" if most of the studies showed the same direction of effect. We rated the consistency of a single study as "not applicable." We rated the body of the evidence as "direct" if most of the studies directly addressed the KQs. We based our rating of precision on the width of the confidence intervals for sensitivity, specificity, and positive and negative predictive values. If the width of the confidence interval was less than or equal to 10 percent, then we considered the body of evidence to be "precise."

We classified evidence pertaining to the KQs into four basic categories: 1) "high" strength of evidence (indicating high confidence that the evidence reflects the true effect and that further research is very unlikely to change our confidence in the estimate of the effect); 2) "moderate"

strength of evidence (indicating moderate confidence that the evidence reflects the true effect and that further research may change our confidence in the estimate of the effect and may change the estimate); 3) “low” grade (indicating low confidence that the evidence reflects the true effect and that further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate); and 4) “insufficient” strength of evidence (evidence is unavailable or does not permit a conclusion).[31]

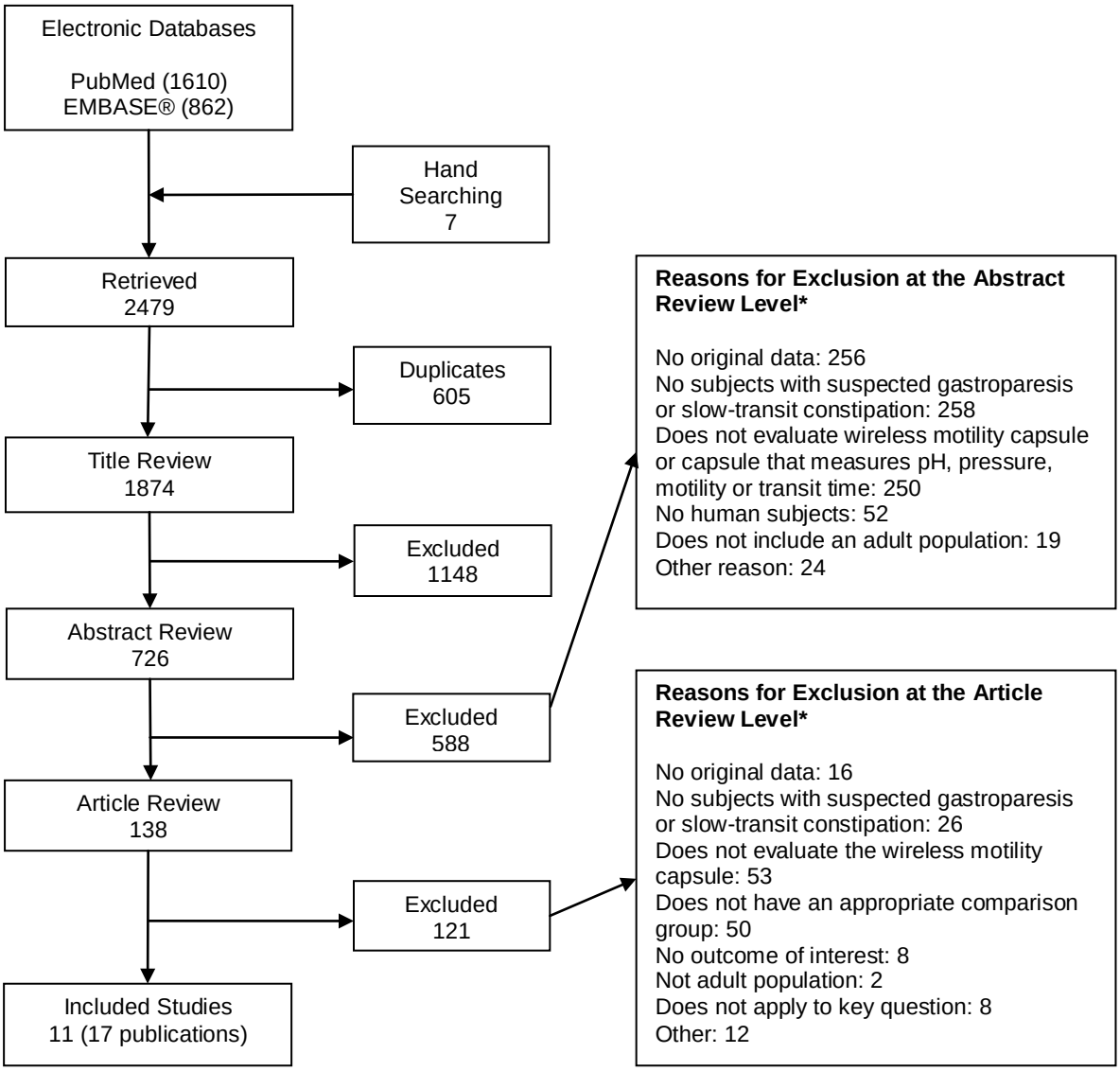
Results

Search Results

Figure 3 summarizes the results of our literature search. Our search retrieved 1874 unique records. After reviewing the titles and abstracts, we considered 138 articles as potentially relevant and we reviewed the full text of each article for eligibility (see Appendix C for a list of the excluded articles). We included a total of 11 studies (in 17 publications)[12, 28, 32-40] in this review. One manuscript[38] conducted additional analyses among the subjects included in another manuscript by Kuo et al.[11] Two manuscripts[41, 42] conducted additional analyses among the subjects included in the manuscript by Rao et al.[12] Two abstracts[39, 43] reported on the same patient population. One manuscript[33] was previously published in two abstracts.[44, 45]

Seven studies (10 publications) evaluated the wireless motility capsule test among patients with gastroparesis,[11, 32-38, 44, 45] and eight studies (13 publications) evaluated the wireless motility capsule test among patients with slow-transit constipation.[12, 28, 32, 33, 35, 37, 39-45]

Figure 3. Summary of literature search (number of articles)



* Total may exceed number in corresponding box, as articles could be excluded for more than one reason at this level.

Study Design Characteristics

A total of 11 studies reported in 17 publications were included (see Appendix D, Evidence Table 1).[11, 12, 28, 32-45] Six studies were prospective,[11, 12, 28, 34, 36, 40] four studies were retrospective,[32, 33, 35, 37] and one did not specify a study design.[39] Five of the prospective studies occurred at multiple study centers[11, 12, 28, 36, 40] and the other prospective studies did not report the number of study locations. All prospective studies applied the tests concurrently. One of the retrospective studies involved chart review from multiple centers[32] with the remainder using

information from single centers.[33, 35, 37] Six studies were reported in meeting abstracts,[34-37, 39, 40] with the remainder reported in peer-reviewed publications.

All studies that reported the study location occurred in the U.S.[11, 12, 28, 32-34, 36, 37] One study took place in multiple countries including the U.S.[28] All studies that reported the location of recruitment occurred in tertiary centers.[12, 32-37]

Three studies reported the start year of recruitment.[11, 32, 33] One began recruitment in 2005[11] with the other two starting recruitment in 2007.[32, 33] Length of followup for the prospective studies and those with unspecified designs included the day of the testing only,[34, 36, 37, 39, 40, 43] 3 days,[11] 14 days,[28] and 21 days.[12]

Prospective studies included patients with known gastroparesis[11, 34, 36] or constipation.[12, 28] Four retrospective studies included patients with suspected gastroparesis or constipation[32, 33, 35, 37] and one included patients with known constipation exclusively.[39] Five of the prospective studies also included patients without gastroparesis or constipation,[11, 12, 34, 36, 40] whereas one study included only patients with known constipation.[28] Two studies that included patients with constipation used the Rome III criteria as inclusion criteria.[12, 28] Two studies reported age restrictions. One allowed patients 18 to 80 years of age[28] and the other included patients older than 65 years of age.[40]

Study Population Characteristics

No gender restrictions were made in the inclusion criteria, although the majority of participants with gastroparesis or constipation were female (Appendix D, Evidence Table 2). The mean age was 40 or greater in all studies that reported an average.[12, 28, 32, 33, 39, 40] Three studies reported on race or ethnicity.[11, 28, 33] Greater than 80 percent of the participants were white in these studies. No study reported a measure of weight, blood sugar, or smoking status at baseline. Two studies reported on the percent of patients with diabetes.[32, 38] Fifteen and 37 percent had diabetes. Two studies reported on defecatory dysfunction.[32, 39] Twenty of 32 subjects had defecatory dysfunction in one study[39] and in another study 64 percent of patients with had defecatory dysfunction.[32] Studies rarely reported use of medications such as prokinetics, narcotics, antidepressants, proton pump inhibitors, and laxatives, prior to and during the studies. Diagnostic testing prior to the study included scintigraphy[11, 32, 33, 36] and radiopaque markers.[32, 33]

Characteristics of Diagnostic Tests

In Tables 2, 3, and 4, we summarized the characteristics of the tests used in the studies, taking into consideration how evaluation of gastrointestinal motility is dependent on multiple factors, including not only the type of test but also the specific protocol employed (Appendix D, Evidence Table 3). The specific protocols employed for these studies often were not standardized. The characteristics of the gastric scintigraphy tests are detailed in Table 2. Characteristics of wireless motility capsule testing for gastroparesis are detailed in Table 3. Characteristics of radiopaque marker testing are detailed in Table 4. Only two abstracts reported on antroduodenal manometry testing, and both provided limited information regarding study characteristics. No included studies reported on colonic manometry.

Table 2. Characteristics of gastric scintigraphy testing in studies of patients with symptoms of possible gastroparesis

Author, year	Duration of test	Tougas protocol*	Patients off tobacco at time of test	Patients off prokinetics at time of test	Patients off narcotics at time of test	Patients off antidepressants at time of test
Rao, 2011[33]	NR	NR	NR	NR	NR	NR
Kuo, 2008[11]	4 hours	Yes	Yes	Yes	Yes	No
Brun, 2011[34]	4 hours	Yes	NR	NR	NR	NR
Mysore, 2010[45] [earlier version of study[33]]	NR	NR	NR	NR	NR	NR
Lee, 2010[35]	4 hours	Yes	NR	NR	NR	NR
Reddymasu, 2010[36]	4 hours	Yes	NR	NR	NR	NR
Lee, 2012[38]	4 hours	Yes	NR	Yes	Yes	NR

NR = not reported

* The Tougas protocol refers to a 4-hour solid state gastric scintigraphy protocol agreed upon by consensus of the American Neurogastroenterology and Motility Society and the Nuclear Medicine Society.[15]

Table 3. Characteristics of wireless motility capsule testing in studies of patients with symptoms of possible gastroparesis or slow-transit constipation

Author, year	Criteria for abnormal	Standardized meal	Type of meal	Ensure® challenge	Off tobacco at time of test	Off prokinetics at time of test	Off narcotics at time of test	Off anti-depressants at time of test	Off PPIs at time of test	Was another study referenced in lieu of providing details within current study?
Kuo, 2011[32]	5 hours	NR	NR	NR	NR	NR	Yes	No	Yes	Yes[11, 12]
Rao, 2011[33]	5 hours	Yes	Bar	NR	NR	NR	Yes	No	Yes	Yes[11, 12, 28]
Camilleri, 2010[28]	5 hours	Yes	Egg Beaters®	Yes	NR	Yes	Yes	Yes	Yes	Yes[12]
Saad, 2010[42] [Sub-analysis of data[12]]	NR	Yes	Bar	Yes	NR	Yes	NR	No	Yes	Yes[12]
Hasler, 2009[41] [Sub-analysis of data[12]]	NR	Yes	Bar	Yes	NR	Yes	Yes	No	Yes	No
Rao, 2009[12]	NR	Yes	Bar	Yes	NR	Yes	NR	No	Yes	No
Kuo, 2008[11]	NR*	Yes	Egg Beaters®	Yes	Yes	Yes	Yes	No	Yes	No
Brun, 2011[34]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mysore, 2010[45] [earlier version of study[33]]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Lee, 2010[35]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Reddymasu, 2010[36]	Gastric cph < 73	NR	NR	NR	NR	NR	NR	NR	NR	NR
Paulson, 2009[43]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Lee, 2009[37]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rao, 2009[39]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rao, 2009[40]	NR	Yes	Bar	Yes	NR	NR	NR	NR	NR	NR
Lee, 2012[38]	5 hours	Yes	Egg Beaters®	Yes	NR	Yes	Yes	NR	Yes	Yes[11]

*Reference article that came up with 5 hour criteria
cph = contractions per hour; NR = not reported; PPI = proton pump inhibitor

Table 4. Characteristics of radiopaque marker testing in studies of patients with symptoms of slow-transit constipation

Author, year	Markers swallowed	Type of markers were used	Timing of ingestion	Days imaging studies were taken	Method of analysis	Considered prolonged colon transit	Was another study referenced in lieu of providing details?
Kuo, 2011[32]	Historically by chart review	ROM	NR	NR	NR	NR	Not referenced
Rao, 2011[33]	NR	ROM	NR	NR	NR	Retention of ≥6 ROM at 120 hrs was defined as abnormal colonic transit	Yes[12, 46]
Camilleri, 2010[28]	Yes	ROM	Ingestion of 24 ROM on 3 consecutive days	Abdominal x-rays taken on day 4 and day 7 (144 hours after ingestion of first markers)	Metcalf method= Count number and distribution of markers. Sum the number of markers visualized on day 4 and day 7 x-rays and equating 1 marker to 1 hr of colonic transit time	Colonic transit time greater than 67 hrs is considered delayed	Yes[47]
Saad, 2010[42] Sub-analysis of data[12]	Yes	ROM	Ingestion of 24 ROM	Abdominal x-rays taken on day 2 and day 5 after ingestion of first markers	See reference	Retention of > 20% of ROM after 5 days	Yes[48]
Hasler, 2009[41] Subset of study[12]	Yes	ROM (Sitzmarks®, Konsyl Pharmaceuticals Fort Worth, TX)	Ingestion of 24 ROM (one capsule)	NR	NR	NR	Yes[12]
Rao, 2009[12]	Yes	ROM (Sitzmarks®, Konsyl Pharmaceuticals Fort Worth, TX)	Ingestion of 24 ROM (one capsule)	Abdominal x-ray 48 hrs and 5 days (120 hrs) after ingestion	Radiographs were reviewed at each location of trial. All radiographs were reviewed by 2 independent investigators who were blinded.	Retention of > 5 markers at day 5 was considered abnormal	Yes[46, 48]
Mysore, 2010[45] [abstract] earlier version of study[33]	Yes	NR	NR	NR	NR	NR	Not referenced
Rao, 2009[39] [abstract]	Yes	NR	NR	NR	NR	NR	Not referenced

NR = not reported; ROM = radiopaque markers

Key Question 1. Evaluation of gastric dysmotility: wireless motility capsule alone versus other diagnostic tests

Key Points

- The diagnostic accuracy of wireless motility capsule is similar to scintigraphy. The sensitivity of wireless motility capsule compared to the reference standard of a clinical diagnosis of gastroparesis ranged from 65 to 68 percent and the specificity ranged from 82 to 87 percent. The sensitivity of gastric scitnigraphy compared to a clinical diagnosis of gastroparesis ranged from 34 to 44 percent and the specificity ranged from 93 to 94 percent. Sensitivity of the wireless motility capsule compared with gastric scintigraphy ranged from 59 to 86 percent and specificity ranged from 64 to 81 percent. (Strength of evidence [SOE]: Low)
- Transit data obtained via wireless motility capsule correlates well with scintigraphic gastric emptying. (SOE: Low)
- Pressure profiles obtained via wireless motility capsule adds to the diagnostic accuracy. Scintigraphy does not measure pressure patterns. (SOE: Low)
- Information derived from wireless motility capsule testing alters management in patients with suspected gastroparesis (50-69 percent change in management for medicine, diet, or surgery). (SOE: Low)
- Wireless motility capsule testing may reduce the need for other testing, but this conclusion was based on one study with a high risk of bias. The need for anorectal manometry may not be reduced by wireless motility capsule testing. (SOE: Low)
- Harms associated with wireless motility capsule were minimal. While no major safety issues were reported, conclusions about harms will likely change with new evidence. (SOE: Low)
- The strength of the evidence was insufficient regarding the effect of wireless motility capsule testing on patient-centered outcomes, as no studies addressed this type of outcome.
- The strength of evidence was insufficient for the comparison of wireless motility capsule with antroduodenal manometry in patients with suspected gastroparesis, as we did not find any studies evaluating this comparison.
- The strength of evidence was insufficient for the comparison of wireless motility capsule with endoscopy in patients with suspected gastroparesis, as we did not find any studies evaluating this comparison.

Wireless Motility Capsule Versus Gastric Scintigraphy

Diagnostic Accuracy

We found seven studies with 560 total patients that examined this outcome for this comparison (Tables 5 and 6).[11, 32-34, 36-38] Diagnostic accuracy was defined in various ways in these studies. Two studies included subjects with and without gastroparesis and evaluated the sensitivity and specificity of the wireless motility capsule and gastric scintigraphy compared with clinical gastroparesis. The sensitivity of wireless motility capsule ranged from 65 to 68 percent

and the specificity ranged from 82 to 87 percent. The sensitivity of gastric scintigraphy compared with clinical gastroparesis ranged from 34 to 46 percent and the specificity ranged from 93 to 94 percent.

All studies looked at diagnostic agreement between the modalities. Diagnostic agreement between wireless motility capsule and gastric scintigraphy ranged from 59 to 86 percent positive test agreement and from 64 to 81 percent for negative test agreement. We estimated the concordance between the two tests to range between 35 and 81 percent. The range reflects the heterogeneity of the studies, which used different definitions of gastroparesis as determined by wireless motility capsule, as well as different study inclusion criteria.

One study[11] examined the specific outcome of diagnostic reclassification for this comparison. The authors recalculated diagnostic accuracy of the wireless motility capsule after reclassifying subjects as gastroparetic or normal based on their 4-hour scintigraphic study results. The receiver operating characteristic area under the curve found for gastric emptying time was 0.94, the sensitivity was 87 percent, and the specificity was 92 percent.

One study[38] estimated the diagnostic accuracy, which they termed "diagnostic gain," of wireless motility capsule compared with gastric emptying scintigraphy (Table 7), using various combinations of gastric emptying time, wireless motility parameters, and gastric scintigraphy. Diagnostic gain was defined as abnormal motility detected by wireless motility capsule, deducting the number of subjects with abnormal gastric scintigraphy but normal wireless motility studies, over the total number of subjects, expressed as a percentage. In patients with confirmed gastroparesis (based on symptoms and prior scintigraphy within 2 years), gastric scintigraphy alone was abnormal in 51 percent of patients whereas 70 percent of patients had an abnormal wireless motility capsule study using a combination of gastric emptying time and motility parameters. The overall diagnostic gain of wireless motility capsule compared with gastric scintigraphy was 19 percent ($P = 0.04$).

One study[34] compared the coefficient of variation (COV) for various measures obtained by gastric scintigraphy and gastric emptying time via wireless motility capsule. This abstract evaluated the relationship between gastric emptying time of the wireless motility capsule and different parameters obtained via 4-hour gastric scintigraphy: namely retention at 2 hours, retention at 4 hours, time of 50 percent emptying, or time of 90 percent emptying. Both studies were obtained simultaneously and they reported that the time of 90 percent emptying by scintigraphy had the COV most similar to that of gastric emptying time by wireless motility capsule (Table 8).

Table 5. Diagnostic accuracy of the wireless motility capsule compared with gastric scintigraphy in the evaluation of gastroparesis comparing patients with known gastroparesis with known non-diseased controls

Author, year	Definition for GP - WMC	Definition for GP - GES	Total N	Sensitivity of WMC compared with clinical GP	Specificity of WMC compared with clinical GP	Sensitivity of GES compared with clinical GP	Specificity of GES compared with clinical GP	Correlation between WMC and GES, (95% CI)	AUC, (95% CI)
Kuo, 2008[11]	Threshold NR; abrupt pH rise (usually >3 pH units) from gastric baseline to a pH >4 as determined by software and 2 reviewers	>10% of meal retained after 4 hr	61 patients with GP 87 subjects without GI dysmotility	65%*	87%*	34% (2-hr), 44% (4-hr)*	93%*	0.63 (0.50-0.75) (2-hr) 0.73 (0.61-0.82) (4-hr)	0.83 (0.74–0.90) (WMC) 0.79 (0.71–0.88) (GES, 2-hr) 0.82 (0.77–0.91) (GES, 4-hr)
Reddymasu, 2010[36]	Motility criteria: gastric cph < 73 or frequency of gastric contractions > 100 mm Hg being less than 2/hr	>10% of meal retained after 4 hr	41 patients with GP 66 subjects without GI dysmotility	68% (motility criteria: 88%)*	82% (motility criteria: 30%)*	46%*	94%*	NR	NR

AUC = area under the curve; CI = confidence interval; cph = contractions per hour; GES = gastric scintigraphy; GI = gastrointestinal; GP = gastroparesis; hr = hours; mm Hg = millimeters mercury; NR = not reported; WMC = wireless motility capsule

* Numerator and denominator not available.

Table 6. Diagnostic accuracy of the wireless motility capsule compared with gastric scintigraphy in the evaluation of gastroparesis including only patients with known or suspected gastroparesis

Author, year	Definition for GP - WMC	Definition for GP- GES	N analyzed with GP	Sensitivity of WMC compared with symptoms	Specficity of WMC compared with symptoms	Sensitiivty of GES compared with symptoms	Sensitivity of WMC compared with GES	Specificity of WMC compared with GES	Concordance of WMC and GES
Kuo, 2011[32]	Emptying time > 5 hr	Based on result of prior testing	83 with suspected GI dysmotility	24/52 (46%)	19/28 (68%)	17/44 (39%)	10/17 (59%)	18/28 (64%)	17/45 (35%)
Rao, 2011[33]	NR	>10% of meal retained after 4 hr	36 suspected	24/36 (66%)	NR	15/36 (42%)	12/15 (80%)	17/21 (81%)	29/36 (81%)
Lee, 2009[37]	NR	NR	32 suspected GI dysmotility	NR	NR	NR	9/14 (64%)	8/10 (80%)	NR
Lee, 2012[38]	WMC emptying time > 5 hr	>10% of meal retained after 4 hr	43 suspected	26/43 (60%)	NR	22/43 (51%)	86%*	66%*	77%*

GES = gastric scintigraphy; GI = gastrointestinal; GP = gastroparesis; hr = hours; NR = not reported; WMC = wireless motility capsule
* Numerator and denominator not available.

Table 7. Diagnostic gain of the wireless motility capsule compared with gastric scintigraphy in the evaluation of gastroparesis

Author, year	Definition for gastroparesis	Total N	GES	GES + GET	GES + G/SB PM	GES + GET + G PM	GET + G/SB PM	GES + GET + SB PM	GES + GET + G/SB PM
Lee, 2012[38]	5 hours	43	51%	67%	65%	67%	70%	75%	74%

GES = gastric emptying scintigraphy; GET = gastric emptying time; G/SB PM = gastric/small bowel pressure measurements; G PM = gastric pressure measurements; SB PM = small bowel pressure measurements

Table 8. Coefficient of variation* of gastric emptying among patients with gastroparesis using gastric scintigraphy and wireless motility capsule

Author, year	Definition for gastroparesis	2h % retention - GES	4h % retention - GES	2h % emptying - GES	4h % emptying – GES	T50 - GES	T90 - GES	GET - WMC
Brun, 2011[34]	Not reported	41%	129%	44%	24%	49%	30%	34%

GES = gastric emptying scintigraphy; GET = gastric emptying time; T50 = time of 50% emptying; T90 = time of 90% emptying; WMC = wireless motility capsule
* The coefficient of variation is a measure of dispersion of a probability distribution, defined as the ratio of the standard deviation of values to the mean of the values in a distribution. The coefficient of variation by itself doesn't tell us which test is better. It only provides a measure of how precisely the test can measure the value of interest, in this case, percent retention or percent emptying.

Motility Assessment

Transit Times

Kuo et al.[11] evaluated 87 healthy subjects and 61 patients with gastroparesis via simultaneous gastric scintigraphy and wireless motility capsule. They compared gastric emptying via scintigraphy at 2 hours (GES-2h) and 4 hours (GES-4h) with gastric emptying time obtained via wireless motility capsule. Normative data for gastric scintigraphy at 2 and 4 hour time points were derived from the Tougas protocol. They reported that the correlation coefficient between gastric emptying time via wireless motility capsule and GES-4h was 0.73 and the correlation coefficient between gastric emptying time via wireless motility capsule and GES-2h was 0.63. Receiver operating characteristic curves were calculated to evaluate the clinical utility of the diagnostic tests for gastric emptying time via the wireless motility capsule and GES-2h and GES-4h cut-offs compared with clinical diagnosis. The area under the receiver operating characteristic curve and the sensitivity and specificity of the three diagnostic tests were reported. No statistically significant difference was observed between the areas under the curve for gastric emptying time via the wireless motility capsule and GES-4h. The authors then compared gastric emptying time via the wireless motility capsule with GES-4h. Using this data, the authors concluded that the area under the curve for gastric emptying time via the wireless motility capsule was 0.94, sensitivity was 87 percent and specificity was 92 percent.

In a subsequent abstract,[34] the investigators reported on variability using additional scintigraphically-derived parameters (T50 or the time of 50 percent emptying of the meal, and T90 or the time of 90 percent emptying of the meal) and reported that gastric emptying time via the wireless motility capsule correlated more closely with T90 than with GES-2h or GES-4h; however, data provided in this abstract was limited.

Lee et al.[38] enrolled 48 subjects with symptoms of gastroparesis and a prior abnormal gastric emptying study. These patients then underwent simultaneous gastric scintigraphy and wireless motility capsule testing. Data from 43 subjects were available for analysis. Looking at transit alone, overall device agreement was calculated at 77 percent (positive agreement 86 percent, negative agreement 66 percent). Seven subjects had a delayed wireless motility capsule with normal scintigraphy, whereas 3 subjects had a delayed scintigraphy but normal transit time on wireless motility capsule.

Rao et al.[33] evaluated 86 patients referred for motility evaluation in a retrospective fashion, comparing the wireless motility capsule with conventional motility testing. Of these patients, 36 had upper gastrointestinal symptoms and also underwent 4-hour gastric scintigraphy. The investigators reported that when wireless motility capsule and gastric scintigraphy results were compared in these patients using transit data alone, both studies were abnormal in 12 of 15 (80 percent) subjects and both tests were normal in 17 of 21 (81 percent) subjects. The overall device agreement was reported as 81 percent using transit alone. There was diagnostic discrepancy in five of the 36 subjects (14 percent).

Reddymasu et al.[36] evaluated 66 healthy subjects and 41 patients with gastroparesis using simultaneous wireless motility capsule testing and scintigraphy. Gastroparetic patients were defined as having symptoms consistent with gastroparesis and a prior abnormal gastric scintigraphy. When wireless motility capsule-derived transit data was looked at in isolation from pressure parameters and compared with clinical symptoms and a prior abnormal gastric scintigraphy test, the sensitivity of the wireless motility capsule was reported to be 68 percent

and specificity was reported to be 82 percent. A current gastric scintigraphy was reported to have a sensitivity of 46 percent and specificity of 94 percent.

Pressure Patterns

Two studies evaluated wireless motility capsule-derived pressure patterns in comparison with gastric scintigraphy alone for patients with gastroparesis. Lee et al.[38] evaluated 43 subjects with symptoms of gastroparesis and a previously-abnormal gastric scintigraphy within 2 years of enrollment. The authors reported that 47 percent of subjects had abnormal gastric or small bowel pressure measurements using the wireless motility capsule. However, a direct comparison between pressure parameters derived by wireless motility capsule (in the absence of transit data) and scintigraphic data alone was not made. The authors did, however, evaluate the additional diagnostic gain achieved by using a combination of transit and pressure parameters. Specifically, 10 of 21 subjects with a normal gastric emptying scintigraphy had pressure abnormalities identified by wireless motility capsule. When compared with gastric scintigraphy alone, this study found a statistically significant improvement in diagnostic gain using a combination of gastric scintigraphy and wireless motility study ($P = 0.002$).

Reddymasu and colleagues[36] evaluated 66 healthy and 41 gastroparetic patients with simultaneous wireless motility capsule testing and scintigraphy. Gastroparetic patients were defined as having symptoms consistent with gastroparesis and a prior abnormal gastric scintigraphy. When gastric pressure patterns were looked at in isolation from transit data and compared with a clinical diagnosis of gastroparesis based on symptoms and a prior scintigraphy, the sensitivity of the wireless motility capsule was reported to be 88 percent and specificity was reported to be 30 percent. This was in comparison with gastric scintigraphy, which was reported to have a sensitivity of 46 percent and specificity of 94 percent. Data evaluating the combination of wireless motility capsule-derived transit and pressure data in comparison with scintigraphy was not reported in this abstract.

Treatment Decisions

Three studies addressed this outcome for this comparison (Table 9). Lee et al. found that, in patients who underwent examination by wireless motility capsule, management was changed in multiple areas compared with “another modality”[37] in a total of 22 of 32 (69 percent) patients. Similarly, Kuo et al. found that examination with wireless motility capsule changed management in 52 of 83 (63 percent) patients.[32] Finally, Rao et al.[33] found that changes in management owing to wireless motility capsule testing were made in 18 of 36 (50 percent) of patients. However, the numbers of patients for whom particular categories of management changes were made were not available in the report.

Table 9. Change in treatment decisions due to examination by wireless motility capsule compared with gastric scintigraphy in the evaluation of gastroparesis

Author, year	Study design	Total N	Total change in management	Changes in medication	Changes in diet	Changes in procedure (G-tube placement, J-tube placement, or surgery)
Lee, 2009[37]	Retrospective cohort	32	22/32 (69%)	18/22 (82%)	6/22 (27%)	4/22 (18%)
Kuo, 2011[32]	Retrospective chart review	83	52/83 (63%)	39/83 (47%)	9/83 (11%)	4/83 (5%)
Rao, 2011[33]	Retrospective chart review	36	18/36 (50%)	NR	NR	NR

G-tube = gastronomy tube; J-tube = jejunostomy tube; NR = not reported

Resource Utilization

One study addressed resource utilization as an outcome.[32] Kuo et al. reviewed outpatient records of patients who had undergone wireless motility capsule testing to determine if capsule testing eliminated needs for additional tests. They assumed that patients who were undergoing evaluation for presumptive gastroparesis would undergo scintigraphy, that patients who were undergoing evaluation for presumptive small intestinal dysmotility would undergo barium studies and that patients with presumed slow-transit constipation would undergo radiopaque marker studies – and that wireless motility capsule testing eliminated the need for these tests if these tests were not performed for patients with the aforementioned symptoms. They found that the need for additional testing via gastric scintigraphy was eliminated in nine of 52 patients (17.3 percent) patients, small bowel barium transit in seven of 13 (53.8 percent) patients, and radiopaque colon marker tests in 41 of 60 (68 percent) patients. The need for additional anorectal outlet function testing was not eliminated by any fraction (0 percent).

Patient-Centered Outcomes

No studies addressed patient-centered outcomes for this comparison.

Harms

The studies had limited data on potential harms of wireless capsule testing. Kuo et al.[11] evaluated 148 patients and reported that 46 percent required an abdominal x-ray to verify passage of the capsule. Five subjects required a second x-ray to ensure passage; however, the capsule did pass in all subjects. Ten adverse events were reported; six were felt to be unrelated to the wireless motility capsule and three were felt probably to be not related. The one event that was felt to be associated was capsule retention in the stomach due to entrapment with a fiber supplement; however, the capsule did pass in this case after administration of intravenous erythromycin. No serious adverse events were recorded.

Rao et al.[33] reported on 86 patients who underwent wireless motility capsule testing in addition to conventional motility testing. No serious adverse events were reported and the capsule was successfully expelled in all subjects.

No other studies reported on this outcome.

Wireless Motility Capsule Versus Antroduodenal Manometry

No included studies addressed this comparison.

Wireless Motility Capsule Versus Endoscopy

No included studies addressed this comparison.

Strength of Evidence

For most of the outcomes included in this Key Question, the strength of the evidence was low or insufficient. Seven studies were included for diagnostic accuracy; however, four of the seven were felt to have a high risk of bias and only two of the seven were felt to be precise studies – both of which were felt to have high risk of bias. With regards to motility assessment, we also felt the strength of evidence was low, primarily due to risk of bias. Similar issues were present with the sub-questions for treatment decisions, resource utilization, and harms. Please see Table 10 for more details.

Table 10. Numbers of studies and subjects, strength of evidence domains, and strength of evidence among studies comparing wireless motility capsule testing with gastric scintigraphy

Outcome	Number of studies	Domains pertaining to strength of evidence				Strength of evidence
		Risk of Bias	Consistency	Directness	Precision	
Diagnostic accuracy	7[11, 32-34, 36-38]	Medium	Consistent	Direct	Imprecise	Low
Motility assessment	5[11, 33, 34, 36, 38]	Medium	Consistent	Direct	Imprecise	Low
Treatment decisions	3[32, 33, 37]	Medium	Consistent	Direct	Imprecise	Low
Harms	2[11, 33]	Medium	Consistent	Direct	Imprecise	Low
Patient-centered outcomes	0	N/A	N/A	N/A	N/A	Insufficient
Resource utilization	1[32]	High	Unknown	Direct	Imprecise	Low

N/A = not applicable

The strength of the evidence was defined as follows: High = High confidence that the evidence reflects the true effect. Further research is unlikely to change our confidence in the estimate of the effect. Moderate = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate. Low = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate. Insufficient = Evidence is unavailable or does not permit a conclusion.

Key Question 2. Evaluation of gastric dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

Key Points

- Adding wireless motility capsule testing to conventional motility testing improves diagnostic accuracy in patients with suspected gastroparesis (sensitivity of scintigraphy compared with symptoms ranged from 42 to 51 percent; sensitivity of wireless motility capsule ranged from 60 to 66 percent). (SOE: Low)
- Adding wireless motility capsule testing to conventional motility testing improves assessment of motility parameters in patient with suspected gastroparesis. Scintigraphy does not measure pressure patterns. (SOE: Low)

- The strength of evidence was insufficient for treatment decisions, harms, patient-centered outcomes, and resource utilization. We did not find any studies addressing these outcomes.
- The strength of evidence was insufficient that the addition of wireless motility capsule testing to antroduodenal manometry or endoscopy affects diagnostic accuracy, motility assessment, treatment decisions, harms, patient-centered outcomes, or resource utilization. We did not find any studies addressing these comparisons.

Wireless Motility Capsule Plus Gastric Scintigraphy Versus Gastric Scintigraphy Alone

Diagnostic Accuracy

Two studies addressed this question with a total of 79 applicable patients.[33, 38] Rao et al. evaluated 86 patients with symptoms of dysmotility and normal baseline endoscopic and radiographic evaluations.[33] Of those 86 patients, 36 had predominant upper gastrointestinal symptoms and underwent evaluation with 4-hour gastric scintigraphy and wireless motility capsule testing. On testing, gastric scintigraphy confirmed clinical suspicion for gastroparesis in 42 percent of patients whereas the wireless motility capsule confirmed suspicion for gastroparesis in 66 percent of patients. The two studies were abnormal in 12 of 15 patients (80 percent) and both were normal in 17 of 21 patients (81 percent) with an overall device agreement of 81 percent. There was diagnostic discrepancy in 5 of 36 (14 percent) subjects, representing at least some degree of diagnostic gain from the two modalities in combination. The statistical significance of this increased diagnostic yield was not calculated.

Lee et al. evaluated 43 patients with symptoms of gastroparesis and previous abnormal gastric scintigraphy.[38] All patients underwent simultaneous gastric scintigraphy and wireless motility capsule study. Twenty-two of 43 patients (51 percent) had abnormal gastric scintigraphy, whereas 26 of 43 patients (60 percent) had abnormal gastric transit on wireless motility capsule. Overall device agreement for transit time was calculated at 77 percent (positive agreement 86 percent, negative agreement 66 percent). Seven of 43 patients had delayed gastric transit on wireless motility capsule and normal gastric scintigraphy. Three of 43 patients had delayed gastric scintigraphy with normal gastric transit on wireless motility capsule. In addition, this study evaluated gastric pressure parameters and found additional gain using those parameters. Ten of 21 subjects with a normal GES had pressure abnormalities identified by wireless motility capsule. When compared with gastric scintigraphy alone, this study found a statistically significant improvement in diagnostic gain using a combination of gastric scintigraphy and wireless motility study ($P = 0.002$).

Motility Assessment

Transit Times

The article by Rao et al. looked only at transit times and did not include pressure patterns in their analysis.[33] Thus, the findings above represent only transit time assessment. The study by Lee et al. looked at both transit times and pressure patterns. However, even when looking at transit times alone and disregarding pressure patterns entirely, there was a statistically significant

improvement in diagnostic gain discovered by scintigraphy plus wireless motility capsule transit time as compared with scintigraphy alone ($P = 0.02$).

Pressure Patterns

The only article to evaluate the role of gastric scintigraphy in combination with wireless motility capsule pressure patterns as compared with scintigraphy alone was that of Lee et al.[38] As stated above, they found that the addition of pressure profile analysis to scintigraphy data significantly increased diagnostic yield. They looked at multiple pressure pattern parameters, including contractile frequency and a calculated motility index. When taken together, the data obtained with scintigraphy plus wireless motility capsule-derived pressure patterns increased diagnostic yield over scintigraphy alone.

Treatment Decisions

We did not find any studies meeting our eligibility criteria that reported on the effect of testing on treatment decisions.

Resource Utilization

No included studies addressed this outcome for this comparison.

Patient-Centered Outcomes

No included studies addressed this outcome for this comparison.

Harms

The article by Rao[33] found no harms from either modality of testing. The article by Lee[38] did not report on harms; however, these numbers are small and insufficient to address this issue.

Wireless Motility Capsule Plus Antroduodenal Manometry Versus Antroduodenal Manometry Alone

No studies addressed this comparison.

Wireless Motility Capsule Plus Endoscopy Versus Endoscopy Alone

No studies addressed this comparison.

Strength of Evidence

We graded the strength of evidence for this Key Question as low. While few studies addressed this question specifically, the ones that did were among the better studies in terms of quality, and demonstrated independent review of the wireless motility capsule and scintigraphy. Risk of bias was assessed as medium and these studies were felt to be consistent and direct. Precision was felt to be low but this is difficult to gauge for this question. Table 11 summarizes our grading of the strength of evidence.

Table 11. Numbers of studies and subjects, strength of evidence domains, and strength of evidence among studies comparing wireless motility capsule testing plus gastric scintigraphy compared with gastric scintigraphy alone

Outcome	Number of studies	Domains pertaining to strength of evidence				Strength of evidence
		Risk of bias	Consistency	Directness	Precision	
Diagnostic accuracy	2[33, 38]	Medium	Consistent	Direct	Imprecise	Low
Motility assessment	2[33, 38]	Medium	Consistent	Direct	Imprecise	Low
Treatment decisions	0	N/A	N/A	N/A	N/A	Insufficient
Harms	0	N/A	N/A	N/A	N/A	Insufficient
Patient-centered outcomes	0	N/A	N/A	N/A	N/A	Insufficient
Resource utilization	0	N/A	N/A	N/A	N/A	Insufficient

N/A = not applicable

The strength of the evidence was defined as follows: High = High confidence that the evidence reflects the true effect. Further research is unlikely to change our confidence in the estimate of the effect. Moderate = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate. Low = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate. Insufficient = Evidence is unavailable or does not permit a conclusion.

Key Question 3. Evaluation of colonic dysmotility: wireless motility capsule alone versus other diagnostic tests

Key Points

- The strength of the evidence comparing wireless motility capsule with colonic or whole gut scintigraphy was insufficient because no articles or abstracts formally evaluated this comparison.
- The diagnostic accuracy of wireless motility capsule is similar to radiopaque markers. Concordance between radiopaque markers and wireless motility capsule was approximately 80 percent in two larger studies. Overall sensitivity and specificity were estimated to be 46 and 95 percent for wireless motility capsule compared with clinical constipation, and 37 and 95 percent for radiopaque markers. (SOE: Low)
- Wireless motility capsule was comparable with radiopaque markers in judgment of colonic transit time and identification of slow-transit constipation. (SOE: Low)
- Wireless motility capsule testing affects treatment decisions based on radiopaque marker testing. Very small numbers made comparison difficult for treatment decisions. Studies reported 7 percent change in nutrition, 21 percent referral to surgery, and 4 percent change in nutritional and behavioral therapies with wireless motility capsule. (SOE: Low)
- Wireless motility capsule testing can affect resource utilization. (SOE: Low)
- Harms and adverse events were infrequently reported for wireless motility capsule or radiopaque markers. (SOE: Low)
- The strength of the evidence was insufficient regarding patient-centered outcomes. We did not identify any studies that met our inclusion criteria and evaluated this outcome.

Wireless Motility Capsule Versus Colonic Scintigraphy

We did not include any studies that addressed this comparison.

Wireless Motility Capsule Versus Radiopaque Markers

Eight studies reported in 13 publications compared the wireless motility capsule with radiopaque markers among colon dysmotility patients (Table 11).[12, 28, 45] One study had three publications, but only one publication is described below. The additional studies compared an unclear subset of patients' results to the Bristol stool test and studied how irritable bowel syndrome may alter pressure results measured by the wireless motiligy capusle among moderate and severe constipation without reporting the corresponding radiopaque marker results. Another full-text publication updated an abstract, so only the full-text publication is reported.

One study included patients with suspected slow-transit constipation, gastroparesis, or intestinal dysmotility. Only the diagnostic accuracy results contribute because the clinical management changes for patients with suspected slow-transit constipation could not be distinguished from the other patients or were reported based on the final diagnosis, not the suspected diagnosis when the test was performed. Two abstracts included patients with suspected gastrointenstinal dysmotility disorders, but did not report results separately for slow-transit constipation. The results from this study are presented under Key Question 1. All other studies enrolled patients who were previously diagnosed with chronic or slow-transit constipation according to Rome criteria.

Diagnostic Accuracy

Tables 12 and 13 summarize data reported on diagnostic accuracy, sensitivity, and specificity within the included studies.

Rao et al.[12] showed that the sensitivity and specificity of colon transit time as measured by the wireless motility capsule compared with clinical suspicion was 46 percent and 95 percent. The sensitivity and specificity of day 5 radiopaque markers was 37 and 95 percent.

Four studies evaluated the diagnostic accuracy of wireless motility capsule testing with radiopaque markers among patients with known or suspect constipation. The sensitivity ranged from 43 to 87 percent and the specificity ranged from 67 to 91 percent. As the concordance between radiopaque markers and wireless motility capsule was determined to be approximately 80 percent in two larger studies,[28, 33] we found the tests to be considered similar by the criteria set out in the methods. One study,[32] which found a lower concordance rate, had a different population focus and much smaller sample size. Another study[12] reported the Spearmen correlation coefficient between colonic transit times recorded by the wireless motility capsule and day 2 and day 5 radiopaque marker counts. The correlation among constipated subjects was 0.74 on day 2 and 0.69 on day 5.

Table 12. Diagnostic accuracy and test concordance of the wireless motility capsule and radiopaque markers in the evaluation of constipation comparing patients with known constipation with known non-diseased controls

Author, year	Definition for slow-transit constipation CTT WMC	Definition for slow-transit constipation ROM	Total N	Sensitivity of CTT WMC compared with clinical constipation	Specificity of CTT WMC compared with clinical constipation	Sensitivity of ROM compared with clinical constipation	Specificity of ROM compared with clinical constipation	Concordance of CTT WMC and ROM
Rao, 2009[12]	44 hours for men and 59 hours for women	Day 2: NR Day 5 ROM sensitivity was based on cut off of 5 or more markers retained	67 with known constipation 81 without gastrointestinal disease	46%*	95%*	Day 5: 22/67 (37%)	Day 5: 95%*	Day 2: 0.78[†] (0.70-0.84) Day 5: 0.59 (0.46-0.69)

* Numerator and denominator not reported.
[†]Spearman correlation coefficient
CTT = colonic transit time; NR = not reported; ROM = radiopaque markers; WMC = wireless motility capsule

Table 13. Diagnostic accuracy and test concordance of the wireless motility capsule compared with radiopaque markers in the evaluation of constipation including only patients with known or suspected constipation

Author, year	Definition for slow-transit constipation WMC	Definition for slow-transit constipation	N analyzed with constipation	Sensitivity of CTT WMC compared with ROM	Specificity of CTT WMC compared with ROM	AUC, CTT WMC compared with ROM	Concordance of CTT WMC and ROM
Rao, 2009[12]	CTT 44 hours for men and 59 hours for women	Day 5 ROM sensitivity was based on cut off of 5 or more markers retained	67 known	Day 5: 19/23=83%*	NR	NR	Day 2: 0.74[†] Day 5: 0.69
Camilleri, 2010[28]	59 hours	Delayed on days 4 and 7	157 known	47/59 (80%; CI, 67 to 98%)	89/98 (91%; CI, 83 to 92%)	NR	136/157 (87%)
Kuo, 2011[32]	59 hours	NR	7 with information on colonic transit time from both ROM and WMC	3/7 (43%)	6/7 (86%)	NR	9/14 (64%)
Rao, 2011[33]	NR	6 or more ROM at 120 hours	50 suspected	20/23 (87%)	18/27 (67%)	NR	38/50 (76%)

*This study also reported that 31 subjects had a colonic transit time greater than 59 hours measured by wireless motility capsule testing, and 21 of these subjects were also delayed based on day 5 radiopaque marker count.
[†] Spearman correlation coefficient
AUC = receiver operating characteristic area under curve; CI = 95 percent confidence interval; CTT = colonic transit time; NR = not reported; ROM = radiopaque markers; WMC = wireless motility capsule

Motility Assessment

Transit Time

Three studies reported data on transit times measured by wireless motility capsule and radiopaque markers (Table 14). One study reported significantly different colonic transit times as measured by wireless motility capsule (median 43.5 hours) compared with radiopaque markers (median 55 hours; $P < 0.001$).[28] However, the correlation coefficient between these numbers was 0.71. Another study reported correlation coefficients between colonic transit time by wireless motility capsule and day-2 radiopaque marker count of 0.74 and between colonic transit time and day-5 radiopaque marker count of 0.69 (Table 13).[12]

Table 14. Transit times recorded by wireless motility capsule and radiopaque markers in the evaluation of constipation

Author, year	Study design	Total N constipated	Wireless motility capsule transit time	Radiopaque marker transit time	Concordance
Camilleri, 2010[28]	Prospective cohort	157	CTT median (25-75 percentiles) 43.5 h (21.7-70.3)	Median (25-75 percentiles) 55.0 h (31.0-85.0)	0.71 ($P <$ 0.001)
Rao, 2009[12]	Prospective cohort	67	Median (25-75 percentiles), hours GET 3.5 (3.0-4.2) CTT 46.7 (24.0-91.9)	Median (25-75 percentiles), Day 5 ROM count 1 (0-17)	NR

CTT = colonic transit time; GET = gastric emptying time; NR = not reported; ROM = radiopaque markers; SBTT = small bowel transit time; SD = standard deviation; WGTT = whole gut transit time

* In a radiopaque marker test, transit delay is measured by counting the number of markers remaining at a certain time interval after the capsule is ingested. There are 24 markers at the start.

Pressure Patterns

No study compared the wireless motility capsule with radiopaque markers and reported on pressure patterns. A substudy that was excluded reported on pressure patterns but was excluded because no radiopaque marker results were reported in the publication. Similarly, an abstract reporting on pressure patterns mentioned that testing with radiopaque markers occurred, but no radiopaque marker results were reported.

Treatment Decisions

Change in Medications

Very few studies offered information about change in medications for wireless motility capsule compared with use of radiopaque markers.[32, 33] All the studies that offered information reported data gleaned from retrospective chart reviews and no studies prospectively assessed whether change in medication was appropriate based on diagnostic testing (Table 15). There was reported an overall change in medications of 71 percent[32] and 40 percent[33] in the two studies that reported on change in medications.

Table 15. Change in medications following a wireless motility capsule for the evaluation of slow-transit constipation

Author, year	Study design	N (%) changed medications after wireless motility capsule test	N (%) changed medications after ROM
Rao, 2011[33]	Prospective cohort	40% overall change, but not specified for LGI or UGI symptoms Treatment Prokinetic agents 6% Prescription laxatives 20% Antidepressants 12% Withdrawal of opioids 6% Antiemetics 6%	Not reported (all patients had previously had ROM)

LGI = lower gastrointestinal; ROM = radiopaque makers; UGI = upper gastrointestinal

Change in Management: Referral, Referral to Surgery, or Change in Nutrition

Very few studies offered information about change in management for wireless motility capsule compared with use of radiopaque markers.[32, 33] All the studies that offered information reported data gleaned from retrospective chart reviews and no studies prospectively assessed whether change in medication was appropriate based on diagnostic testing (Table 16). There was a report of one person changing their nutritional intake and three people being referred to surgery in the Kuo study.[32] The other study reported that 28 percent of the patients were referred for anorectal manometry and 16 percent for breath testing based on the wireless motility capsule results. Four percent received new nutritional or behavioral therapies.[33]

Table 16. Change in other management following wireless motility capsule and radiopaque markers for evaluation of slow-transit constipation

Author, year	Study design	WMC change in nutrition	WMC referral to surgery	ROM
Rao, 2011[33]	Prospective cohort	Nutritional and behavioral therapies 4%	Not specifically reported	NR

NR = not reported; ROM = radiopaque markers; WMC = wireless motility capsule

Resource Utilization and Patient-Centered Outcomes

Table 17 summarizes the changes in resource utilization based on wireless motility capsule or radiopaque marker testing in the evaluation of slow-transit constipation. Two studies reported on unreadable results from the wireless motility capsule test and problems with following up for the radiopaque marker testing. Unreadable results from the wireless motility capsule ranged from 4 to 8 percent, and problems with radiopaque marker followup ranged from 3 to 7 percent. Another study reported patients being referred for anorectal manometry (28 percent) and breath testing (16 percent). This study also reported that 26 out of 50 patients (53 percent) received new information on their diagnosis based on the wireless motility capsule test.

Table 17. Change in resource utilization following wireless motility capsule and radiopaque marker testing for evaluation of slow-transit constipation

Author, year	Study design	WMC subsequent tests	ROM subsequent tests	WMC new diagnoses	ROM new diagnoses	Unreadable results from WMC (for resource utilization section)	Failure to attend followup ROM radiographs or read on wrong day (for resource utilization)
Camilleri, 2010[28]	Prospective	NR	NR	NR	NR	8/180 (4%)	5/180 (3%)
Rao, 2011[33]	Prospective	Anorectal manometry, 28%* Breath testing for bacterial overgrowth or carbohydrate intolerance, 16%*	NR	Prolonged gastric emptying, 14/50 (28%) Rapid gastric emptying, 2/50 (4%) Prolonged small bowel transit, 7/50 (14%) Prolonged colon transit, 3/50 (6%)	NR	N/A (based on chart review of completed tests; had to have readable result to be included)	N/A (based on chart review of completed tests)
Rao, 2009[12]	Prospective	NR	NR	NR	NR	14/165 (8%)	12/165 (7%)

* Numerators and denominators not reported.
N/A = not applicable; NR = not reported; ROM = radiopaque markers; WMC = wireless motility capsule

Harms

Among the articles reporting on the comparison of wireless motility capsule testing and use of radiopaque markers, very few harms were reported (Table 18).

The types of harms most frequently mentioned were inability to swallow the capsule, technical failure or data loss, and failure to pass the capsule within the timeframe of initial testing.[12, 28] X-rays at day 21 were required to exclude capsule retention in some cases, but this was based on simultaneous radiopaque marker testing during the study (and a day 5 x-ray showing retention of the capsule). No deaths were reported from exposure to the wireless motility capsule or radiopaque markers. The Rao et al article[12] reported a technical failure rate of 3.4 percent in the literature, and a study rate of 10 percent technical failure.[12] No serious adverse events were reported in any of the studies that reported on harms.[12, 28, 39] The only reported adverse events were from Camilleri et al.[28] with two patients suffering dysphagia with ingestion attempts for the wireless motility capsule, and one patient suffering abdominal pain after ingestion of the capsule. These were determined by the authors to be "definitely related" to the capsule itself.

In comparison of harms, although the articles discussed the radiation exposure risk between wireless motility capsule and radiopaque markers, the difference in actual exposure was not reported in any unit of measure for comparison on a person by person basis. Theoretically, wireless motility capsule should not require x-ray exposure in standard use, however delay or failure of passage is possible and may need documentation of passage with x-ray. The research protocols evaluated in the included studies used sequential x-rays to assess radiopaque marker transit with between 1 and 3 x-rays to capture data. Study protocols mandated that if wireless motility capsule is not observed to pass by the patient, then x-rays at day 7 or 21 were used to ensure lack of retention in the studies under investigation. This x-ray exposure was needed in 4 patients at day 7[28] and in 14 patients at day 21.[12]

Table 18. Summary of the adverse events from wireless motility capsule testing in the evaluation of slow-transit constipation

Author, year	Serious adverse events	Other adverse events	Retained capsule	Retained capsule requiring intervention	Radiation exposure	Mortality
Rao, 2009[12]	None	NR	0 non-constipation 14/67 constipated	11/67	NR	NR, presumably 0
Camilleri, 2010[28]	None	31 adverse events (could have more than 1 per person)	NR	0/180	At least 1 person	NR, presumably 0
Rao, 2011[33]	None	NR	0	0	NR	NR, presumably 0
Rao, 2009*	None	None	0	0	NR	NR

* Results were not reported for radiopaque marker testing.
NR = not reported

Strength of Evidence

Although relatively few articles compared the diagnostic accuracy of the wireless motility capsule with the use of radiopaque markers for evaluating slow-transit constipation, Table 19 shows that the strength of evidence was low in support of the diagnostic accuracy of the wireless motility capsule in evaluating slow-transit constipation. The risk of bias in these studies was low, but the total amount of evidence was sparse. The strength of evidence also was low regarding the accuracy of the wireless motility capsule in assessing motility times in patients with possible slow transit constipation, and regarding the low risk of harm associated with use of the device. The strength of evidence was low or insufficient regarding other outcomes associated with use of the device.

Table 19. Numbers of studies and subjects, strength of evidence domains, and strength of evidence among studies comparing wireless motility capsule testing with radiopaque markers

Outcome	Number of Studies (Participants)	Domains Pertaining to Strength of Evidence				Strength of Evidence
		Risk of Bias: Design/ Quality	Consistency	Directness	Precision	
Diagnostic accuracy of slow-transit constipation	4 (281)[12, 33, 45]	Moderate	Consistent	Direct	Precise	Low
Motility time assessment	3 (282)[12, 28, 42]	Moderate	Consistent	Direct	Precise	Low
Treatment decisions	2 on medications & referrals (169)[32, 33]	Moderate	Consistent	Direct	Imprecise	Low
Harms	4 (363)[12, 28, 39]	Moderate	Consistent	Direct	Imprecise	Low
Patient-centered outcomes	0	N/A	N/A	N/A	N/A	Insufficient
Resource utilization	3 (274)	Moderate	Consistent	Direct	Imprecise	Low

N/A = not applicable

The strength of the evidence was defined as follows: High = High confidence that the evidence reflects the true effect. Further research is unlikely to change our confidence in the estimate of the effect. Moderate = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate. Low = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate. Insufficient = Evidence is unavailable or does not permit a conclusion.

Key Question 4. Evaluation of colonic dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

Key Points

- Strength of evidence was insufficient because no studies directly addressed the outcomes for this comparison.

Summary

We reviewed eight studies (13 publications) that looked at the comparison of wireless motility capsule with scintigraphy or radiopaque markers in the evaluation of colonic dysmotility.[12, 28, 32, 33, 35, 37, 39-45] However, no studies specifically looked at the incremental value of wireless motility capsule testing in addition to radiopaque markers or scintigraphy in terms of diagnostic accuracy of slow-transit constipation. Additionally, no studies looked at the incremental value of also using the wireless motility capsule in addition to radiopaque markers or scintigraphy in terms of motility, treatment decisions, patient-centered outcomes, harms, and resource utilization. One study[33] attempted to answer this question by comparing the wireless motility capsule with conventional motility tests, including both scintigraphy and radiopaque markers. However, the data was incomplete and did not directly answer the key question regarding incremental value specifically. Thus, the evidence was insufficient to determine the incremental value of using the wireless motility capsule in combination with other conventional tests of colonic motility.

Study Quality (For All Key Questions)

Study quality is reported separately for the full-length publications and the abstracts because the abstracts had limited information about study methods (Appendix D, Evidence Table 4). The overall study quality was fair.

Of the 10 full-length publications,[11, 12, 28, 32, 33, 38, 41, 42, 44, 45] six stated that a goal was to compare the diagnostic accuracy of the wireless motility capsule with a reference standard.[12, 28, 32, 33, 38, 41] Five publications excluded healthy controls from the diagnostic accuracy analyses,[32, 33, 38, 44, 45] with the remainder including both healthy controls in the comparison of diagnostic tests. Two publications excluded severely ill patients,[11, 33] one publication[41] included these patients and the remainder had unclear reporting. Five publications used the same reference standard for all patients,[11, 12, 28, 41, 42] one publication allowed different reference standards,[38] and four publications did not report on the reference standard with enough detail to determine if the same reference standard was used for all participants. No publication analyzed all patients. The wireless motility capsule and reference standard were performed within three months of each other in seven of the publications,[11, 12, 28, 33, 38, 42, 44] often with the tests performed concurrently. Six publications reported a threshold for disease positivity or cited that a threshold from a previous publication was used.[12, 28, 33, 38, 41, 42] Only three publications reported that the wireless motility capsule results were interpreted independently from the reference standard.[12, 28, 33] One of these publications was a retrospective chart review.[33] Four publications explicitly stated that the test results were not interpreted independently.[11, 32, 38, 41, 42] For the two publications with unclear reporting[44, 45] and those publications that stated that results were not interpreted without knowledge of the other test results, we contacted the authors to obtain information on

independent assessment of the tests. We were able to confirm from the authors that the results were interpreted independently in three publications where blinding was not reported.[11, 38, 42]

Eight full-length studies reported on conflicts of interest.[11, 12, 28, 32, 33, 38, 41, 42] Five were funded by a commercial source related to motility testing, one was not[33] and two were unclear.[32, 38] One of the studies with unclear commercial funding[38] was reported to be commercially funded in a related publication.[11] All of the studies that reported on conflict of interest included an author employed by industry or an author who received funding or fees from at least one commercial source related to motility testing.

The seven abstracts did not provide sufficient details to evaluate all domains of study quality. One abstract excluded healthy controls from the analyses,[37] whereas five abstracts included healthy controls[34, 36, 39, 40, 43] and one had unclear inclusion.[35] Two abstracts reported that all patients received the same reference standard,[34, 36] with the remainder having unclear consistency of a reference standard. No abstract stated that results of the wireless motility capsule were interpreted independently of the reference standard. Two studies reported that the wireless motility capsule assessment and reference standard occurred within three months.[34, 36] One study stated a threshold for disease based on the wireless motility capsule in the abstract.[36] Three studies stated the aim was to compare the diagnostic accuracy of the wireless motility capsule with a reference standard.[35-37]

No abstract reported on conflict of interest. However, many of the abstract authors were authors of the full-length publications we reviewed, and some of those publications reported potential conflicts as noted above.

Discussion

Potential Niche for Wireless Motility Capsule

The wireless motility capsule has the potential to be an improvement over previous testing modalities for patients with possible gastroparesis or slow-transit constipation because it is small and can be transported to patients wherever they live. Also, the capsule does not involve any radioactive material or x-ray exposure, and can record information about pressure, transit, and location simultaneously. Other testing modalities for gastric emptying and colonic motility assessment do not share these characteristics. Scintigraphy is often used for assessment of gastric transit abnormalities and in certain academic centers also extended to evaluate whole gut motility; however, this involves radiation exposure, significant patient time requirements, and significant cost. Antroduodenal manometry allows assessment of gastric pressure parameters but has limited availability and is more invasive than other testing modalities. Radiopaque markers are portable and small, but require radiation exposure, access to fluoroscopy, and radiology interpretation. In addition, all other studies used in evaluation of either gastric or colonic motility evaluate either transit or pressure, but not both – yet both are involved in disease pathogenesis. The wireless motility capsule has the potential to evaluate both transit and pressure simultaneously, which in theory could allow more optimal assessment of motility than evaluation of either parameter independently. Likewise, by recording both parameters, the wireless motility capsule has the potential to replace a combination of studies and provide more accurate diagnosis with less resource utilization and enhanced patient convenience.

In light of this potential niche, the wireless motility capsule is becoming much more readily available in both academic and community centers. However, questions remain about the position of the wireless motility capsule in the diagnostic algorithm for suspected motility disorders such as gastroparesis and slow-transit constipation. Is the wireless motility capsule equivalent to conventional testing? Is it superior? Is it more likely to establish a concrete diagnosis or guide medical therapy than conventional motility testing? Should it be used as a stand-alone test or is it better used as an adjunct test after conventional testing has been completed in cases where the diagnosis remains in question? These are questions that have not been clearly addressed in previous clinical practice guidelines.

The potential limitations of the wireless motility capsule must also be considered. The modality is of limited utility in patients with severe gastroparesis as this is listed by the manufacturer as a contraindication to capsule placement due to fear of capsule retention. In addition, by definition, the wireless motility capsule evaluates motility at only a single point, as opposed to antroduodenal manometry which has multiple recording points, or scintigraphy which looks at transit of an entire meal. One assumes that the single point of measurement is representative of motility parameters as a whole; however, this is an assumption only and not clearly established in the literature. In the assessment of constipation, one cannot separate patients with slow-transit constipation from defecatory dysfunction based on only colonic transit time so further motility testing and clinical judgment is needed to evaluate defecation. Finally, parameters of motility for a non-digestible solid are different than those for either liquids or a meal – implying that patients can have abnormalities with one modality that would not be seen with another. In short, while the potential of wireless motility capsule testing is exciting, many questions remain as to whether it is equivalent or superior – and as to the appropriate place in the diagnostic algorithm where it should be used.

Key Findings and Implications

Few studies met our criteria for evaluation. The paucity of full length articles with independent data limited our ability to answer the key questions definitively.

Key Question 1. Evaluation of gastric dysmotility: wireless motility capsule alone versus other diagnostic tests

Wireless Motility Capsule Versus Scintigraphy

We found low strength of evidence from seven studies[11, 32-34, 36-38] to support that wireless motility capsule has comparable diagnostic accuracy with gastric scintigraphy. The sensitivity was moderately greater in some studies, but there was slightly lower specificity reported. The test agreement and diagnostic gain were moderate. Diagnostic agreement between wireless motility capsule and gastric scintigraphy ranged from 58 to 86 percent positive test agreement and from 64 to 81 percent for negative test agreement.

We found low strength of evidence from five studies[11, 33, 34, 36, 38] that transit data obtained via wireless motility capsule testing correlates well with scintigraphic gastric emptying. The reporting of the results in these studies was heterogeneous. One study reported a correlation coefficient of 0.73 between gastric emptying time measured by the wireless motility capsule and 4-hr gastric emptying measured by gastric scintigraphy.[11] Other studies reported sensitivity, specificity, and device agreement between wireless motility capsule transit data and gastric scintigraphy.[33, 36, 38] All three studies examining transit time showed similar sensitivity and specificity for wireless motility capsule and scintigraphy, and some studies reported increased diagnostic gain of sensitivity with wireless motility capsule.

Low strength of evidence from two studies supports the utility of wireless motility capsule versus scintigraphy in measuring pressure profiles.[36, 38] Pressure patterns are reported by wireless motility capsule, but scintigraphy can not detect pressure patterns. It does appear, however, that abnormalities are more likely to be seen with wireless motility capsule than scintigraphy – especially if one adds assessment of pressure patterns to the equation. However, based on the literature there remains questions as to whether this increased diagnostic detection rate has clinical implications.

Low strength of evidence supports the changes in treatment that may result from testing with wireless motility capsule versus scintigraphy. Change in treatment was identified in three studies,[32, 33, 37] in which use of the wireless motility capsule was associated with a change in management ranging between 50 and 69 percent of patients, change in medication in 47 to 82 percent of patients, and change in diet in 11 to 27 percent of patients. Since scintigraphy is the reference standard, presumably all decisions would be made based on clinical symptoms and scintigraphy testing. There was low quality evidence suggesting that wireless motility capsule is comparable with scintigraphy in directing a change in management. Although Kuo et al.[32] reported that testing was avoided in a large percentage of patients in their study, they accepted the results of the individual test as definitive and elected not to pursue additional testing. As discussed by the authors, an ideal trial of the comparative effectiveness of the tests would involve randomizing subjects to either get care guided by wireless motility capsule and others guided by reference standard testing (which could be uniformly applied), and then assess outcomes, including the need for additional tests, using blinded reviewers.

There is low strength of evidence when looking at harms from wireless motility capsule as compared with scintigraphy. Harms were mentioned in many articles, but overall no serious

adverse events, deaths, bowel obstructions, or rehospitalizations were reported in patients using the wireless motility capsule or gastric scintigraphy. Minor symptoms such as nausea, abdominal discomfort, or bloating were present among a measurable portion of the study participants who received the wireless motility capsule. Loss of data capture or device failure was also noted; however this does not seem to qualify as a true harm.

Overall, we had graded the strength of evidence for many outcomes addressing KQ1 to be low because we considered the evidence to have medium risk of bias, consistent reporting, direct nature of the data, and imprecise findings. The main limitation weighting the risk of bias was that enrollment of patients was not prespecified or done in a random fashion; in fact many studies did not report how patients were selected for testing and study. Another limitation was the lack of advance prespecification of criteria and values of positivity of the tests being used. The final major limitation was that few studies mentioned whether a person without conflict of interest was selected to manage the data collected. Most studies had limited followup duration, which hampers our ability to draw conclusions about some of the outcomes that are really important to patients. A major strength of the full length articles was that there was reporting of independent review of the results to perform analysis.

We could not conduct a meta-analysis because of the heterogeneity of the data and patient populations in the studies. Our ability to compare studies was limited by lack of consistency in how the reference standards were defined. The reference standard was often reported as a community based gastric scintigraphy testing performed within 2 years of enrollment into a study. Local standards for scintigraphy vary greatly, and this introduced heterogeneity into the patient populations under investigation. Many studies had different definitions for key outcomes such as diagnostic agreement, sensitivity, and specifity, as well as different diagnoses based on similar test results. This latter discrepancy can be explained by changes over time in how investigators considered the cut off values for detection of gastroparesis with wireless motility capsule. It is uncertain if the full spectrum of patients is captured in the available examinations of motility testing as academic referral centers were the primary recruitment site for studies. Overall, seven studies with 560 patients addressed the question of diagnostic accuracy.[32-38] For a rare illness, the large number of patients included for evaluation reflects the great length that researchers have taken to assess the quality of this modality. Several studies suggested there was some diagnostic gain with wireless motility capsule as compared with scintigraphy, assuming all additional cases identified were correct and not false positives.[11, 32, 33, 36, 38] Employing simultaneous scintigraphy and wireless motility capsule at the time of assessment, the investigators attempted to minimize the impact of having a heterogenous population; sensitivity and specificity for both scintigraphy and wireless motility capsule compared with symptoms in these studies is expectedly low given the issues above and the fact that the denominator may not have truly reflected entirely gastroparetic patients. Device agreement is a more useful parameter to measure in these papers than sensitivity and specificity.[27] However, agreement is likely to be imperfect because these two modalities look at different mechanisms of transit.

Regarding treatment decisions, we did find that, in three studies, wireless motility capsule testing altered management in patients with suspected gastroparesis (50 to 69 percent change in management for medicine, diet, or surgery). However, the strength of evidence was low (i.e., likely to be changed by future evidence).

The evidence was insufficient to draw conclusions regarding the differences or similarities between gastric scintigraphy and wireless motility capsule with regards to patient-centered

outcomes or resource utilization. Very little research examined resource utilization, and no studies specifically examined this outcome with any rigor.

The findings reported in the literature are consistent with what would be expected based on the pathophysiology of gastroparesis and the comparative methods of wireless motility capsule and gastric scintigraphy. Comparing scintigraphy with wireless motility capsule is fundamentally a challenging endeavor. Both modalities evaluate different parameters. Scintigraphy looks at transit of a test meal and does not assess pressure. When the stomach processes a meal, fundic accommodation is followed by antral contractions that break up the food into small particles that are then propelled from the antrum to the duodenum. In comparison, the wireless motility capsule is not digested and is believed to exit the stomach when the gastric motility patterns change from a fed to fasting state and migratory motility complexes resume. As such, these two technologies are evaluating different parameters and a direct comparison may be challenging if one looks at transit alone.

Wireless Motility Capsule Versus Anteroduodenal Manometry or Endoscopy

No head-to-head comparison of antroduodenal manometry (which can record pressure patterns) and wireless motility capsule was found in patients with suspected gastroparesis in our review. This makes a more definitive assessment of the ability of wireless motility capsule to detect abnormalities in pressure patterns in our defined populations more difficult at this time. Similarly, we did not find any studies that compared wireless motility capsule testing with endoscopy among patients with suspect gastroparesis.

Key Question 2. Evaluation of gastric dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

Wireless Motility Capsule Plus Gastric Scintigraphy Versus Gastric Scintigraphy Alone

Two studies[33, 38] assessed the incremental value of using the wireless motility capsule with gastric scintigraphy. We found low strength of evidence to suggest that wireless motility capsule is associated with modest improvement in diagnostic accuracy over use of scintigraphy alone for patients with suspected gastroparesis. Low strength of evidence was also present to support the incremental benefit of wireless motility capsule in evaluation of transit times and pressure patterns. The two studies that did attempt to address this question had a method of data collection that may not have allowed for full understanding of diagnostic discrepancy. Discrepancy is when one test shows disease and the other test does not show disease. The authors assumed that in a population of patients with gastroparesis diagnostic gain (when wireless motility capsule was positive but scintigraphy was not) was always present when there was discrepancy with results.[33] This assumption is difficult to confirm without having an independent gold standard for establishing the diagnosis.

While few studies addressed this question specifically, the ones that did were among the better studies in terms of quality, and demonstrated independent review of the wireless motility capsule and scintigraphy. Risk of bias was assessed as medium and these studies were felt to be consistent and direct. Precision was felt to be low but this is difficult to gauge for this question. The overall strength of evidence was low for this key question. It is very hard to prove an

incremental benefit of the test when used in addition to other testing modalities becauseit is hard to determine how clinical decision making was performed. It may be unclear which test the clinician used to form an opinion of the case, and it may be unclear how much the incremental information contributed to the decision making process. The retrospective nature of studies also limited the strength of evidence..

The incremental benefit for wireless motility capsule in diagnostic evaluation of suspected gastroparesis is consistent with the nature of the disorder and the tests, since the wireless motility capsule offers pressure data and motility data which are not discernible by scintigraphy alone, as well as lower gastrointestinal motility data which can be implicated as a cause of symptoms in patients with combinations of motility disorders. Measurable benefit may be gleaned from the additional reported information in combination with scintigraphy especially with regard to identification of a more diffuse motility disorder. The evidence was limited and there was no information to guide any conclusions regarding treatment decisions, utilization, patient-centered outcomes, or harms when evaluating the incremental value of also using the wireless motility capsule.

Incremental Value of Wireless Motility Capsule Compared with Antroduodenal Manometry Alone or Endoscopy Alone

We did not find any studies that evaluated the incremental value of adding the wireless motility capsule test to testing with either antroduodenal manometry or endoscopy in patients with suspected gastroparesis.

Key Question 3. Evaluation of colonic dysmotility: wireless motility capsule alone versus other diagnostic tests

Wireless Motility Capsule Versus Radiopaque Markers

The strength of evidence was low from four studies (six publications) containing 522 patients comparing wireless motility capsule with radiopaque markers in assessment of diagnostic accuracy of identification of slow-transit constipation.[12, 28, 32, 33, 42, 45] The diagnostic accuracy of the wireless motility capsule was similar to radiopaque markers (concordance was about 80 percent in two of the larger studies). Sensitivity and specificity were estimated to be 46 and 95 percent for wireless motility capsule compared with clinical constipation, and 37 and 95 percent for radiopaque markers.[12] Of these reported studies, only three were true independent studies and the remainder were abstracts or ad-hoc analysis of already included studies, which impaired the strength of evidence due to a smaller pool of patients under analysis. The wireless motility capsule was comparable with radiopaque markers in assessment of diagnostic accuracy, and matched the sensitivity in different target populations in a reliable way.

The strength of evidence was low to suggest that the colonic transit time estimated by wireless motility capsule correlates well with the colonic transit times recorded by radiopaque markers. The correlation coefficients between these two measures ranged from 0.69 to 0.71.

The strength of evidence was low regarding the effect of wireless motility capsule testing on treatment decisions based on radiopaque marker testing. We are unable to draw conclusions because only two retrospective chart reviews offered information about change in management for the wireless motility capsule compared with use of radiopaque markers.[32, 33] These two studies differed in the patient populations and the reporting of the outcomes. One of the studies

reported few events, providing imprecise results. The data was further limited because not all patients underwent both diagnostic tests of interest. We found low strength of evidence that wireless motility capsule can affect resource utilization.

The strength of evidence was low in the three studies reporting on any harms relevant to wireless motility capsule or radiopaque markers.[12, 28, 39] Harms and adverse events were infrequently reported for the wireless motility capsule or radiopaque markers. The wireless motility capsule is comparable to radiopaque markers with regard to low frequency of harms, as no serious adverse events and no mortality was reported. Radiopaque marker testing involves exposure to at least one x-ray by definition. Day 21 x-ray was required in a small proportion of patients who received wireless motility capsule by protocol if the capsule had not spontaneously passed, but may not be required in practice if a capsule passage is witnessed. Technical failures were reported in prototype devices with reported rates between 3 and 10 percent depending on the study.[12] Other harms or adverse events reported included dysphagia, abdominal discomfort, bloating, or nausea, which happened infrequently. These all resolved spontaneously when reported.[28]

The strength of evidence was insufficient to make any conclusions about patient-centered outcomes like symptom improvement, quality of life, patient satisfaction (0 studies). No included studies addressed these outcomes of interest. These are difficult outcomes to assess without using dedicated symptom scores or mining large sources of data on hospital and physician visits. Longer duration studies will also be needed to address questions about change in quality of life or symptoms, which requires assessment along multiple time points.

Many factors contributed to the overall grading of evidence for outcomes assessed as having low strength of evidence in reference to Key Question 3. The evidence was considered to have moderate risk of bias because many of the studies were retrospective, lacked random patient selection, did not report if there was blinding of assessment, and did not apply the same reference standard to all the patients. Furthermore, many studies recruited patients from academic referral centers; it is uncertain if the full spectrum of patients were captured in the available examinations of motility testing. Most studies had limited followup duration, which hampered our ability to draw conclusions about some of the outcomes that are important to patients such as patient satisfaction or change in symptom scores. We had only imprecise estimates of the effects on treatment decisions and harms. Our conclusions were limited by how the reference standards were defined. The reference standard was often reported as a community based radiopaque marker study of varying protocol. The multiple protocols had different assessment methods, which could have influenced the results. We could not conduct a meta-analysis because of the heterogeneity of reported data and patient populations in the studies. Although the strength of evidence was low, it is impressive how well these devices correlated given limitations of the studies.

Much like the comparison between scintigraphy and wireless motility capsule, radiopaque markers and wireless motility capsule are assessing different components of transit. Some of the points of assessment coincide and provide comparable data, but the additional pressure and transit data offered by the wireless motility capsule make it a different and possibly complementary modality. Overall, the studies showed diagnostic agreement between wireless motility capsule and radiopaque markers for assessment and diagnosis of slow-transit constipation.

Wireless Motility Capsule Versus Colonic Scintigraphy

We found no evidence to evaluate the wireless motility capsule in comparison with colonic scintigraphy in patients with suspected slow-transit constipation. The reported studies on scintigraphy in the literature were excluded from our analysis because they compared testing in healthy subjects separately from those with constipation or slow-transit constipation and thus were not eligible for inclusion.

Key Question 4. Evaluation of colonic dysmotility: wireless motility capsule in combination with other diagnostic tests versus other diagnostic tests alone

No studies directly addressed any outcomes of interest related to Key Question 4. The little data that was available from small trials about these outcomes were heterogeneous and did not specify the specific patient populations of interest and thus, it was impossible to generalize based on this data. Assessing the incremental value of a new technology could be assessed by diagnostic gain. However, when trying to judge whether a new test can be a replacement or adjunct to an old test, it is difficult to get a clear picture of which test was most helpful in making a diagnosis without a blinded comparison or without follow up that can assess the validity of the diagnosis and or treatment effects over time.

Applicability (For All KQ)

The applicability of the literature is limited based on the use of the wireless motility capsule test in referral centers and no prospective testing of the wireless motility capsule as a diagnostic tool in patients with suspected disease. All studies occurred at referral centers. All prospective studies involved patients with known disease. When a comparison group without constipation or gastroparesis was used, “healthy” controls were included, instead of patients who may have similar presenting symptoms who do not have constipation or gastroparesis. These controls tended to be college-aged men compared with middle-aged females with suspected disease. Additionally, it is unclear how previous treatments or comorbidity, including diabetes, affect test performance or how the test results ultimately affect management.

Limitations and Strengths of our Review Process

Our review had two major limitations.

(a) No standards exist in the field of motility assessment for determining the minimum improvement of diagnostic accuracy that will identify one test as superior to another test. There are also no standards to establish the equivalence of motility tests. We arbitrarily chose a 10 percent difference in sensitivity or specificity as a clinically meaningful difference between tests.[28] We felt this threshold was a conservative minimum improvement over a reference standard with moderate diagnostic accuracy (between 50 percent and 80 percent). If the reference standard had a larger diagnostic accuracy (90 percent or greater), a 10 percent absolute difference is too large to expect.

(b) We excluded studies that included non-diseased participants exclusively as our review focused on studies that compared the diagnostic accuracy of the tests for patients with gastroparesis or slow transit constipation. We recognize that many of the most commonly cited studies in the field included non-diseased participants.[13, 14, 49-62] Thus, we excluded a number of studies that evaluated characteristics of the wireless motility capsule.

The major strength of our review process was the comprehensiveness. We included abstracts, contacted industry for unpublished studies, and contacted study authors for missing data.

Limitations of the Identified Literature

Our aim was to compare the diagnostic accuracy of the wireless motility capsule to other testing modalities to diagnose and manage gastroparesis and slow transit constipation. The identified literature limited our ability to answer our key questions for several reasons.

(a) No study directly addressed the incremental value of using the wireless motility capsule in addition to using a radiopaque marker or scintigraphy in the evaluation of colonic dysmotility (KQ4). Only limited data addressed the incremental value of using the wireless motility capsule in addition to using gastric scintigraphy, antroduodenal manometry, or endoscopy in the evaluation of gastric dysmotility (KQ2).

(b) All study sites were referral centers that tend to have patients with more severe disease. The study results have limited generalizability to general gastroenterology or primary care clinics where a greater spectrum of disease severity is observed. The sensitivity and specificity of the wireless motility capsule may be different in referral center settings than in other settings, and the positive and negative predictive values will be different when the prevalence of disease is different.

(c) Many studies included non-diseased patients in the comparison of the diagnostic accuracy of the wireless motility capsule with other tests, using a clinical diagnosis of disease as the reference standard rather than the results of the other diagnostic tests.

(d) The non-diseased participants had very different demographic characteristics than the gastroparesis and slow transit constipation patients. For example, the majority of the non-diseased participants were college-aged males whereas the gastroparesis and slow transit constipation patients were middle-aged women. Using clinical diagnosis as the reference standard, it is difficult to determine if the wireless motility capsule and other tests are distinguishing disease from non-disease or measuring differences in motility by demographic differences such as age and sex.

(e) Variability in the administration of the motility tests and outcome assessments may explain some of the heterogeneity in the study results. Many studies used similar protocols to perform the wireless motility capsule testing and other tests, but with slight modifications, such as in the contents of the meal. Frequently, the timing of the motility assessment differed for the wireless motility capsule and the alternative test within and between studies, which may explain differences in the test results and the diagnostic accuracy differences between studies.

(f) The abstracts we included did not report enough data to fully understand the study population, answer our key questions, and assess the quality of the studies.

(g) We were unable to compare the results of studies with and without industry or investigator conflicts of interest because most studies were sponsored by the company that manufactures the wireless motility capsule. The other studies did not report on conflicts of interest. No study stated that it was performed independent of industry sponsorship with authors who had no previous or current financial relationships with the manufacturer of the wireless motility capsule.

(h) We attempted to assess publication bias by contacting the manufacturer of the wireless motility capsule and requesting any unpublished data, but received no response. Therefore, publication bias may affect our findings, and this is a limitation as well.

Future Research Needs

Future research should ideally emphasize a cure to these diseases that is nontoxic, cheap, easily available, and safe without major surgery or implanted devices. As far as diagnostic testing, the goal is always to find accurate, effective, inexpensive tools to diagnose or exclude cases and qualify their severity in a reproducible way, especially when treatment is expensive, unavailable, or accompanied by great risks. Studies that compare the diagnostic modalities should have blinded interpretation of the results and make every attempt to classify patients by identical criteria and standardized protocols that can be repeated and verified at other centers. We recommend that research focus more on prospectively studied patients in larger numbers with an appropriate spectrum of symptoms and adequate follow up to determine whether the diagnosis was accurate over time. Due to the difficulty enrolling patients, carefully crafted retrospective analyses should also be considered.

Research also is needed to evaluate how the wireless motility capsule should be used in combination with or instead of other testing modalities for evaluation of slow-transit constipation. The studies we reviewed used alternative measures to assess anorectal function, such as anorectal manometry, as wireless motility capsule does not capture data about this region reliably. Thus, wireless motility capsule will likely be used in combination with this test.

Eventually, outcomes studies are needed to see if testing helps to improve quality of life or symptom control. It is unclear at present whether a more sensitive diagnostic test might just provide lead-time bias for diagnosis but not actually change the outcomes or management steps overall for the patient. As other targeted therapies are identified, the value of testing will need to be reassessed. We are aware that a new therapy is in Stage II trials for patients with diabetes and gastric emptying delay, which may increase the need for research into this area if it becomes available for use.[63] Currently, most patients with nausea- and vomiting-predominant symptoms of gastroparesis receive similar first-line treatment with antiemetics or prokinetics. As treatment options for gastroparesis expand (some at great expense), then more accurate detection of disease prior to initiation of therapy may play a more prominent role in disease management. Resource utilization with and without using the wireless motility capsule is not currently reported in the literature, and more studies evaluating these measures will be needed.

Little data is available to support determination of the optimal timing of wireless motility capsule testing in the diagnostic and therapeutic approach to patients with symptoms of possible gastroparesis or slow transit constipation. Further work needs to be done to classify the types of patients within subgroups of gastroparesis or slow-transit constipation to identify severe cases that may need more urgent evaluation. Finally, little is known about whether testing should be used to assess the effectiveness of treatment or if subsequent testing would offer any benefit in long-term management of patients. Currently, symptoms and symptom resolution guide therapeutic decisions, but these require careful interpretation.

Conclusions

Based on the current literature, the wireless motility capsule appears to be accurate in detection of gastroparesis and slow-transit constipation and may provide increased diagnostic gain as compared with standard motility testing. While the strength of evidence is low, the data were relatively consistent and suggested that this modality is no less sensitive than conventional testing. The evidence is insufficient to determine whether use of the wireless motility capsule will improve outcomes of care.

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Abbreviations

ACG = American College of Gastroenterology
AGA = American Gastroenterological Association
AHRQ = Agency for Healthcare Research and Quality
ANMS = American Neurogastroenterology and Motility Society
AUC = area under the curve
CI = confidence interval
COV = coefficient of variance
cph = contractions per hour
CTT = colonic transit time
EPC = Evidence-based Practice Center
FDA = U.S. Food and Drug Administration
G PM = gastric pressure measurements
G/SB PM = gastric/small bowel pressure measurements
GES = gastric emptying scintigraphy
GES-2hr = gastric emptying via scintigraphy at 2 hours
GES-4hr = gastric emptying via scintigraphy at 4 hours
GET = gastric emptying time
GI = gastrointestinal
GRADE = Grading of Recommendations Assessment Development and Evaluation
hr = hours
KQ = key question
min = minutes
mmHg = millimeters of mercury
NA or N/A = not applicable
NR = not reported
PPI = proton pump inhibitor
ROC = receiver operating characteristic
ROM = radiopaque markers
SB = small bowel
SB PM = small bowel pressure measurements
SBTT = small bowel transit time
SD = standard deviation
T50 = time of 50% emptying
T90 = time of 90% emptying
U.S. = United States
WGTT = whole gut transit time
WMC = wireless motility capsule